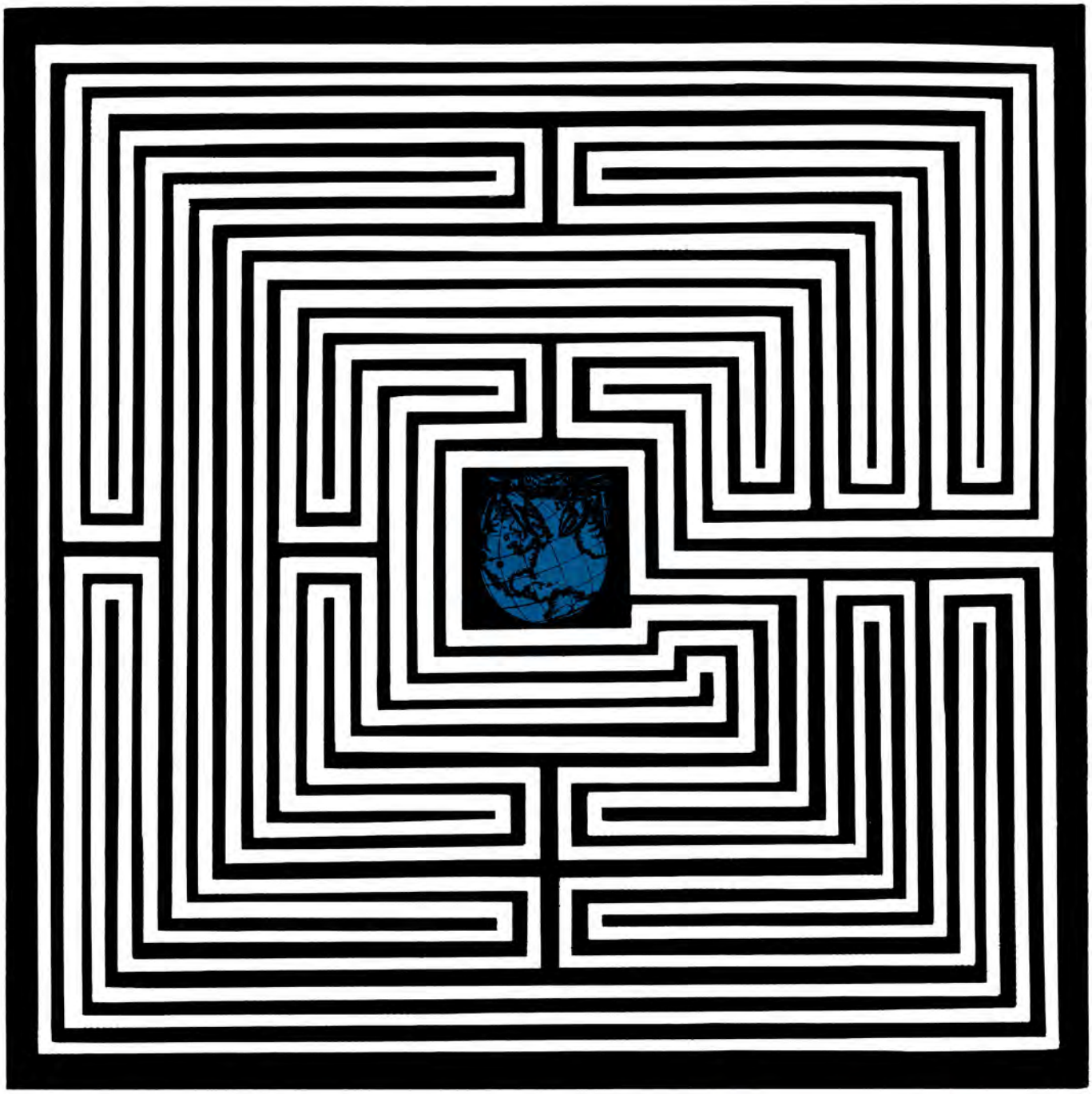

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Sisters of Charity

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Juan A. del Regato, *Editor*

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Lyle A. French, M.D.

TUMORS OF THE CENTRAL NERVOUS SYSTEM

Considerable progress has been achieved in the past few years in the development of new techniques in radiodiagnosis of tumors of the brain and spine; radioisotopic scanning has been added as an additional tool by which information may be gathered before an intervention is decided upon. Histopathologists have not been idle and new concepts have been introduced which have brought about better understanding of these tumors.

On November 7, 1970, this CANCER SEMINAR took place at the Broadmoor Hotel of Colorado Springs. Dr. Harold O. Peterson, Professor of Radiology, University of Minnesota, proved once again his keen ability to extract information from submitted roentgenograms, in spite of the limitations imposed by this exercise. Dr. Lucien J. Rubinstein, a recognized authority in the exclusive field of neuropathology, was most generous with his time in the study of the histopathologic material. Besides, we owe him the excellent photomicrographs of this issue and the carefully composed captions. Dr. Lyle A. French proved a stimulating extemporaneous speaker and commentator with a wealth of experience in the surgical treatment of the tumors on discussion. We are very thankful to these three gentlemen for contributing most fruitful hours of presentation and discussion.

These CANCER SEMINARS have now been held for 22 consecutive years. Although there is a participation of old faithfuls who have attended most or all of them, the greater part of the audience is usually formed by a new crop of young radiologists, histopathologists or surgeons who are attracted by the format of our conference and the quality of our speakers. As in the past we wish to thank those who by their contribution or participation have made these CANCER SEMINARS fruitful and enjoyable.

J. A. del Regato, M.D.
Colorado Springs, Colorado
July, 1971

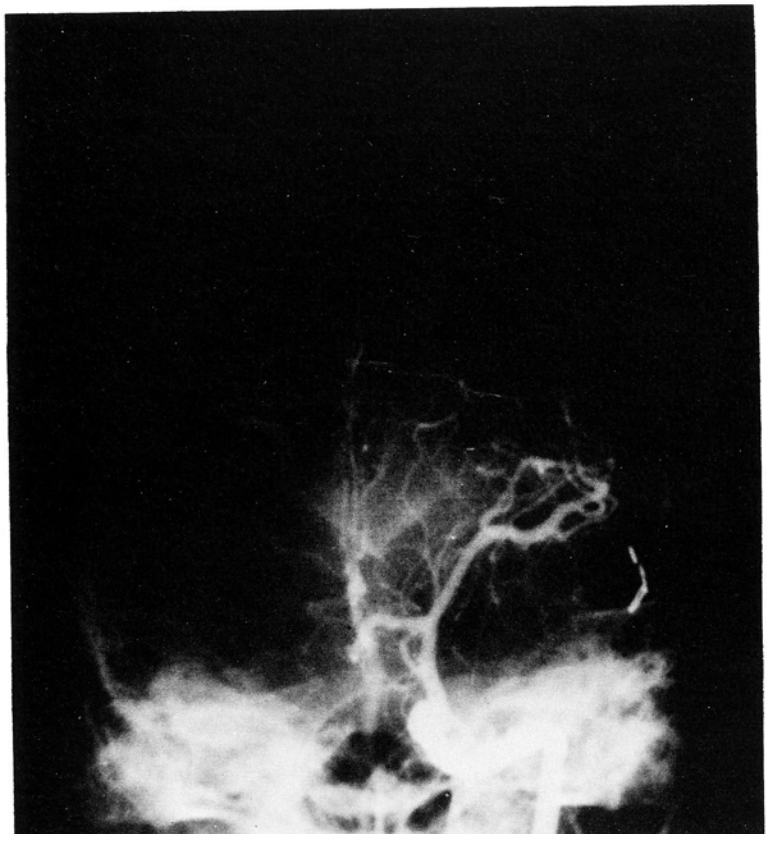
1. *Meningioma, Transitional Type, of the Sphenoid Wing Area*

Contributed by **S. Chamblin, Jr., Col., M.C.** and **C. R. Vest, Maj., M.C.**
U. S. Army, Fort Sam Houston, Texas

THE PATIENT was a 20-year old man in September, 1969 when he complained of pains of a few minutes duration of the left side of his head, following trauma. At the age of ten he had suffered from headaches and seizures; he had been put on Dalantin and later operated upon: a meningioma had been removed. On examination the optic disks and visual fields were normal.

Dr. Peterson: A single, anteroposterior film in the early arterial phase of a left carotid angiogram demonstrates a marked elevation of the middle cerebral artery beginning immediately at its point of origin and becoming relatively less marked more laterally, together with a medial displacement of the terminal segment of the internal carotid artery. There is a relatively slight displacement of the anterior cerebral vessels to the right. There are only a few very tiny vessels, possibly arising from the middle cerebral artery which extend inferiorly, some of which appear a little stretched. Some of these are very poorly defined but it is not definite that any of them represent tumor vessels. There is no clearly recognizable filling of the middle meningeal artery, particularly intracranially, although there are three unusual vascular-like structures visible in the area of the mandible and base of the skull extracranially which are not well understood. There is evidence of a previous craniotomy with a rather large flap in the parieto-temporal area and some surgical clips remain in the operative site. There is also some evidence to suggest there may have been a previous ventriculogram with almost obliterated trephines in the parieto-occipital region.

Fig. 1—Left carotid angiogram showing elevation of middle cerebral artery.



These findings clearly indicate a rather sizable mass in the middle cranial fossa anteriorly and somewhat medially which is avascular at least on injection of the internal carotid system. A large menigioma or a large astrocytoma in the temporal lobe, possibly associated with some cysts, would seem to be the most likely probabilities. The relatively marked displacement of the middle cerebral artery with correspondingly slight displacement of the anterior cerebral suggests a long standing process which in turn would favor a mass of low-grade malignancy. An intracerebral hemmorrhage or a subdural hematoma would seem to be unlikely.

Dr. Peterson's impression: Neoplastic process in the tip of the temporal lobe anteriorly and medially. 1) MENINGIOMA 2) ASTROCYTOMA

Roentgenologic impressions submitted by mail:

Temporal lobe tumor	38
Subdural hematoma (with tumor?)	38
Astrocytoma	27
Glioblastoma	10
Meningioma	9
Extradural tumor	6
Others	18

Dr. Peterson: I didn't really think there was much evidence for a subdural hematoma, none really, because what few vessels you can see are stretched over the tumor, over the mass, rather than being displaced away from the surface like a subdural hematoma would do. We don't see any vascular pattern of any extent at all which should present for glioblastoma. Meningioma is a fine diagnosis; the reason we can't do better is that we don't have external carotid filling, or probably don't have any external carotid filling.

Dr. Regato: Drs. P. Hodes, of Philadelphia, and P. Roesler, of Colorado Springs, offered an impression of meningioma of the temporal lobe. Dr. T. O. Gabrielsen, of Ann Arbor, suggested extradural hematoma.

Operative findings: On October 21, 1969, a left temporal craniotomy was carried out: a tumor 6 cm in diameter was found apparently arising from the sphenoid wing; it was very vascular and it was attached to the dura. A dural graft was fashioned from the temporalis fascia in order to close. The surgical specimen consisted of several tumor fragments, the largest being 4x3x2.5 cm; it weighed 97 grams; it was rubbery in consistency and pale gray in color. Bone biopsies were done.

Dr. Rubinstein: This circumscribed, coarsely lobulated tumor is of moderate cellularity and relatively homogeneous. The cell walls are indistinct. The general appearance often suggests a syncytial pattern. The cytoplasm is eosinophilic and homogeneous. The shape of the cells varies from polygonal to fusiform. Nuclei are prominent, of moderate size, usually spheroidal or slightly elongated. They have a pale nucleoplasm, are frequently vacuolated and have a distinct delicate nuclear membrane. They often contain one small prominent central nucleolus. In places, the nuclei are enlarged, with an apparently empty nucleoplasm and one to three prominent central nucleoli.

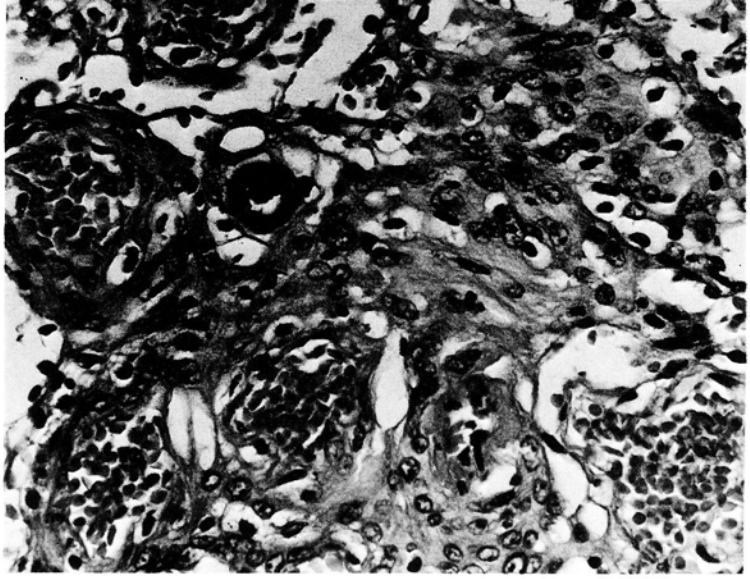


Fig.2—Transitional meningioma showing arrangement in whorls, centered around capillary blood vessels. One psammoma body is seen to the left of center. H & E x 300.

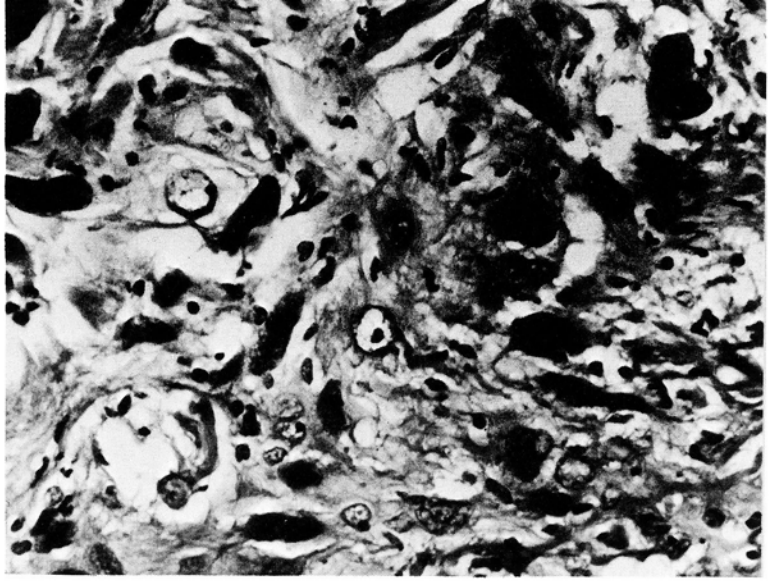


Fig. 3—Irregular giant cells with bizarre hyperchromatic nuclei in this meningioma. No increase in cellularity, mitotic figures or other forms of cellular atypia. Giant cells, as seen here, are not necessarily associated with clinical malignancy. H & E x 300.

In a few fields, especially at the periphery of the fragments, an arrangement in whorls is seen. The whorls are centered around a central capillary blood vessel. In a few others, they show calcification, with the appearance of typical psammoma bodies.

In the central areas, degenerative changes are found, consisting in a loss of cellularity and a fine reticulated network of fibers among which clusters of capillaries are seen, and cells with a stellate or elongated outline. In these fields, the appearances mimic somewhat those of a poorly cellular astrocytic tumor, but the fibers which are found throughout these less densely cellular areas are formed by reticulin or collagen, and are not neuroglial.

The appearances therefore, are characteristic of a meningioma, consisting of a mixture of syncytial and fibroblastic elements. A few features are, however, unusual: (1) Central areas in the tumor occasionally contain foci of calcification. These are different from the small isolated calcified psammoma bodies which can be identified elsewhere: (2) The tumor contains in places fairly conspicuous giant cells. These fall into two categories: a) a simple enlargement of the nuclei, as already described, in which the nucleoplasm retains its "empty" appearance; and b) scattered irregular multinucleated giant cells in which the nuclei, which are markedly hyperchromatic, are heaped upon each other. Accompanying these giant cells, there are no obvious areas of necrosis, no increase of cellularity, and no mitoses, or other forms of cellular atypia. (3) Rare mitotic figures are found, a feature which is unusual in otherwise benign meningiomas. These are present at an approximate rate of one per twenty high power fields. (4) The reticulin pattern is more abundant than is usually the case in syncytial meningiomas. In the latter reticulin fibers are generally confined to the vascular stroma. By contrast a very abundant reticulin network is demonstrated, suggesting that many of the tumor cells are fibroblastic. It also emphasizes the transitional morphological features that bridge the various histological types of meningiomas.

The main diagnostic problem on this case hinges on whether it has features indicative of malignancy. The presence of giant cells might lead one to suspect so, and one might be supported by the finding of an occasional mitosis. However, giant cells of this type are sometimes found in meningiomas in which the subsequent clinical course has shown that the tumor was entirely benign. I am therefore inclined to discount the presence of giant cells in this case as significant of a malignant, or invasive, meningioma. Despite the presence of an occasional mitotic figure, I would not anticipate that this particular example has a likelihood of recurrence greater than what is usually estimated in the group of meningiomas as a whole, i.e. approximately 20%.

As regards the histological classification of this meningioma, the microscopic appearances suggest that it should be placed in a transitional category between the syncytial, or endotheliomatous, and the fibroblastic forms.

Dr. Rubinstein's diagnoses: MENINGIOMA, Transitional type.

Histopathologic diagnoses submitted by mail:

Meningioma	61
Meningioma (Meningothelial, endotheliomatous, syncytial, meningocytic, epithelioid, cytoplasmic, atypical, peculiar, pleomorphic, myxomatous, transitional)	47
Malignant meningioma	32
*Astrocytoma	3
Others	8

Dr. Rubinstein: The vast number of subvarieties which are listed here and would illustrate I think the difficulty in coming to an exact designation of the histological type of meningioma. Instead of adopting all these various sub-classifications, you call it transitional to include them all.

Dr. Regato: Dr. K. Jollinger, of Vienna, made a diagnosis of cytoplasmic meningioma with questionable transition to meningosarcoma. Drs. B. B. Banson, of Manila, A. O. Severance, of San Antonio, and V. F. Lopez, of Columbia, Missouri, preferred the designation of meningotheliomatous meningioma. Dr. J. B. Frerichs, of El Paso, thought it to be a peculiar variant. Dr. E. B. Blizard, of Denver, considered it as a potentially malignant menigioma while Dr. W. J. Pepler, of Pretoria, preferred to call it a meningeal sarcoma.

Subsequent history: The patient made a rapid recovery and in November, 1969 was discharged. In October, 1970, he was reported in good condition.

Dr. French: This patient gave a history of being on Dalantin; he is in the Army, which sort of throws you a little bit—what's a fellow doing in the Army with seizures; those seizures probably came on after he got into the service—that's the way a neurosurgeon looks at it. Looking at this film you can see that he had a craniotomy; sometimes you can tell the age of a craniotomy by looking at the sharpness of the clip. A meningioma arising in a 20-year old boy is pretty unusual; it can happen, but not too often. Actually he had the tumor operated on 10 years ago when 10 years of age. Meningiomas occur in children, not quite as frequently as in adults by any means but when they do occur they are more apt to be multicentric in origin or multiple, or tend to be more malignant. They tend to be sort of neurofibromatosis. I think it would be important to know from a neurosurgical point of view if this lad did have other stigmas, of neurofibromatosis, for example, or if he had other potential evidence of a lesion. The type of seizures is important. If this were a meningeal tumor the patient probably should have what we call uncinate type of seizures, with olfactory phenomena, but if the attacks were true temporal lobe attacks, having with it possibly some visual loss, some taste phenomenon, hallucinations, a peculiar inter-seizure personality, you could tell that it most likely is a glioma. It would be nice to have an external carotid study. I would have turned the flap—the craniotomy flap to sort of a transfrontal going down along the sphenoid wing and followed in and we would have come down on the tumor. The lesion is well located; it turned out to be a meningioma, one would know that at the time of surgery because of its attachment to the sphenoid wing, the dura. This is quite a large tumor, especially when its the second time around; the probabilities are the tumor is twice the reported size because a lot of it will go up the suction apparatus.

C.R. Vest, Maj., M.C., Fort Sam Houston, Texas: We apologize for not having additional radiologic studies. The patient had a grand mal seizure in the midst of the carotid angiogram; it was elected not to attempt additional studies and to explore immediately. As far as we know, he is doing well.

C. Araoz, M.D., Little Rock, Arkansas: Would you please comment on the calcifications or hyperostosis adjacent to meningiomas?

Dr. Peterson: I would have liked to have seen some plain films to see if there was any hyperstosis along the sphenoid wing, which there might well have been; they would really have given away the diagnosis. My impression is that meningioma cells invade the bone and provoke a bone reaction, which is the hyperostosis that we see radiologically.

Dr. Rubinstein: I would say there are two basic pathogenic mechanisms that are responsible for the hyperostosis. On one hand you may have simply an excessive amount of osteoblastic proliferation due to the contiguous tumor which may infiltrate the periosteum, but may actually not infiltrate the bone; this, therefore, may simply be a reaction of the bone to an underlying tumor and why this reaction takes place one does not know. It is quite a well-known feature, of course, that one form of tissue may induce a strong reaction to another. We shall discuss all of this later on and perhaps this osteoblastic reaction to an underlying tumor may be regarded as similar to fibrous tissue reaction, due to underlying tumors as well. Quite frequently, there is a second feature, the bone and the bone marrow spaces are actually infiltrated by meningioma cells. This is only one of several characteristic invasive features of meningiomas which must be regarded benign despite these invasive features. Meningiomas tend to invade also the dura; they may even invade the muscle; in cases of orbital meningioma you can find invasion of the extraocular muscle but it doesn't mean histological malignancy.

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2. *Malignant Angioblastic Meningioma (Hemangiopericytoma of the Leptomeninges)*

Contributed by **M. J. McNally, M.D.** and **M. Berthrong, M.D.**
Colorado Springs, Colorado

THE PATIENT was a 67-year old man in April, 1970, when he was hospitalized because of progressive mental confusion, drowsiness and urinary incontinence of, at least, four weeks duration. Examination revealed mild tremor and diminished sensory responses of the left upper extremity; there was bilateral Babinski response.

Dr. Peterson: Films demonstrate a right carotid arteriogram in the arterial phase with the injection in the common carotid artery with some filling of both the internal and external carotid system. There is a marked elevation of the middle cerebral vessels beginning at the point of origin of the right middle cerebral artery. There is a moderate displacement of the anterior cerebral vessels toward the

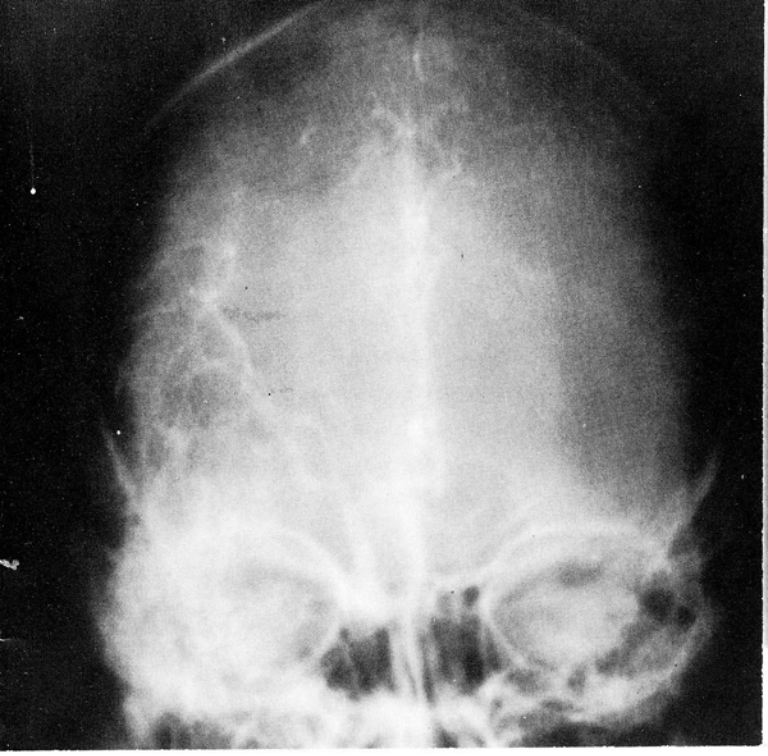

Fig. 1—Right carotid arteriogram showing displacement of anterior cerebral artery to the left.

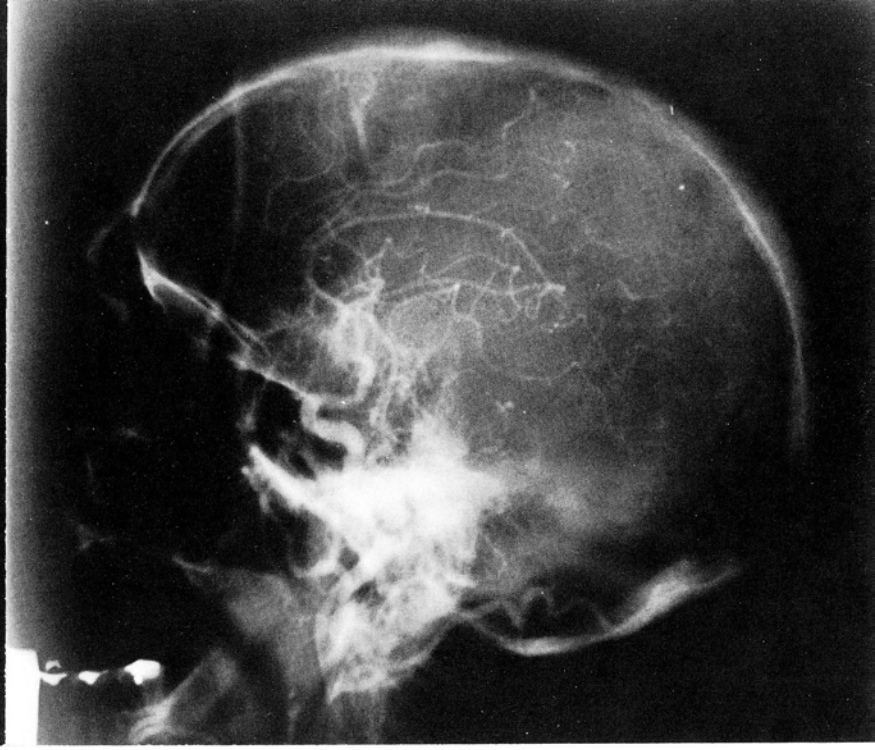

Fig. 2—Right carotid arteriogram showing elevation of the middle cerebral vessels.

left side. There are some abnormal vessels rather poorly demonstrated in the area of the middle fossa or temporal lobe on the right side which are located about in the central position of the temporal lobe or posterior central location in the middle fossa. There is rather vague evidence to suggest a large vessel leading into this area which may well be the middle meningeal artery. The findings are quite accurate with regards to location of the tumor in the middle fossa or temporal lobe on the right side and are definitely indicative of a neoplastic lesion; the differential diagnosis would lie between a glioma in the temporal lobe or a meningioma. The suggestion, which actually is not sharply demonstrated, that there are vessels coming to the lesion from the external carotid system would favor a meningioma.

Dr. Peterson's impression: Neoplastic process in the right middle fossa or temporal lobe, probably a MENINGIOMA.

Roentgenologic impressions submitted by mail:

Glioblastoma	32
Meningioma, sphenoid wing	19
Temporal lobe tumor	18
Metastatic tumor	12
Others	13

Dr. Peterson: Glioblastoma is all right, there were a number of what looked like tumor vessels, not really sharply brought out. Temporal lobe tumor—that's a great diagnosis; histologically, that's got to be right. Metastatic tumor is maybe a little less likely. I have a feeling that most metastatic tumors should be rather sharply circumscribed. They look like round masses that grew from a focus; they get bigger but the edges end abruptly and most of them don't have a diffuse margin.

Dr. Regato: Dr. P. H. Remenschneider, of Santa Barbara, California, and Dr. J. W. Sala, of Springfield, Missouri, also offered an impression of temporal meningioma. Dr. A. Schlessinger of Cincinnati, designated it as a sphenoid wing meningioma.

Operative findings: On April 13, 1970, a left temporal craniotomy was performed. There was no visible tumor, but a mass was felt underlying the surface. Fragments of the tumor were removed by finger dissection; the bone appeared eroded. There was considerable bleeding necessitating the administration of 4 pints of blood. The surgical specimen consisted of four irregular gray-tan hemorrhagic fragments of rubbery consistency measuring 5 cm in their greatest diameter.

Dr. Rubinstein: The circumscribed and coarsely lobulated tumor has a fairly high cellular density and a remarkably homogeneous cytology. There are central areas of necrosis. Under the low power, the cellular areas show two histological patterns. Some areas show a very uniform cell population, the cells being compact, with very ill-defined cytoplasmic outlines and prominent packed nuclei with a delicate nuclear membrane, a frequently vacuolated nucleoplasm, and a very delicate or ill-defined chromatin network. The nuclei are often somewhat spindle-shaped, and often appear to surround very thin-walled blood vessels lined by normal flattened endothelial cells. The second histological pattern results from an apparent concentration of cellularity around the blood vessels, with a relatively decreased cellularity further afield. In these less cellular areas, the tumor cells form a reticulated pattern, the neclei being small and elongated and delicate fibers appearing to arise from their cytoplasmic processes.

The reticulin preparation outlines in a striking manner the presence of an extremely abundant vascular network. The reticulin fibers appear to radiate from the walls of the blood vessels and to form an intense meshwork separating the tumor cells both singly and in small groups. The pattern of reticulin fibers thus demonstrated is much more intense than might have been surmised from the H & E preparation.

An important feature is the presence of numerous mitotic figures, frequently amounting to two or three per high power field.

The microscopic appearances are highly typical of the angioblastic meningioma as originally described by Bailey,

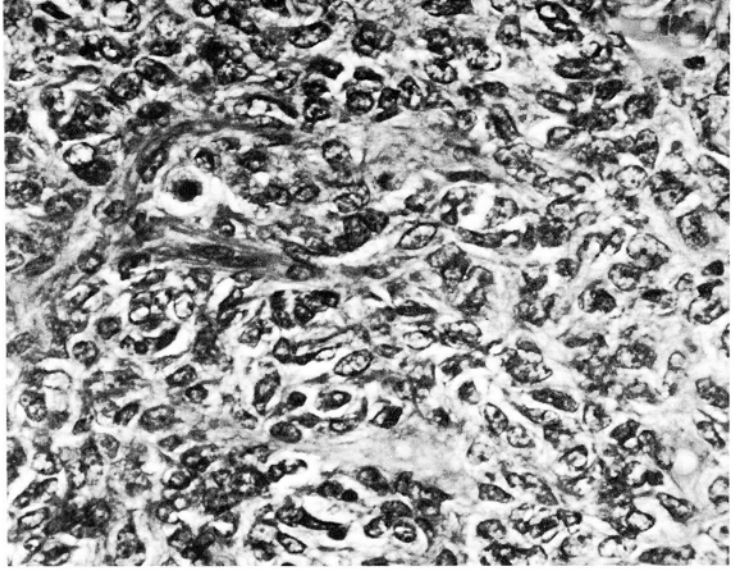

Fig. 3—Angioblastic meningioma showing a compact arrangement of cells with ill-defined cytoplasmic outlines and spindle-shaped nuclei containing a pale nucleoplasm and delicate chromatin. Thin-walled blood vessels lined by normal endothelial cells are present. Note mitotic figure. H & E x 400.

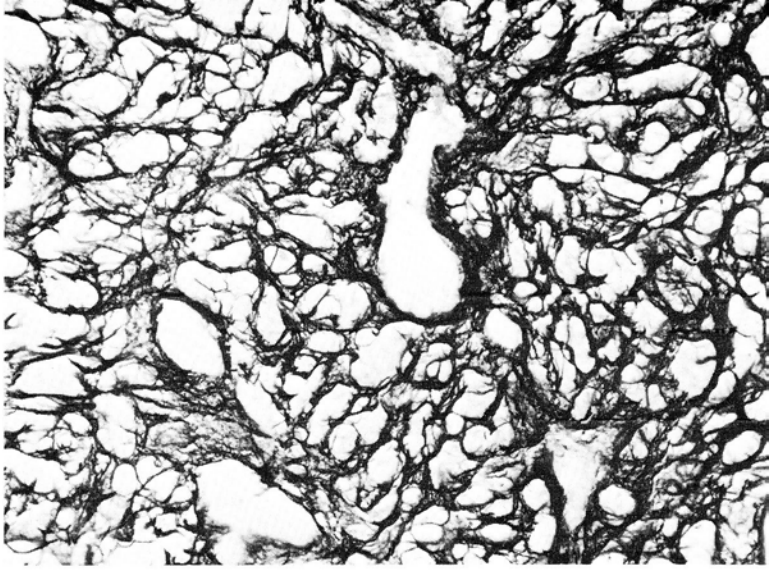

Fig. 4—Reticulin pattern in angioblastic meningioma. The fibers appear to radiate from the blood vessel walls and form a close-meshed network encompassing the tumor cells in small nests. Gordon-Sweets' silver method for reticulin x 300.

Cushing and Eisenhardt. This type of meningioma has long been known to exhibit a more aggressive type of growth than other forms of meningioma, to show mitotic figures, to be prone to recurrence and, in a number of cases, to give rise to extraneural metastases. It corresponds to variant 1 of the angioblastic form of meningioma as described by Cushing and Eisenhardt.

More recently, the same tumor has been reclassified, by Kernohan and Uihlein and others (see references in Pitkethly et al.), as a hemangiopericytoma of the leptomeninges. It is included by Kernohan among the primary sarcomas of the brain.

A recent paper by Pitkethly et al. (1970) reviews the clinico-pathologic features of 81 cases of angioblastic meningioma, and subdivides them into a hemangioblastic and a hemangiopericytic type. This case would fall into the second type. These authors found that it appears at an earlier age and has a more rapid involvement of symptoms than the hemangioblastic variety. They confirmed its tendency to recur. Four of their cases had extracranial metastases. In three such cases referred to me for consultation, distant metastases had developed.

There is some disagreement as to whether this type of tumor should be included among the meningiomas. It has been claimed that its parent cell, the pericyte, should be regarded as a component of the capillary wall, and thus these tumors have been considered to arise from the blood vessel walls, or to be a form of sarcoma. Other workers regard it still as a variant of meningioma. Tissue culture studies of an example (quoted by Pitkethly et al) have reported the presence of delicate whorls, typical of meningiomas. Transitional forms can also sometimes be seen between this form and the more common type of meningioma.

Dr. Rubinstein's diagnosis: MALIGNANT ANGIOBLASTIC MENINGIOMA or HEMANGIOPERICYTOMA OF THE MENINGES.

Histopathologic diagnoses submitted by mail:

Hemangiopericytoma	48
Angioblastic meningioma	29
Meningioma (malignant 12)	28
Hemangiosarcoma	11
Other sarcomas	10
Ependymoma	9
*Astrocytoma	8
Others	5

Dr. Rubinstein: Most of the participants had no difficulty in recognizing the main features of this tumor. Hemangiopericytoma, alternatively angioblastic meningioma, or malignant meningioma: the opinions are roughly divided by half. Some called it hemangiosarcoma, other forms of sarcoma. I think what this illustrates is that although there is no difficulty in recognizing this tumor, there are some conceptual differences as to what to call this tumor and also as to its origin.

Dr. Regato: Drs. G. Vogt-Hoerner, of Tunis, Sister Joseph Ignatius, of Dayton, and Y. LeGal, of Strasbourg, made a diagnosis of hemangiopericytoma. Drs. R. D. Schultz, of Sioux Falls, and C. R. Vest, of Fort Sam Houston, Texas, considered it a malignant meningioma. Dr. H. M. Zimmerman, of New York, and Dr. J. M. Loizaga, of Madrid, made a diagnosis of dural hemangiosarcoma. Dr. Dorothy Russell, of Surrey, England, also suggested a malignant angioblastic meningioma.

Subsequent history: Post-operatively the patient did well but complained of epigastric pain; a renal shut down developed which failed to respond to medication. On April 17, 1970 he expired. No autopsy was done.

Dr. French: This is a 67 year old man who had progressive mental confusion, drowsiness and urinary incontinence. It could mean anything, so you rely on the neurological examination but it showed only mild tremor which, in a 67 year old, doesn't mean much; you need to know whether there was really a loss of perception of pain, temperature, light touch, etc. Your Babinskis get a little bit more positive as you get older and it is probably indicative of some sort of cortical spinal tract involvement. One of the things that a neurosurgeon must learn always is to talk to his radiologist; whether the radiologist does the angiogram, or the neurosurgeon, it makes no difference. But what to do when you get an angiogram like this, can you be certain what the lesion is? It would worry me a little bit, but I'd talk to the radiologist about it and if he felt pretty confident of it, I then would go ahead and turn a craniotomy flap over this area and we would come down to the neoplasm, we would remove it and we wouldn't be sure really from the gross appearance what type of lesion it was. We probably would be worried about how much we were taking out and as to whether or not we were getting it all out or not. And here we would turn to the neuropathologist. If this turns out

to be an angioblastic sort of meningioma or hemangiopericytomous type of meningioma, I would wonder if indeed we had taken out all the tumor. Now what else do you do? I would not irradiate him. I would simply follow him along to see how he got along. If he had any recurrence, I would then irradiate him. If this gentleman were 47 years of age, I would irradiate him right off the bat.

M. J. McNally, M. D., Colorado Springs: This patient's wife had not at first noticed any personality change until about a month or so before he came in. Afterwards we requestioned her and she admitted that friends did feel that he had changed in personality for about a year. I did a temporal craniotomy, there was a fair amount of pressure and looking down to the middle fossa floor I did not see any obvious tumor laterally. I did feel the firmness of the lobe and found it very hard to work. I removed the lower portion of the temporal lobe for better exposure and found it to be an extremely vascular tumor. As I tried to remove it piecemeal, it just kept bleeding furiously and I felt I was going to lose too much blood, so I used my index finger and peeled it out of the area. It was firmly attached to the medial and middle aspect of the floor of the middle fossa; I was extremely sorry to have peeled it off because then the bone bled profusely. It took a great deal of cauterizing, bone wax and finally some muscle and allowing the lobe to drop back in place to control it, but we did lose four units of blood. Postoperatively the first few days the patient was drowsy but then he did progressively improve; about the fifth day he started complaining of chest pain, had a renal shut down and hypotension and in spite of vigorous attempts by the internist all that day, he did expire.

Dr. French: I would like to ask from Dr. Rubinstein, how in the world do people get mixed up, how could anyone call this an ependymoma?

Dr. Rubinstein: I can only answer for my own misdiagnoses. My impression from the literature is that these aggressive meningiomas have a tendency to recur and do not respond to irradiation. I would like to have further information, for if indeed these tumors are not radiosensitive, I wonder what is the rationale for irradiating.

Dr. Regato: We have irradiated meningiomas successfully and we feel that this should be taken into consideration. In this instance, however, the patient died promptly after his operation, so there was no question for us to take the blame for that one. Provided the irradiation is vast enough and throrough enough, I think this is to be attempted any time when there is obvious evidence that tumor has been left behind. The tumor is not particularly radiosensitive in the sense that it does not regress rapidly. There is a rule of thumb: a tumor regresses under irradiation in relation to the speed with which it develops before being irradiated. If the tumor is slow growing, its regression will be slow. Meningiomas are slow developing, with some variability, some slower than others; the tumor may be expected to regress very slowly, but they should be irradiated if there is evidence of residual disease.

Dr. Rubinstein: The pathologists sometimes are regarded as some-what hypercritical on irradiation; I do not belong to those pathologists at all. One can find reasonable objective evidence that irradiation has actually had an effect on some tumors. This is certainly so on certain gliomas, and in the case of tumors of the lymphoma group. But when you come to estimate the effect of irradiation on a tumor of this kind, where the post-operative course is so unknown, when it is so chancy as to whether it is going to recur quickly or not. It becomes very difficult to get some objective evidence as to what irradiation does, so I would sort of express a certain amount of skepticism at the moment, until I've seen more, as to whether this tumor really does respond to irradiation and as to whether the results do mean that irradiation has done something to the patient.

Dr. Regato: You are absolutely right in your skepticism, also you are absolutely right in your expectation. However, few of these cases are ever irradiated because they do not go to the therapeutic radiologist. Few radiotherapists like Dr. Jean Bouchard, of McGill, have had an opportunity to irradiate a great number of intracranial tumors. When more such tumors are irradiated neurosurgeons as well as neuropathologists will become more appreciative of the possibilities of radiotherapy in this area. But there are not enough figures, as you said, to prove it to anybody.

John Kepes, M. D., Kansas City, Kansas: I think that this case is very instructive for more than one reason; one particular point all of us should appreciate, is the fact that in many areas this is not a completely pure hemangiopericytoma. Dr. Rubinstein emphasized that they are not always pure: in some areas we see the classical hemangiopercytoma and in other areas it is more like a primitive mesenchymal tumor possibly looking like a very primitive fibrosarcoma. And ever since Arthur Purdy Stout brought to our knowledge the existance of this tumor, this is generally thought about as a hemogenous lesion. It is either this or it is something else. I recently had a case in a young man who had a hemangiopercytoma in the parotid gland and looking at another section it looked like a fibrosarcoma; this mixed behavior is an important feature to recognize. Dr. French asked: how could anybody call this an ependymoma? Whenever you hit a tumor that has blood vessels surrounded by tumor cells in a radiating fashion to the blood vessel, the question of ependymoma comes up. In this lesion the nuclei are much closer to the blood vessel than in an ependymoma, but, nevertheless, it is something that surrounds blood vessels. I feel that a strong stand should be taken against the term hemangiosarcoma in a tumor like this. I don't think it one of the synonyms for this tumor as long as the endothelium is not neoplastic. I think in a hemangiosarcoma you should have a malignant endothelium.

Dr. French: I would like to explain why I asked that question between the meningioma and ependymoma. In general it is nice, not only if the neurosurgeon talks to the pathologist, but the reverse too. The neurosurgeon can be very helpful by telling the pathologist the location of the tumor and simply reporting that it is attached to the dura. I would probably recommend irradiation in a younger patient because in this location it is probably not as disadvantageous to the patient as in other locations.

Dr. Regato: May I add that what is disadvantageous to the patient very often is not the irradiation, but the man who does it and the manner in which it is done. To give you an example, there is evidence, more than 30 years old, that medulloblastomas of the cerebellum are curable by radiotherapy, whereas they are seldom curable by surgery. One of the pioneers of this work in this country, Dr. Lampe of the University of Michigan, treated his first cases rather intensively and he cured them, but the patients were damaged; they remained mental children and sort of living vegetables. Having learned his lesson,

he subsequently irradiated less intensively, the disease was controlled and the patients were not damaged; depending on how intensively these brains are irradiated, permanent and progressive subsequent damage may be observed.

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3. *Malignant Sincytial (Endotheliomatous) Meningioma*

Contributed by **Harold O. Peterson, M.D.,** Minneapolis, Minnesota

THE PATIENT was a 45-year old man in February, 1970, when he was hospitalized for persistent headaches and personality changes over a period of 3 months. On examination the pupils were dilated and there was marked papilledema. The spinal fluid had a pressure of 420 mm and 86 mgm% proteins.

Dr. Peterson: Right carotid angiogram in a mid arterial phase demonstrate a huge mass lesion on the right side with a large number of tumor vessels located in the frontal and temporal area inferiorly, probably arising laterally, displacing and elevating the middle cerebral vessels markedly and showing a marked displacement of the anterior cerebral vessels to the left side. There are tumor vessels in the antero-posterior projection which extend from the lateral aspect of the cranial cavity to a point just across the mid line. In the lateral projection, tumor vessels extend anteriorly almost to the tip of the frontal pole area and posteriorly well into the central portion of the temporal lobe to a level of the mastoids from a standpoint of a bony landmark.

The problem here is one of attempted differentiation of a histologic type of neoplasm since the size and location of the tumor is extremely well demonstrated by the tumor vessels. The tumor vessels are moderately small but reasonably well formed and the entire tumor is reasonably well demarcated. Anteriorly and superiorly there is a relative lack of vascularity in the brain substance outside of the tumor which might suggest cerebral edema. All of these features would favor a meningioma. The tremendous size of the tumor might also be in favor of a meningioma. The vascular pattern might also occur with a glioma, although it is not as wild looking as a Grade IV glioblastoma. There probably is a lack of vascularity in the central portion of the mass as compared to the periphery which would be in favor of some degeneration taking place centrally. The massive displacement of the middle cerebral vessels and the demarcation of the tumor vessels from the surrounding brain would tend to favor a meningioma.

Dr. Peterson's impression: Huge mass involving the frontal and temporal lobes inferiorly consistent with a MENINGIOMA.

Roentgenologic impressions submitted by mail:

Glioblastoma multiforme	60
Fronto-temporal tumor	16
Meningioma	10
Others	12

Dr. Peterson: Most of the radiologists favored a glioblastoma multiforme and, as I say, that's what our own neuroradiologist at the Veterans Hospital also thought it was. The location of this tumor is no problem. Some of the little points I brought out are not bad. It is perhaps the art of radiology, but I think they do tend to point towards a meningioma.

Dr. Regato: Dr. J. Marshall, of Colorado Springs, also offered an impression of meningioma. Drs. B. A. Zickerman, of Bronx, New York, and K. Hehman, of Cincinnati, suggested a fronto-temporal glioblastoma.

Operative findings: On February 4, 1970 a right frontotemporal craniotomy was done. After incision of the dura a tumor was found attached to the sphenoid wing. With the help of the "sucker and Bovie" a large amount of granular and vascular tissue was removed from the frontal and temporal lobes. A frozen section was reported as "glioma" and no further attempts at complete removal were made. The specimen consisted of numerous hemorrhagic and necrotic fragments under 1 cm in diameter.

Dr. Rubinstein: In certain areas this tumor is composed of a characteristic pattern of rather flattened epithelial-like cells with very ill-defined cell margins, regular spheroidal nuclei and a delicate chromatin network. A suggestion of whorling is seen, but this is not very frequent. In other areas the architecture is less distinctive. The cells are arranged in homogeneous sheets. Their cytoplasmic margins remain indistinct, but here again a suggestion of whorling is present. In a number of fields, the cells are arranged to form multiple layers around blood vessel walls, and have a somewhat papillary architecture.

The tumor shows extensive vascularization. Some of the blood vessels are abnormally thick and apparently malformed, their walls being greatly fibrosed. Occasionally, they contain mural thrombi in various stages of organization. Extensive necroses are found, particularly in the center of the fragments. There is a considerable amount of central fibrous tissue proliferation, some of

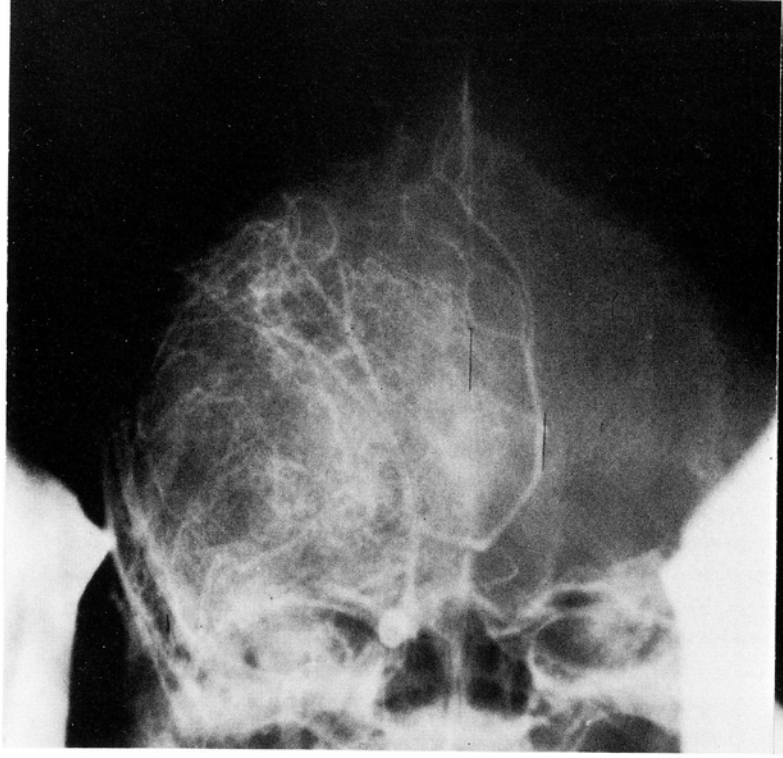

Fig. 1—Right carotid angiogram demonstrating displacement of anterior vessels to the left.

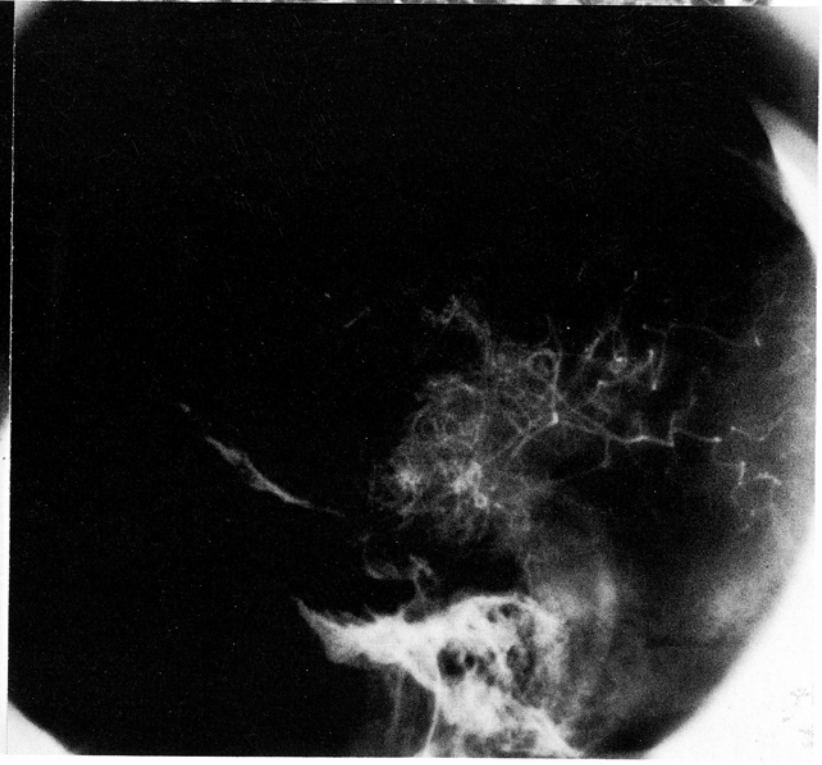

Fig. 2—Right carotid angiogram showing tumor vessels extending anteriorly to the frontal lobe.

which appears to originate from degenerated, thickened blood vessel walls, and some forming rather closely intermeshed bundles of coarsely staining fibers.

In the above mentioned areas, the cytology is usually benign, and without atypia. However, mitotic figures are found in fairly abundant numbers throughout, amounting in some cases to two or three per high power field. In other areas, however, the tumor pattern is less well organized, the cells being larger and more irregular, the nuclei more hyperchromatic. In a few places the cell outlines become better defined, and acquire the irregular, almost mosaic pattern of squamoid cells. Finally, in a few areas at the periphery of the tumor, there is a definite suggestion of invasion of the adjacent brain. The tumor cells here tend to cluster around the advancing blood vessels that appear to invade the neural parenchyma.

The reticulin preparation shows a fairly abundant reticulin network intersecting the tumor, particularly obvious where blood vessels are abundant. The almost telangiectatic pattern seen in places is well demonstrated. Interesting fibrillated stromal structures that stain intensely with eosin are formed by the fibrous connective tissue. The reticulin pattern varies from field to field. It is rather less well developed in the more epithelial-like areas.

All the above features point foremost to a malignant endotheliomatous, or syncytial, meningioma. A confusion might possibly arise at first with a metastatic squamoid carcinoma. This is a well-known differential diagnosis, because of the superficial resemblance between the syncytial, or endotheliomatous, meningioma and some of the less differentiated squamoid carcinomas. The problem may be complicated by the presence of numerous mitotic figures. The papillary pattern in this tumor is also interesting because it is occasionally found in aggressive, or malignant, meningiomas. These features, as well as the presence of necrosis suggest therefore an aggressive form of meningeal tumor, in which recurrence and even remote metastasis might be anticipated.

Dr. Rubinstein's diagnosis: MALIGNANT SYNCYTIAL (or endotheliomatous) MENINGIOMA.

Histopathologic diagnoses submitted by mail:

Malignant meningioma (blastoma, sarcoma, angioblastic)	52
Meningioma	17
Glioblastoma	35
Ependymoma	18
Metastatic carcinoma	10
*Astrocytoma	17
Others	12

Dr. Rubinstein: The majority have emphasized the presence of malignant features in this meningioma, but there is quite a wide group of pathologists who interpreted this tumor as a form of glioma; they evidently have been impressed by the malignant features and I can't entirely blame them for coming to this conclusion. I find it less easy to understand the diagnosis of astrocytoma and ependymoma, although as Dr. Kepes has pointed out to you, it is possible that the very vascular arrangement may have induced the diagnosis of ependymoma. You notice that quite a few offered metastatic carcinoma, which I think does come to a differential diagnosis in a few fields.

Dr. Regato: May I point out that there is an asterisk there. I am thus calling your attention to the fact that someone, somewhere in everyone of the cases made a diagnosis of astrocytoma.

Dr. Regato: Dr. L. B. Henley, of San Antonio, offered a diagnosis of meningothelial meningioma. Dr. R. Reicher, of Sofia, called it a meningeal blastoma. Dr. B. B. Banson, of Manila, saw evidence of malignancy and placed it as intermediate between syncytial and transitional meningioma. Dr. Cammoun, of Tunis, concluded simply to malignant meningioma.

Subsequent history: Slides of this case were submitted to the A.F.I.P. (Accession No. 1339785) and a diagnosis of meningioma was rendered by Dr. K. M. Earle. On March the 4th the patient was reoperated: residual tumor was resected from the middle cerebral fossa and sphe-

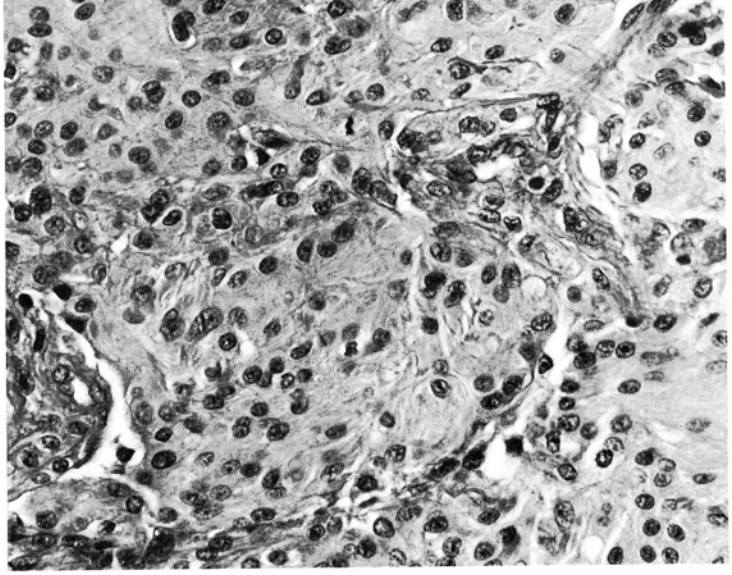

Fig. 3—Field of typical syncytial, or endotheliomatous, meningioma. Note mitotic figure in upper central portion of photograph. H & E x 300.

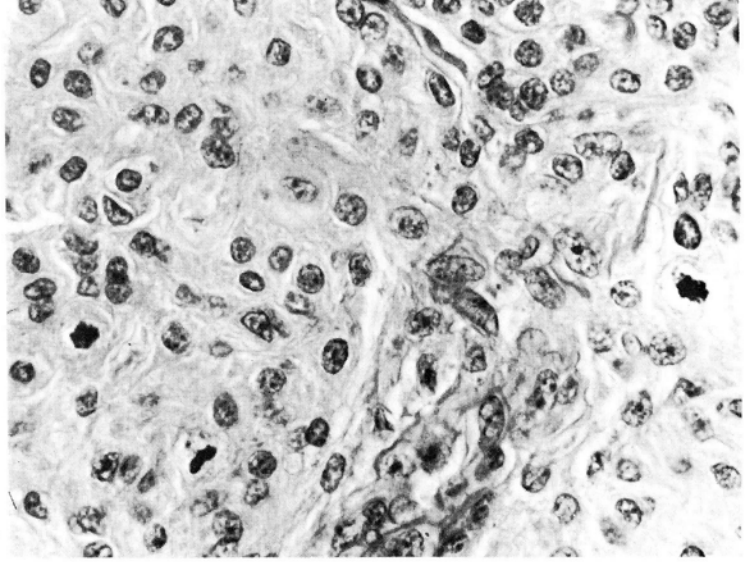

Fig. 4—High power view of syncytial, or meningotheliomatous meningioma, showing three mitotic figures. van Gieson x 480.

noid wing. Six weeks later he was discharged. In August, 1970, he had to be reoperated because of infection of the craniotomy flap; the bone was resected and the flap debrided. On September 18, 1970, he was reported well.

Dr. French: This case came from our service in the Veterans Administration Hospital which is part of our University service. I had never seen the case. Basically, this is a frontal lobe symptomatology. It could be due to early degenerative changes, from too much whiskey, or it could be due to subdural hematomas or it could be due to an intracerebral neoplasm and I don't think one can tell from the history. But, pupils were dilated and there was marked papilledema, so you know he has increased pressure. The spinal fluid had a pressure of 420 millimeters and 86 milligrams percent of proteins. Most neurosurgeons would think that when you have a patient with bilateral papilledema and when the pupils are getting fixed and dilated, you should not stick a needle into the spine to measure the pressure or find out the protein. There is just no sense in it and probably the patient is going to get worse. I think you can do a lumbar puncture in the face of increased pressure under certain circumstances, but not this one. I would criticize our service for that very seriously and severely. This should not be done. The location was well delineated by the angiogram. You will turn the same type of craniotomy flap. We would get a frozen section on most of the tumors we operate upon. The pathologist's report was that of a glioma and it must not have been too far from what the surgeon thought it was; I gathered from his description, that he thought it was attached to the meninges, but a malignant type of glioblastoma will sometimes develop this adherence to the meninges.

Before I came to this CANCER SEMINAR I talked to the surgeon who operated on the patient; he thought it was a glioblastoma, but there was something wrong with it. About a week later when the patient was doing all right he asked the pathologist if he was sure of that diagnosis, and the pathologist said, "Well no, it is kind of funny. I'm not sure if it is a glioblastoma or just what it is." About a week later over a cup of coffee, the surgeon asked again and the pathologist replied, "Well, you know, it looks kind of like a meningioma of some sort, but not a really good meningioma." And after another week and several cups of coffee the surgeon blurted: "Can't you fellows tell the difference?" And the pathologist said, "Well, we sent it to Dr. Earle and he phoned and said he wasn't sure." A week later a report stated that it was probably a meningioma and our pathologist by this time had come to the same conclusion. Our men accepted the fact that they were wrong and reoperated on the patient. I think that this is something you need to appreciate, that whenever you have a probability that you are wrong, or even a possibility, you ought to accept this, talk to the patient and reoperate if necessary. I don't know if they removed all the tumor or not. I don't know why he had an infection of flap, but I can imagine why. It is two craniotomies in a period of about six weeks. I presume both of these operative procedures were fairly long operative procedures where the scalp and the incision were exposed to the air and all the contaminants. The thing to do is to re-excise the edge of the bone and it usually clears up.

Dr. Rubinstein: I demonstrated that there was invasion of the neighboring brain. These tumors are known to recur (although when would they recur cannot be predicted) even though they have been apparently completely removed. This is the problem with these aggressive meningiomas, some do recur, some of them don't and even when they do, we may wait 20 years before they do so. The same thing is true of metastases. There are quite a few cases reported in the literature of tumors that have metastasized and where the metastasis presented several months or years after the primary had been removed. It is true that in the majority of these cases, there was recurrence locally, but this need not be necessarily the most impressive presenting symptom, and since these tumors may sometimes be slowly growing particularly in extracranial sites, you may have to wait a long time before a clinical recurrence becomes obvious. In this kind of case we hope that the slides are given to us on a Thursday, because then we can ask the technician to do a very slow and very careful PPH stain. We generally get the slides next Wednesday, thus allowing plenty of time to think about it.

Leo Lowbeer, M.D., Tulsa, Oklahoma: The last three cases were more or less classical cases of large meningiomas in which a radiologic diagnosis can be made to a

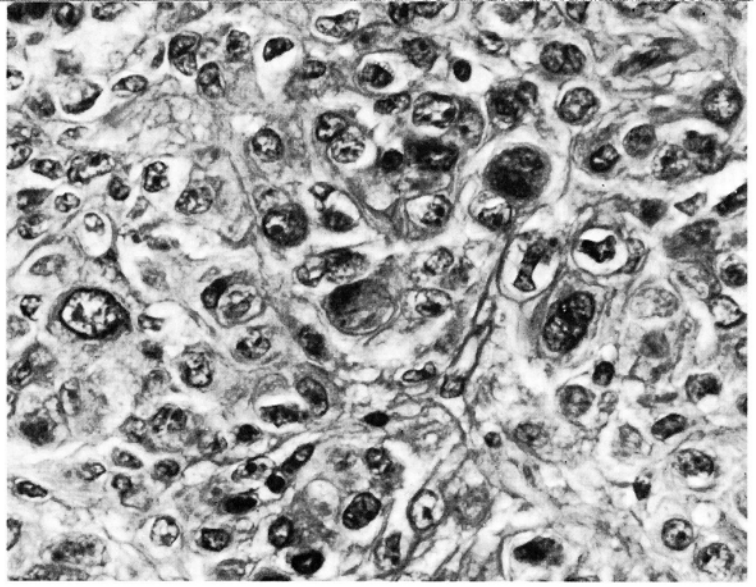

Fig. 5—Area of malignant meningioma showing enlarged irregular cells with hyperchromatic nuclei. H & E x 480.

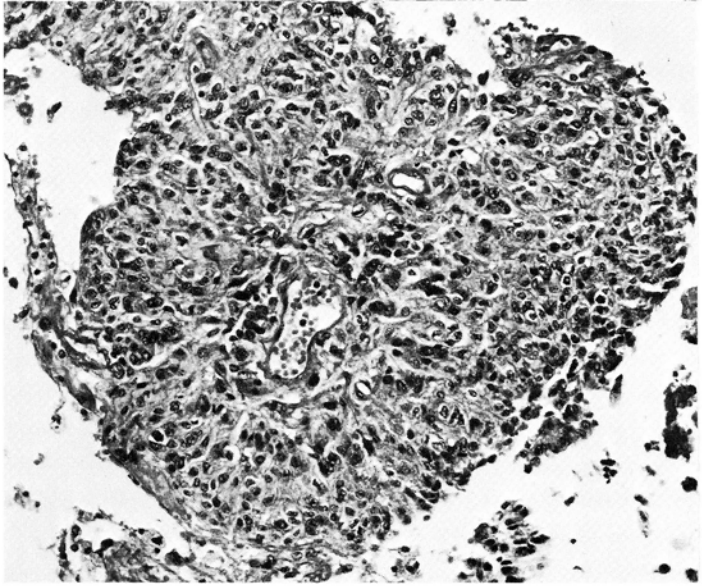

Fig. 6—Papillary arrangement of irregular and hyperchromatic tumor cells to form several layers around a thin-walled blood vessel. This papillary pattern is almost invariably associated with malignant meningiomas. H & E x 160.

certain degree from the films. Now I have a question to the radiologist. There is a smaller group of meningiomas *en plaque* which behave like an iceberg, where most of the tumor is outside the cranial cavity, or rather the cranial vault, some in the orbit, some in the nasal cavity, and some in the middle ear. The pathologist sometimes erroneously diagnose it as a chemodectoma. Are there radiological signs to make a tentative diagnosis of such a meningioma *en plaque*?

Dr. Peterson: My experience with the meningioma *en plaque* is that you don't see much on the angiogram other than some displacement and usually not as much displacement as you would like to have. There are usually no tumor vessels and the tumor intracranially is relatively flat so there isn't a lot of shift; this is a tough diagnosis to make unless there is a bone lesion, but angiographically it is a poor one.

Kenneth M. Earle, M.D., Washington, D.C.: We have been frequently impressed with the discrepancy between the histological criteria of malignancy in a number of meningiomas and the subsequent behavior of the tumor. In some cases where the tumor appeared histologically benign, there has been rather rapid recurrence and in other cases where we have had many mitoses and evidence of invasion, the tumor has gone along quite well. In trying to study why this is so, we have uncovered a number of reports; Frazier and Grant very carefully documented their 240 cases of meningioma, very much like Cushing had, with elaborate follow-up. Using Dr. Rubinstein's classifications we set out to see if these various adjectives really did tell us much about the prognosis of the tumor, when we were through we had a lot of statistical figures which showed only that the location of the tumor seemed to be a greater indication of its behavior than did the histological features, with two exceptions: One was that the angioblastic group seemed to be a bit more aggressive, as has always been pointed out, and the other that a few of the tumors were obviously sarcomatous from the outset, recurred very rapidly and frequently went to regional nodes. The meningioma that is sarcomatous is no more than one or two percent of what you see and yet they constitute one out of five of those that are sent to the AFIP. Even Cushing's series tend to show that the numerous varieties in which he divided meningiomas did not predict the prognosis. If you look over his table of 300 and some meningiomas, the histology was not as great an indication as was the location of the tumor. We very much like to know the location and we are reluctant to make an absolute prognosis upon the histological criteria alone.

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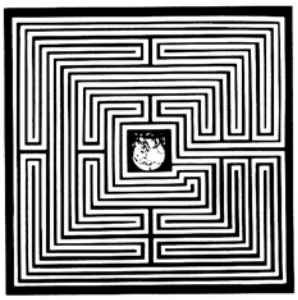


4. *Primary Tumor of the Reticulum-Cell Sarcoma (Microglioma) Group*

Contributed by **L. I. Gottlieb, M.D., W. W. Copeland, M.D.** and **W. C. Williams, M.D.**
Salt Lake City, Utah

THE PATIENT was a 27-year old man in January, 1970, when he complained of headaches of six weeks duration, and slurred speech and blurred vision of a few days duration. On examination there was severe papilledema, left-sided dysmetria and faint nystagmus in left and upward gaze; all reflexes were normal.

Dr. Peterson: A right carotid arteriogram with two films in the arterial phase demonstrate a modest shift of the anterior cerebral vessels to the left, the shift being a little more marked proximally. There is possible slight lateral displacement of the middle cerebral vessels. There is slight straightening of the usual undulations of the frontal polar branch of the anterior cerebral artery and perhaps a slight posterior displacement of the anterior cerebral as it curves around the anterior part of the corpus callosum. The anterior, larger division of the middle cerebral group in the position of the so-called candelabra vessel or fronto-parietal branch may be elevated slightly in its position in the anterior part of the sylvian fissure. No tumor vessels are recognizable. The injection was in the common carotid artery and there is filling of both the external and internal carotid vessels. The lenticulostriates are partially visualized and may be shifted slightly posteriorly.

The findings are suggestive of a mass lesion in the frontal lobe on the right side medially, inferiorly and extending posteriorly into the anterior part of the temporal lobe. A likely probability would be an astrocytoma which is infiltrating the frontal and temporal lobes medially. Another, much less common, avascular lesion would be a reticulum cell sarcoma.

Dr. Peterson's impression: Infiltrating, avascular, low-grade ASTROCYTOMA in the right frontal and temporal area.

Roentgenologic impressions submitted by mail:

Astrocytoma	28
Third ventricle tumor (cyst)	24
Glioma with hydrocephalus	10
Glioma (frontal, temporal, suprasylvian, thalamic, hippocampal, of basal ganglia, corpus callosum)	31
Others	21

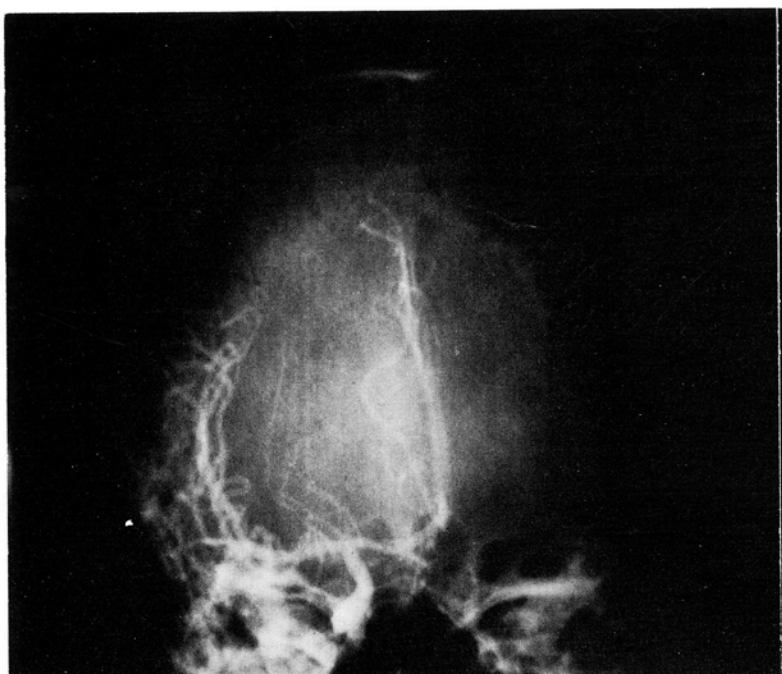
Dr. Peterson: Many radiologists thought of an astrocytoma in this area, which would be my first impression also. Unless it was felt that there was a midline mass which perhaps was causing hydrocephalus and the rounding of that anterior cerebral artery. I don't know how else to explain a third ventricle tumor, but I am not too much impressed with that rounding. Hydrocephalus isn't too impressive to me; otherwise, glioma is all right. Basal ganglia, they can be involved in this location. The corpus callosum is involved very often, so it is easy to throw in the corpus callosum most any time.

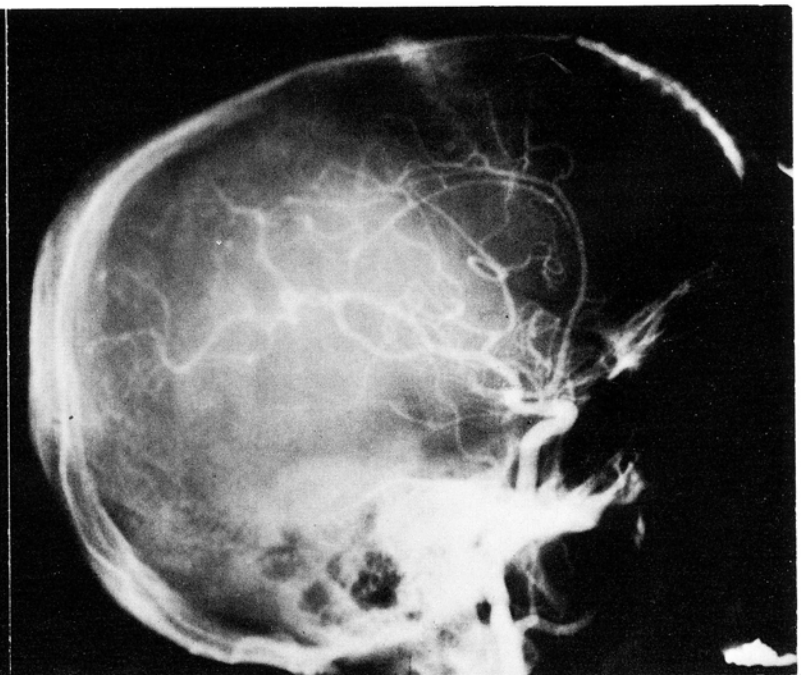
Dr. Regato: Drs. L. O. Martinez and J. Seldon, of Miami, offered also an impression of astrocytoma. Dr. T. O. Gabrielsen of Ann Arbor, preferred to call it a low grade glioma with extension from right frontal to left frontal lobe through the corpus callosum.

Operative findings: This patients ventriculogram showed no air in the right lateral ventricle. The isotope encephalogram showed increased activity over an area 4 cm in

Fig. 1—Right carotid arteriogram showing shift of anterior cerebral vessels to the left.

Fig. 2—Right carotid arteriogram showing straightening of the undulations of the frontal polar branch of the anterior cerebral artery.





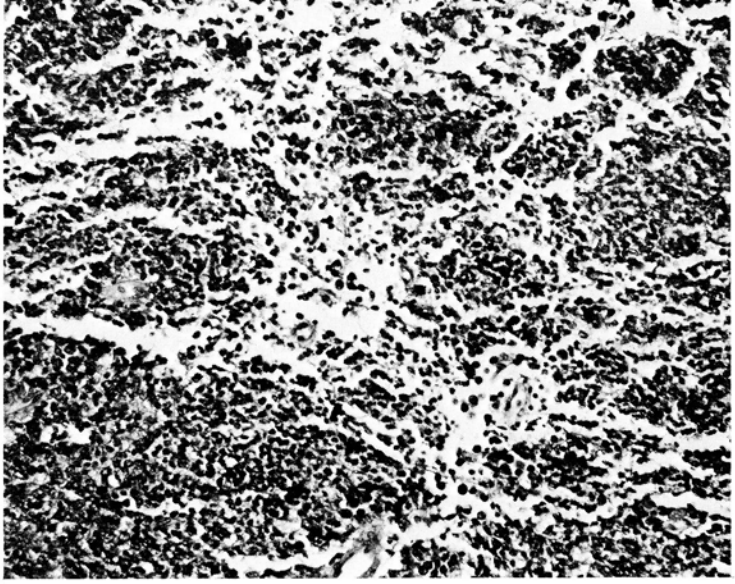


Fig. 3—Low power at periphery of the tumor, showing darkly staining cells arranged in small groups, often surrounding blood vessels. H & E x 120.

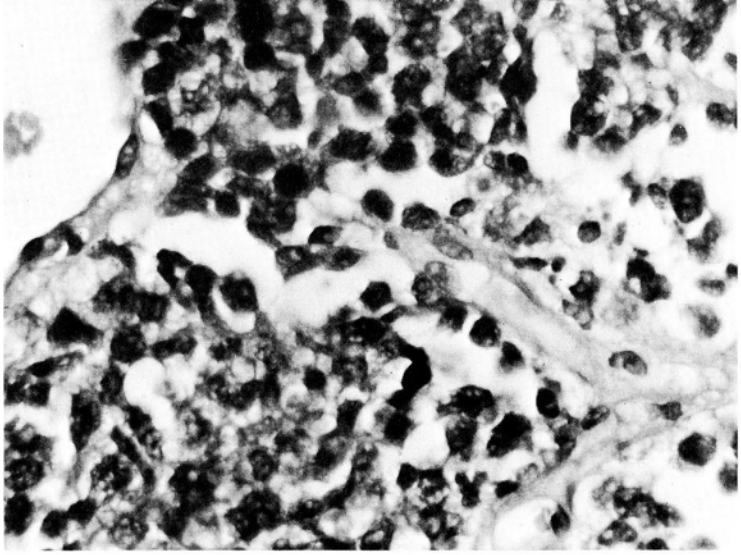


Fig. 4—Tumor cells forming a thick collar around a blood vessel (lumen at left upper corner). They have prominent nuclei with a dusky nucleoplasm, and often well-define nuclear membranes and a very ill-defined cytoplasm. H & E x 480.

diameter at the midline. On January 7, 1970, a craniotomy was done along the sagittal suture; a small opening was made in the corpus callosum and "as much as possible" of the tumor was removed for decompression.

Dr. Rubinstein: These are fragments of highly cellular tumor, which, in the more compact areas, demonstrates a monotonous histologic picture. The nuclei are closely packed without any distinctive architectural pattern. In some fragments, the tumor cells are more loosely arranged, and, in places, a perivascular arrangement around thin-walled vessels can be discerned. At its periphery the tumor has no capsule, but is still relatively well demarcated from the adjacent brain, although discrete cellular invasion is clearly demonstrated.

Under high power, the tumor cells present mainly as nuclei, the cytoplasm being extremely ill-defined. In the more central and homogeneous areas, the cells show as pale nuclei with an "empty" nucleoplasm and a fine delicate nuclear membrane. These appearances may partly be due to inadequate fixation. At the periphery of the fragments, where the fixation is better, the nuclei show a more dusky nucleoplasm, but the nuclear membrane remains well defined. A slight degree of pleomorphism is present, the nuclei being usually oval or round, but occasionally bilobed or notched. Mitotic figures are fairly frequent, and necrotic cells are also present. Occasionally, at the periphery of the tumor, neoplastic cells are arranged in small distinct groups, again with a tendency to arrange themselves around blood vessels.

The PTAH stain does not reveal any obvious cell processes or fibers in the central areas, but cells at the periphery are found to be closely associated with a fibrillary background. This is closely contiguous to the obvious fibrillary gliosis which is present in the adjacent brain. Neuroglial fibers are not found in the more compactly cellular central parts of the fragments.

The microscopic features do not suggest a primary neuroectodermal neoplasm. The differential diagnosis essentially lies between a metastatic tumor and a neoplasm belonging to the lymphoma group, most likely of the reticulum-cell sarcoma-microglioma group. It is important to know whether a primary tumor was found elsewhere in the body of this patient, and the possibility of a metastatic melanoma should be kept in mind.

If a metastatic tumor is excluded, the diagnosis of tumor of the reticulum-cell sarcoma-microglioma must come to the fore. The reticulin preparation supports this diagnosis, as it demonstrates a moderately abundant reticulin network throughout the tumor, and, in a few places, an enlargement of the perivascular spaces with the typical "hoop-like" arrangement of increased reticulin fibers in the distended Virchow-Robin spaces, characteristic of microgliomatosis.

Silver impregnations on wet tissues are, however, essential to determine whether the cells are of microglial origin, or of the more primitive reticulum-cell sarcoma kind.

To exclude a metastatic tumor, a request was made for any possible lesion previously removed from this patient. It transpired that a pigmented lesion of the skin, and cervical and axillary lymph nodes had been excised in 1959. The slide from the skin lesion showed a compound benign nevus, without any suggestion of malignancy, quite different from the subsequently removed brain tumor. The lymph nodes showed reactive follicular hyperplasia only.

Dr. Rubinstein's diagnosis: PRIMARY TUMOR OF THE RETICULUM-CELL SARCOMA-MICROGLIOMA GROUP.

Histopathologic diagnoses submitted by mail:

Reticulum-cell sarcoma	27
Lymphoepithelioma (transitional cell)	21
Microgliomatosis	17
Ependymoma (anaplastic, malignant)	17
Glioma	12
Pinealoma	9
Neuroblastoma	8
Various sarcomas	16
*Astrocytoma	9
Others	27

Dr. Rubinstein: Quite a large number of pathologists came to the same conclusion without benefit of special stains. There is a minority group in favor of a tumor of the glioma group, this is understandable and certainly one of the differential diagnosis from histological point of view. Ependymoma I would not have seriously entertained. Apart from the very vascular arrangement I see no resemblance to ependymoma; ependymomas are tumors which I can recognize fairly easily, although, of course, my criteria are not quite those as shared by others. I think in certain areas an undifferentiated anaplastic astrocytoma is suggested. Neuroblastoma is worth thinking about in

tumors that have no distinctive cytological features and consist mainly of cells which might be of neuroepithelial origin.

Dr. Regato: Dr. R. M. Sherwin, of Fort Huachuca, Arizona, also made a diagnosis of malignant lymphoma, stem-cell type. Dr. P. B. Putong, of Chicago, preferred microgliomatosis. Drs. Magda and John Kepes, of Kansas City, Kansas, suggested a variant of medulloblastoma. Drs. J. B. Frerichs and F. P. Bornstein, of El Paso, suspected it to be a metastasis from a pharyngeal tumor of the lymphoepithelioma type. Dr. H. M. Zimmerman, of New York, requested an unstained slide and reported that a Wilder stain revealed a complex mesodermal stroma which rules out glioma; he felt that the cells strongly suggested a metastatic epithelial neoplasm. Dr. S. W. Kowierschke, of Bryan, Texas, offered a diagnosis of cellular ependymoma. Dr. J. Cabanne, of Dijon, France, suggested ependymoglioma.

Subsequent history: From January 21st to February 26th, 1970, the patient was irradiated through two lateral cranial fields including the entire brain: a dose of 5200 rads in 34 days, in the sagittal midplane, was calculated to have been received. In August, 1970, he was reported in good condition.

Dr. French: Clinically, we have too much data to make a clear decision. I read the symptoms and I thought this probably was a lesion of the left posterior fossa. I could get this mixed up with right frontal lesion; a right frontal and a left cerebellar are sometimes difficult to distinguish. It is not difficult in the reverse, a left frontal and right cerebellar are easy because the left frontal gives an aphasia. But this gentleman has slurred speech which suggests to me something in the brain stem or in the twelfth nerve area, not a cortical function. I probably would have thought clinically this patient had a left posterior fossa lesion. I would have done the routine skull films but if they were normal, we might have done an isotope scan, although our results of isotope scans in the posterior fossa are not nearly as accurate as they are in the anterior or middle fossa. This was a good surgical approach to the lesion. I don't think that I could tell what lesion it was from the angiogram. The biopsy showed obviously abnormal tissue and histologically suggested reticulum-cell sarcoma. I would worry about a microgliomatosis and I would wonder about whether this were indeed a right frontal and also had other lesions. If I were handling this case, after removing the frontal lesion, we would probably irradiate on the basis that this may be a multiple lesion and that we had not totally removed the lesion. I would think the gentleman's prognosis was quite poor overall.

L. Gottlieb, M. D., Salt Lake City, Utah: The patient was seen about a week ago and is perfectly well. A postoperative scan was performed in March and there was no evidence of tumor at the time. The patient comes in to be seen and then doesn't wait to get his scan, so we haven't been able to get a scan since that time. He has had personality changes following the surgery rather than before.

L. Lowbeer, M. D., Tulsa, Oklahoma: Recently I was consulted on a 50 year old man who had been operated in New Mexico for a tumor which developed readily; he was operated upon and there was a deep seated neoplasm found which was inoperable and a needle biopsy was performed from which no diagnosis was made other than an undifferentiated neoplasm. Subsequently the patient was irradiated and all his symptoms disappeared miraculously. But five months later he developed a large tumor of the testicle which was removed and showed a typical reticulum-cell sarcoma. When the sections were then reviewed from New Mexico, they also turned out to be reticulum-cell sarcoma. The symptoms then reappeared and the patient died a year later. The irradiation had a very unfortunate and unforseen effect—he lost his hair and the pathologist in that hospital refused to do an autopsy because it would show on the head!

Dr. Rubinstein: There is increasing evidence that this tumor does respond to irradiation.

Dr. French: I would like to have Dr. Rubinstein tell us his philosophy of whether such a lesion is indeed primary in the brain and what the relationship of this type of lesion is to microgliomatosis?

Dr. Rubinstein: Tumors of the lymphoreticular system is wide spread throughout the body. With the exception of Hodgkin's disease, in which, in the last few years, there is convincing evidence that the multifocality of Hodgkin's disease may be the result of metastases in other lymphomas, the process arises on a multifocal basis. Lymphoid tissue is not present in the brain, but you do have tissue of the reticuloendothelial system, and they include microglial cells and the perivascular cells which are presumably of primitive reticular origin, both in the perivascular spaces and in the leptomeninges. So that is the tissue in the central nervous system which may give rise to tumors of the reticuloendothelial system. There is no reason why a tumor of this general group should not begin within the central nervous system and then appear elsewhere by a process which I believe to be multifocal neoplasia, rather than metastatic. You could in fact call all of these tumors malignant lymphoma, some of which may start in the lymph node, in the bone marrow, in the spleen, and some of them might start within the central nervous system; a proportion of these, in due course, might show evidence of deposits elsewhere. From the practical point of view, there are two different patterns and they are well recognized: One group shows the pattern of reticulum-cell sarcoma or lymphosarcoma arising in the body and finally tending to form deposits usually over the spine, in the epidural space, over the dura; in the last few years we have seen a number of such cases with extensive infiltration of the leptomeninges, the cranial and the spinal nerve roots: you might call these primary somatic tumors of the lymphoreticular system with deposits within the central nervous system. And then there is another group of cases of which this seems to be one, in which the tumor occurs first within the central nervous system. The majority of these cases, by the time they come to post-mortem, show no evidence of deposits elsewhere, but a proportion of them do, I would estimate it roughly about half of them. In relation to microgliomatosis, I take a very conciliatory view of this semantic quarrel and for practical purposes regard reticulum-cell sarcoma and microglioma as virtually synonymous. It is my personal opinion that the majority of them are really deserving of the name microglioma. Many cells do impregnate positively for microglial cells, and therefore microglioma or microgliomatosis rather, which emphasizes the multifocality of this tumor, seems to be a good name. I would also admit that there are a few cases which have been examined carefully and which are truly reticulum-cell sarcomas. But the distinction I think is entirely semantic.

When you call this microglioma or microgliomatosis, or primary lymphoma of the brain, or reticuloendothelial sarcoma, or reticulum-cell sarcoma, you are certainly thinking along the same lines.

Dr. Regato: The matter of responsiveness to irradiation has been brought up and for semantics sake, I would like to say that responsiveness or radiosensitivity of a tumor, is, of course, a sine qua non circumstance for a tumor to be treated successfully by means of radiations. We have evidence that the radiosensitivity of tumors of the central nervous system varies considerably but, of course, a reticulum-cell sarcoma would be at the highest level of radiosensitivity. There is evidence that tumors of this sort when they are localized are not only responsive, but at the same time curable by means of radiations. The matter of success of radiotherapy, here as elsewhere, depends also on the extent of the lesion, the more or less important structures that the tumor might have already invaded or destroyed and often the extent of the surgical interference that has preceded the radiotherapy. If you assume that they are always multicentric, regional radiotherapy should always fail; in fact when these tumors originate in the upper air passages the proportion of successfully treated cases is rather high. It remains to be shown that what is usually assumed to be multicentric malignant tumors of the lymphoid structures are the same thing, or as we think, an entirely different bag of marbles.

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5. *Oligodendroglioma with Part Astrocytoma*

Contributed by **E. Reilly, M.D.** and **U. T. Slager, M.D.**, Downey, California

THE PATIENT was a 64-year old man in March, 1968, when he was hospitalized because of a right sided hemiplegia; there was a history of convulsions for 7 years previously. On examination there was slow speech, nystagmus to left, ataxia, positive Romberg but no papilledema; reflexes were normal.

Dr. Peterson: Carotid arteriograms are available in the early arterial phase. There is filling of both the internal and external carotid arteries. There is no displacement of the anterior cerebral vessels to the opposite side but there is slight depression of the anterior branches of the middle cerebral. There is a large zone of avascularity occupying the anterior half to two-thirds of the left frontal lobe with straightening of the branches of the anterior cerebral artery on the medial aspect of this lobe and straightening and stretching of some of the smaller branches of the middle cerebral on the lateral aspect of the frontal lobe. No tumor vessels are recognizable. A mass lesion in the frontal lobe is compatible with these findings.

The avascularity of the mass suggests a large, infiltrating, low-grade astrocytoma. One would expect more shift of the anterior cerebral artery for most cerebral lesions, such as reticulum cell sarcoma, although it is possible to have a lesion in both frontal lobes, which would thus counteract any displacement of the anterior cerebral artery. For this purpose a carotid angiogram on the opposite side would be helpful. Intracerebral hemorrhage will result in an avascular mass but should also cause displacement of the anterior cerebral artery.

Dr. Peterson's impression: Infiltrating, low-grade neoplastic process occupying a large part of the left frontal lobe, probably an ASTROCYTOMA.

Roentgenologic impressions submitted by mail:

Astrocytoma	30
Tumor (frontal, temporo-parietal, para-sagittal)	10
Oligodendroglioma	19
Hematoma, infarct, cyst	20
Could not care less!	1
Others	18

Dr. Peterson: Most favored an astrocytoma but I don't know how anybody could be that strong for an oligodendroglioma on the basis of the angiogram. Hematoma, infarct, cyst are all right. If you can locate a lesion from a radiologic standpoint you feel awfully good about it; many times you have nothing to go on and then you can understand why you would say you couldn't care less.

Dr. Regato: Drs. J. J. Senyszyn, of New York City, and J. Marshall, of Colorado Springs, also suggested frontal astrocytoma.

Operative findings: On May 28, 1968, a craniotomy was done: there was a nodular mass in the left frontal region which was removed in multiple fragments. In the aggregate the fragments measured 6 x 4 x 4 cm.

Dr. Rubinstein: These are multiple fragments of tissue, some of which show a characteristic histological picture. A regular pattern of moderate homogeneous cellularity is seen, in which sheets of uniform tumor cells are regularly partitioned by a delicate, highly vascular connective

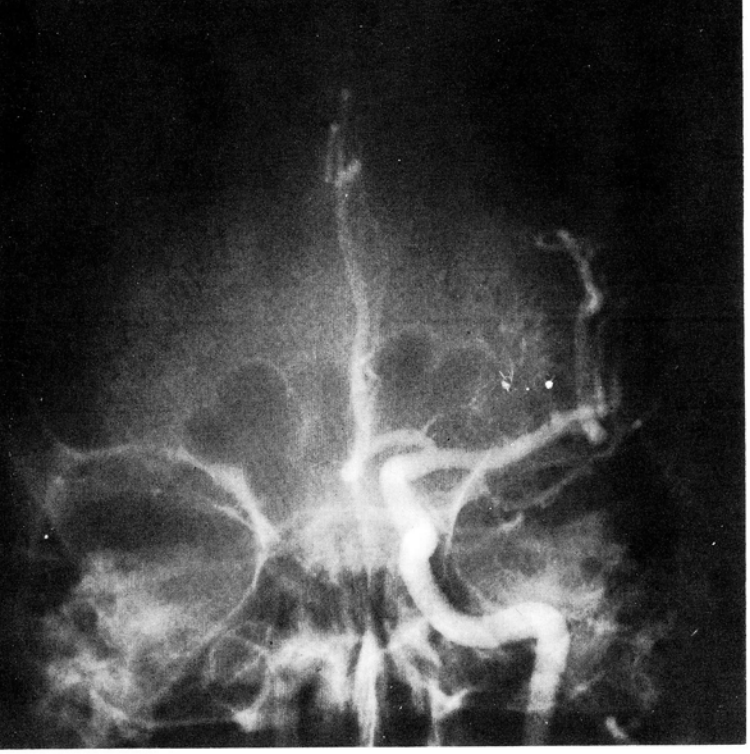


Fig. 1—Carotid arteriogram showing no lateral displacement of the anterior cerebral vessels.

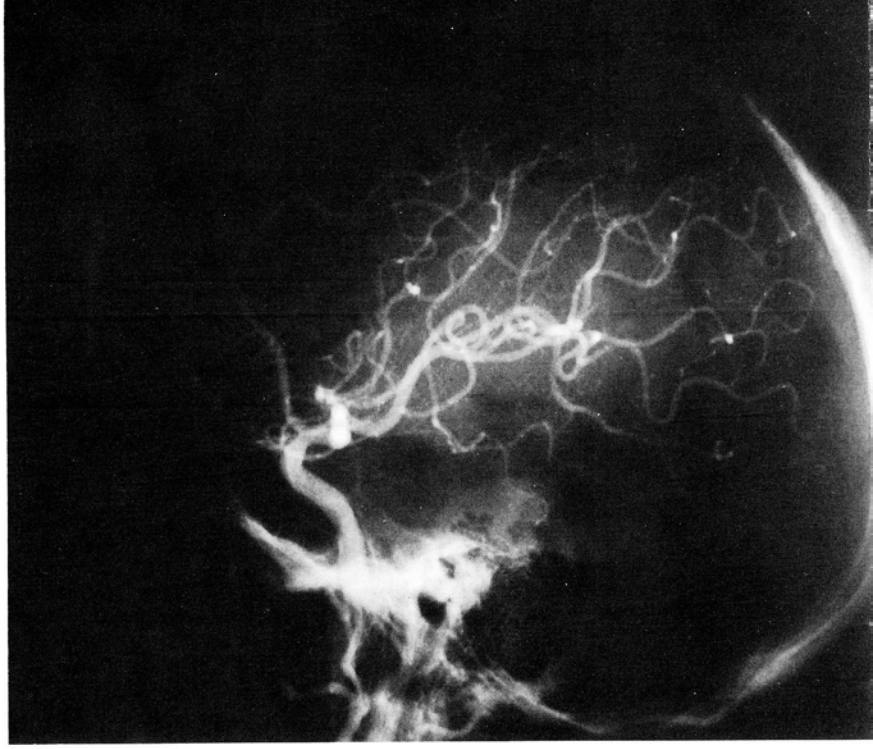


Fig. 2—Carotid arteriogram showing slight depression of anterior branches of the middle cerebral artery and large zone of avascularity of the frontal lobe anteriorly.

tissue stroma. The picture is that of a characteristic honeycomb pattern. The cells present as very regular, central spheroidal nuclei surrounded by a pale perinuclear halo. This separates the nuclei from a distinct regular cytoplasmic membrane, giving the cell a polyhedral shape. There are no atypical cells, or mitotic figures. The appearances are typical of an oligodendroglioma. In support of this diagnosis is the presence of calcospherite particles, which are discrete in places and very numerous and clustered in others. The PTAH confirms that the areas of pure oligodendroglioma are devoid of astrocytic fibers. In places, the tumor appears to abut on a relatively acellular connective tissue, presumably meningeal.

Many fragments contain brown hemosiderin and golden yellow hematoidin pigment. Areas of necrosis containing foamy macrophages are also found. Vascular granulation tissue is present nearby. These features are indicative of previous episodes of hemorrhage and necrosis either in or adjacent to the tumor.

In addition, adjacent to these foci of old hemorrhage and necrosis, tumor cells are intermingled in places with large gemistocytic astrocytes. Their significance is not absolutely clear cut. They are in close proximity to blood pigment-containing macrophages and to fine capillaries showing calcification of their walls. In a number of places too, these large astrocytes appear to contain blood pigment. They could therefore conceivably be reactive to a past episode of hemorrhagic infarction. However, their unusual numbers, their arrangement in compact masses, and, in places, their close admixture with clearly oligodendroglial tumor cells invite the definite suspicion that they too might be neoplastic. This tumor is then primarily an oligodendroglioma, but I would also strongly suspect that part of it is astrocytomatous.

Dr. Rubinstein's diagnosis: OLIGODENDROGLIOMA, with mixed astrocytoma, with evidence of past hemorrhage and necrosis.

Histopathologic diagnoses submitted by mail:

Oligodendroglioma	112
Hematoma	6
Pituitary tumor	12
Metastatic carcinoma	3
*Astrocytoma	3
Others	18

Dr. Rubinstein: The vast majority of pathologists have agreed with the diagnosis of oligodendroglioma. The diagnosis of hematoma was caused by the evidence of previous hemorrhage and there is, in fact, quite a lot of granulation tissue with this tumor. The other diagnoses are interesting—pituitary tumor, presumably chromophobe adenoma; metastatic carcinoma, particularly a renal-cell type, may in some cases present differential diagnostic difficulties with oligodendroglioma. Certainly some pituitary tumors of diffuse type, the chromophobe adenoma of diffuse type may certainly mimic and place very closely to an oligodendroglioma.

Dr. Regato: Almost without exception and only with slight variations in spelling, the experts agreed on a diagnosis of oligodendroglioma.

Subsequent history: The patient did relatively well but in August, 1969, he was incontinent, could not walk and there was ventricular dilatation; because of this a ventriculo-atrial shunt with Pudenz valve was placed. He died on October 21, 1969. The autopsy revealed a cystic defect of the left frontal lobe; there were adjacent tumor nodules extending into the brain stem and cerebellum.

Dr. French: This 64 year old man had seizures of seven years duration; the duration of symptomatology is signnificant if it is of long duration. A very chronic tumor can give symptoms of short duration, but a malignant tumor seldom will give symptoms of long duration. This long duration means a more slowly growing lesion, probably involving the cortical or subcortical areas. He has a hemiplegia which means a fairly large surface lesion, or a small-

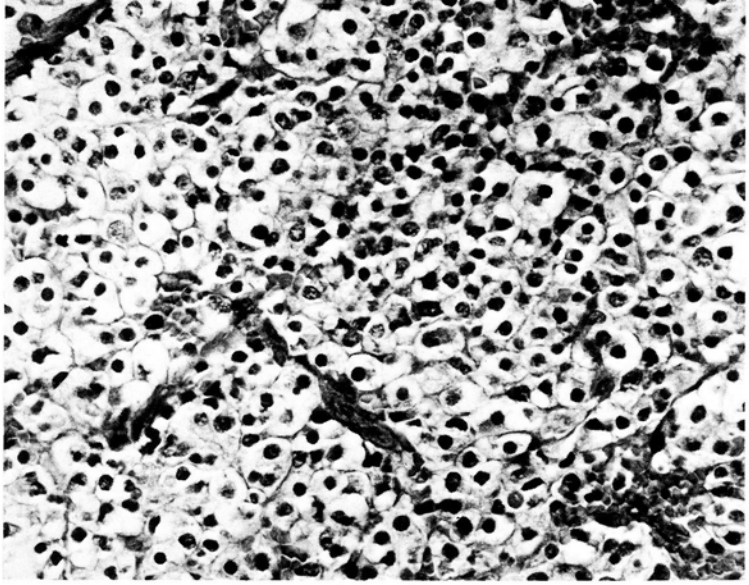


Fig. 3—Regular pattern of homogeneous cellularity in oligodendroglioma, with a characteristic honeycomb pattern. The tumor is intersected by a delicate vascular stroma. H & E x 300.

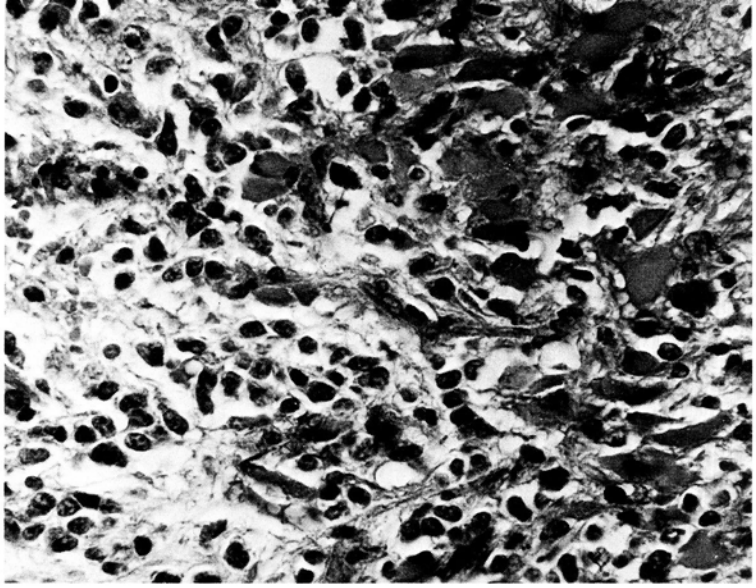
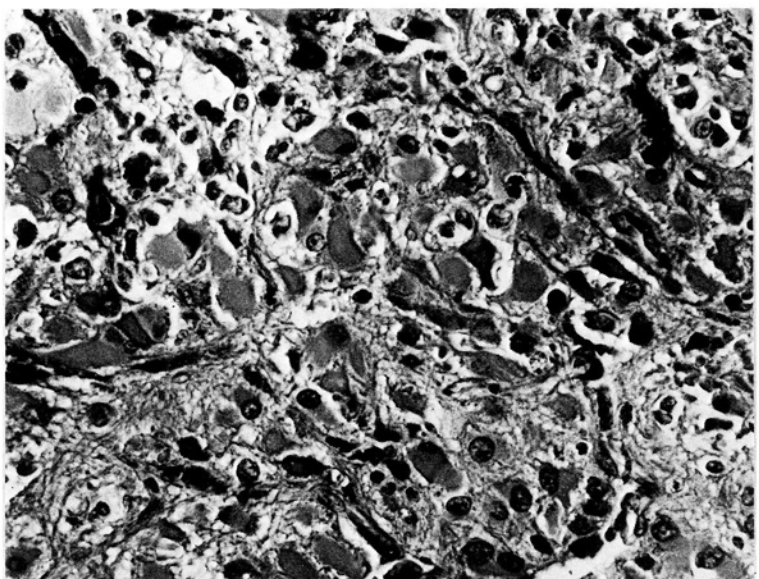


Fig. 4—Adjacent fields of oligodendroglioma (left) and gemistocytic astrocytoma (right) in this mixed oligodendroglioma and astrocytoma. H & E x 300.

er central lesion. Otherwise you wouldn't have a hemiplegia; you might have a paresis, but not a paralysis. With a combination of seizures and hemiplegia this is going to be a peripherally located lesion. I don't really know what slow speech is, so that sort of leaves me cold. With a patient like this we would probably get an isotope scan first. This lesion may scan or may not scan positively, because it is of low malignancy and it is a very slow growing lesion. From the angiographic picture I might be a little hung up, but I wouldn't be quite so positive of it as Dr. Peterson was. That anterior cerebral is very much in the midline and true these are pushed down; I probably would then do an air study. You are going to say you're doing scanning, angiograms, air—you're a typical neurosuregeon. That's right! But by that time I pretty well know where this lesion is. I would turn a craniotomy flap, come down on the tumor, would remove as much of it as possible, recognizing that it is an extremely large lesion, that the patient is 64 years of age, with a long history, and that the probability of removing this lesion totally is very remote. This tumor probably had hit the ventricular surface and it will go along the sub-ventricular area, it simply isn't possible to remove all of it. Would we irradiate a patient like this? I'd say no. What I meant to do, Dr. del Regato, is to ask you whether or not you thought radiations would help this patient.

Fig. 5—Focus of pure gemistocytic astrocytoma in this tumor, which was largely oligodendrogliomatous. Some of the smaller capillary blood vessels show calcification of their walls. H & E x 300.



Dr. Regato: In most instances of brain tumors there is the question of whether or not you know that tumor has been left behind. When you know that to be the case the patient has nothing to lose and radiotherapy can be carried out skillfully, giving the patient the benefit of our doubts and of our ignorance. It is difficult to predict the individual response and result. A great deal depends not only on the tumor response but also on the degree of tumor infiltration and destruction and the extent of the surgical interference. These are the factors that really decide. We have patients who were paraplegic after operation and having received radiotherapy have remained well for several years, and improved, but there is no possibility of restituting sight when this resulted from the operation. This week I saw a young lady whom we irradiated, in 1957, at the request of her neurosurgeon, when she was 8 years old, for a recurrent astrocytoma with extension to the hypothalamus (PCH 57-648). She has remained a mentally retarded child, as she was before irradiation, has mild seizures, has recovered her hair and is well adjusted with no sign of tumor 13 years later. Oligodendrogliomas develop so slowly that one would have to follow them for a lifetime before one is sure that they have been controlled.

Perhaps this is the best place, Dr. French, for me to ask you this question. There used to be a time when the abdominal and gynecological surgeon would come out of the operating room with the statement, 'I removed as much of it as I could.' Today no abdominal surgeon will feel proud of such a statement. If he sees a disease that is beyond his means he will take a biopsy and withdraw modestly. This is not the case in neurosurgery. The neurosurgeon takes pride in not only removing with his fingers, but sucking out as much tumor as he can. In the process I am certain that some damage may be inflicted to the patient. If the lesion is beyond curability by means of surgery wouldn't it be better to simply biopsy and withdraw?

Dr. French: This is very easy to answer. You would never hear me say that I removed as much of the tumor as I could. I would say that I removed the grossly visible tumor or that I subtotally removed the tumor. I have the same criticism that Dr. del Regato has on this. As far as the philosophy of biopsying the tumor and moving out, it has been proved many years ago the immediate mortality is extremely high, and immediate morbidity is high

compared to the subtotal removal of the lesion. I appreciate that it is a greater operative procedure, but in the long run, or in the short run, the patient is better off as far as morbidity and mortality. Very few surgeons who have an interest in cancer, will do this type of biopsy with a needle or with an open biopsy and no further. It is much better, with all of them, even if it is a patient with glioblastoma multiforme, to do a wide resection of the lesion, not going into viable tissue so that you aggravate the neurological loss, but stopping ahead of that.

U. Slager, M.D., Downey, California: The neurosurgeon who did the original operation in this case felt very sure that he had removed the entire tumor. When it recurred a year later in the posterior fossa, mostly in the cerebellum and fourth ventricle, and when we saw the histology of it, he was convinced that there were two separate primaries. Now I don't know whether Dr. Rubinstein saw the autopsy slides or not, but they do show a fairly different pattern from the original and one of the questions we had was how many times do oligodendrogliomas that look almost pure as this one did, really recur as either a mixed malignant glioma or with a superimposed glioblastoma component; is this a recurrence? How often do we see these types of tumors behaving like this?

Dr. Rubinstein: There are two ways of answering your question. First, in regard to this particular case. I made my diagnosis, showing a diffuse tumor, in the original specimen; in my opinion, there was already a mixed tumor there. If you ask me how frequently are oligodendrogliomas pure, I would say they are rather rarely pure. The majority, in fact, have mixed elements and a number of them, one has to render a diagnosis of mixed astrocytoma and oligodendroglioma; you see very clear cut contiguous areas of astrocytoma and oligo side by side. There are some of them, probably a minority, that are really pure oligodendrogliomas. Even in those more pure oligodendrogliomas you often see a mixed cell population. If this is true, then you would expect that when recurrence takes place quite a high proportion either show a mixed picture or the final common pathway, so to speak, of the glioblasto-multiforme. Now as to whether or not this tumor was totally removed. It is impossible for the pathologist to make such a statement on fragments of the tumor. It may be possible to make this kind of presumptive statement if the neurosurgeon is careful to send to the pathologist all the pieces he removed. Even if you do use a sucker extensively, these pieces are still worth collecting and should be sent to the pathologist; the more tissue he has the better his diagnostic skill is going to be. In the absence of information, whether there were bits taken from the margins or the bed of the tumor, I cannot say whether a tumor was entirely removed. Occasionally in a frontal tumor, or in a very posterior tumor, the surgeon practices, or used to practice, a lobectomy. Then you can actually cut the margin of the resection and really see whether or not the tumor has been entirely removed. When recurrences take place it is reasonable, I think, to conclude that recurrence consist essentially in a further activation of a neoplastic field, as a result of which, after certain time, the residual field now becomes neoplastic.

Dr. Peterson: I think that the decision as to what is to be done when a patient comes in with a neurological problem is up to the clinician, it shouldn't be made by a radiologist. A radiologist might be consulted and he might indicate what he can do but the ultimate decision is up to the clinician. As radiologists we are gaining great ability to do procedures, but I think it is time now, that we have had enough experience to call a halt on this tremendous number of procedures that are done. Let's think a little more about how much we really need. I doubt if we can, as you do in laboratory medicine, where twenty-five procedures are run routinely on a sample of blood, and you get twenty-five answers that you don't want to know. These procedures require personalized decisions. Let's say we have made a diagnosis of meningioma on an angiogram. Do we need a scan? A scan costs $80.00 to $100.00—what is it good for? We have the diagnosis and the surgeon has what he needs to know. Let's quit at some point. There are problems where you need to keep on going, but again the clinician has to decide in consultation with the radiologist.

S. Black, M. D., Columbia, Missouri: I agree with Dr. French that the best way to treat some of these gliomas is by a wide internal decompression compatible with no further loss of neurological function. I did not understand the cause of the blindness of the patient discussed.

Dr. Regato: Over six years ago we irradiated a young lady, 18 years of age, for post-operative residual of a glioblastoma multiforme of the right lateral ventricle; she had paresis of the left upper and lower extremities, left facial paralysis and marked loss of vision particularly on the right side (PCH 64-684). We irradiated the entire brain to a total dose of about 5500 rads at the midplane in 54 days. Following her treatment she walked with braces. She has now married and performs all duties of a housewife without difficulty in spite of her hemiparesis which no longer requires braces. Her vision remains impaired; her discs appear normal but vision of the right eye is greatly limited laterally. It is probable that many of her symptoms are simply a result of the tumor but when we first saw her it was believed that some of them had worsened after operation. Her blindness is quite probably related to prolonged papilledema which is no longer present. I think that some of this extensive damage to the brain caused by the operative procedure might be avoided if the surgeon admits upon exploration that this is beyond him. There is the mistaken point of view that the radiotherapist would be better off if there is less tumor. Actually it takes just as much to cure any residual amount, no matter how microscopic, than it will take to treat the whole tumor.

Dr. French: If you have a third nerve paralysis, this is a localizing sign, but if you have papilledema and then development of the third nerve or sixth nerve palsy, this is not localizing. In other words, it is the sequence of development of symptoms that is important. In this case the symptomatology is a little bit unusual. We mentioned seizures, the hemiplegia, but this patient also had nystagmus to the left, ataxia, positive Romberg. I would think the patient had a lesion in the posterior fossa. The trouble is that the patient had a hemiplegia ahead of time, I gather.

Dr. U. Slager: The patient originally came in with a hemiplegia. This resolved completely before the operation. I believe he probably had a hemorrhage into his tumor. The tumor was removed surgically and most of the symptoms mentioned occurred post-operatively within about eight months. I think we maybe condensed it a little too much.

Dr. Regato: I apologize for my part of the confusion, Dr. Slager.

Dr. Slager: The surgeon rather than the pathologist got confused a little.

J. Stern, M. D., El Paso, Texas: At the risk of having the roof fall in on us, I wonder whether someone here shouldn't mention an innocuous, non-destructive, inexpensive procedure which is useful in screening lesions of the anterior and middle cranial fossae: I'm referring to an electroencephalography.

Dr. French: The probabilities of an EEG being really focalizing and being of objective benefit to the surgeon at the time of surgery, as compared to angiography, is comparably low. In general we do not do electroencephalographic studies for that reason. We go more towards angiographic studies where we would find the site of origin, of vascularity and could do a better operative procedure.

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6. *Oligodendroglioma with Intense Desmoplastic Reaction*

Contributed by **John F. Wilson, M.D., V. R. Condon, M.D.** and **L. F. Shurtliff, M.D.,**
Salt Lake City, Utah

THE PATIENT was a 3-year old girl in May, 1970, when she was hospitalized because of headaches, vomiting and fever; drowsiness had been noted for several weeks. Examination revealed a fluctuant mass, 3 cm in diameter, on the left side of the occipital region, there was blurring of the optic disks but no neurologic signs.

Dr. Peterson: A left carotid angiogram shows moderate displacement of the anterior cerebral vessels across the midline toward the right, more of a distal type of shift. There is a massive displacement of the middle cerebral vessels forward and superiorly and there is marked stretching of all the branches of the middle cerebral as well as the posterior cerebral. The entire posterior two-thirds of the cranial cavity shows relative avascularity with thinning and stretching of the surface vessels. The posterior communicating vessel is probably displaced downward moderately. There is considerable separation of the sutures. There is some thinning of the parietal bone posteriorly near the lambdoid suture but from this one projection it is not possible to determine whether this represents a lytic lesion in the bone or simply thinning of the calvarium from an underlying process. There are no tumor vessels.

The differential diagnosis would lie between a huge, perhaps cystic, astrocytoma or a brain abscess with a large amount of associated edema. The characteristic cockade vessels surrounding an abscess are not recognizable on the available films but might be present on later films and occasionally are also absent in patients with an abscess. The minimal amount of displacement of the anterior cerebral artery as contrasted to the extensive size of the lesion in the lateral view is difficult to explain. The brain scan shows one positive area which corresponds with the parietal region on the left side which is superiorly and somewhat peripherally located on this single scan and certainly it does not correspond with the massive size of the overall abnormality. There may be two other areas of somewhat increased activity on the scan but these might be explained on other bases.

In summary, this is a very extensive process involving the parietal, occipital and temporal lobes on the right side with stretching of vessels and no new vessels which because of its extreme size and evidences of rather acute pressure as demonstrated by the spreading of the sutures would probably be more compatible with an abscess with associated edema than with an astrocytoma. The question of actual bone involvement in the posterior parietal region would depend on more plain film studies of this area.

Dr. Peterson's impression: CYSTIC GLIOMA

Roentgenologic impressions submitted by mail:

Epidural, parieto-occipital abscess	27
Neuroblastoma	24
Medulloblastoma	13
Tumor (temporo-parietal, temporo-occipital, retro-intra-sylvian, aqueductal)	21
Inflammatory lesion	6
Others	35

Dr. Peterson: You see a number of radiologists favored abscess for the history suggests it and the lesion is so huge. I really don't know any explanation for neuroblastoma, we would need to see some typical bone changes; they get marked separation of the sutures and enlargement of the calvarium due to extensive metastases in the dura and meningeal area, but not due to expansion of the brain itself, which must have taken place in this case to stretch these vessels as they are. Medulloblastoma is a possibility, but certainly wouldn't occur to me as a probability. Inflammatory lesion, that goes along with the abscess.

Dr. Regato: Dr. J. Lemon, of Denver, Dr. P. Roesler, of Colorado Springs, and Dr. P. Hodes, of Philadelphia, suspected a parietal abscess.

Operative findings: On May 13, 1970 a craniotomy was carried out. A large cystic lesion of the left parietal lobe was found: it measured 7 x 7 cm and had caused bone erosion: 58 cc of xanthochromic fluid were aspirated. The specimen weighed 55 grams; it measured 6.5 x 4.7 x 4 cm. The growth was soft and gray-pink in some areas, rubbery and gray-yellow in others.

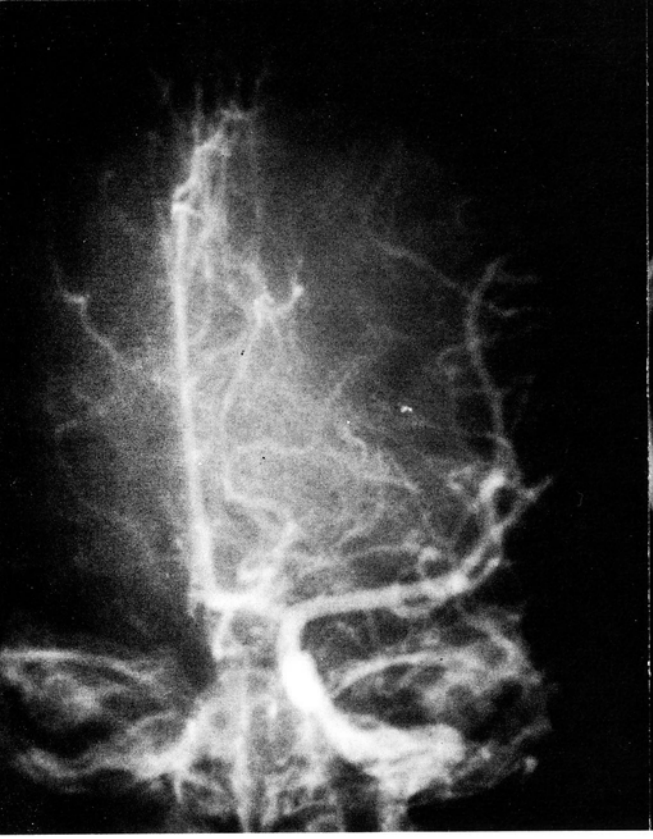


Fig. 1—Moderate displacement of the left anterior cerebral vessels toward the right across the midline.

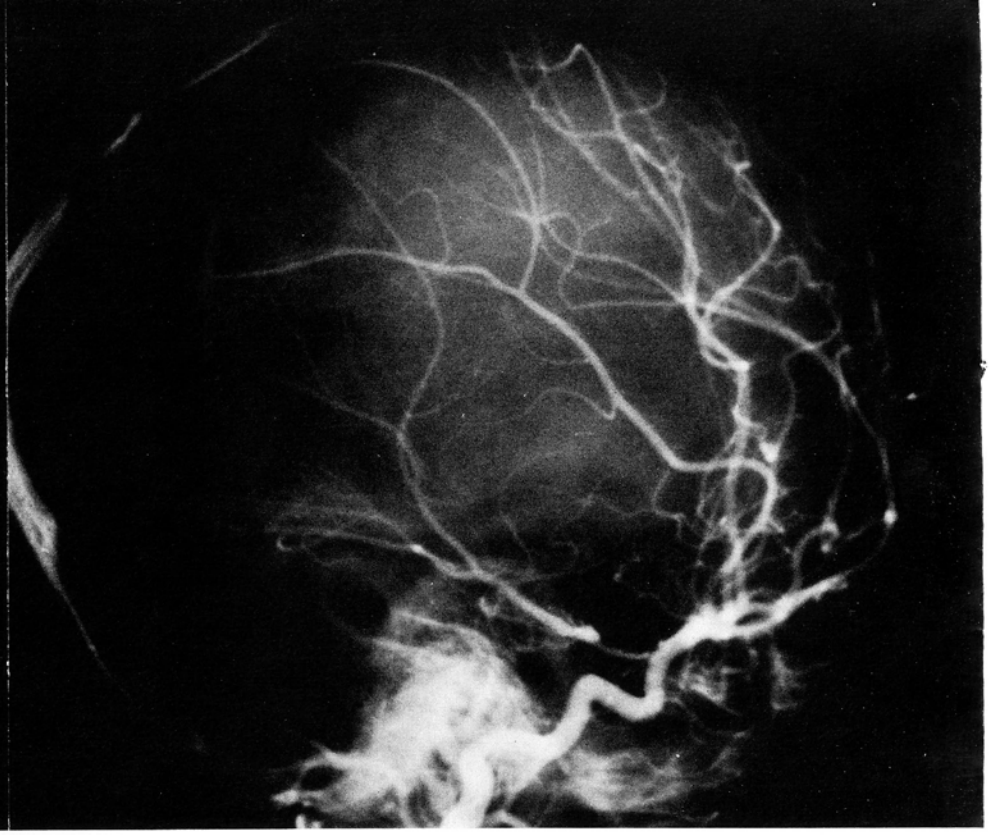


Fig. 2—Massive forward and superior displacement of the middle cerebral vessels and stretching of the branches of the middle and posterior cerebral.

Dr. Rubinstein: The fragments consist of tumor tissue which shows essentially two different patterns: The first type consists of moderately cellular homogeneous tumor with prominent spheroidal nuclei, frequently clear perinuclear halos and distinct cytoplastic membranes arranged in many fields in a typical "honey-comb" pattern. This results from their arrangements in nests intersected by a thin delicate vascular connective tissue stroma. In a few places, the stroma is somewhat more abundant and the perinuclear halos are less prominent, the tumor cells being arranged on a background of fine fibrillary material, even suggesting in places rosette formation. Nevertheless, the picture throughout is fairly uniform, and is classical for an oligodendroglioma. In a few places, the vascular network shows marked capillary endothelial proliferation.

The second type of tissue consists again of a fairly homogeneous arrangement of tumor cells, which are, however, separated by a very abundant, and in places relatively acellular, connective tissue stroma. This is demonstrated most convincingly with the reticulin preparation. The tumor cells are found either to lie singly amidst this very rich connective tissue, or to form small nests encompassed by it. In some areas the cells form elongated intersecting trabeculae, whose appearances very much mimic under the low power those of a fibroblastic tumor, such as a low grade fibrosarcoma.

The cytological features of the tumor cells showing the second pattern do not, however, differ greatly from those in the first. Careful examination under the high power demonstrates that, amidst darkly staining tumor cells, paler elongated cells with a clear nucleoplasm, a distinct nuclear membrane and slightly irregular outlines can be demonstrated. These are very numerous in places. Their appearance suggests that they are fibroblasts.

The reticulin preparations demonstrate not only the very abundant connective tissue stroma in the tissue of the second pattern but also the conspicuous vascular network in the tissue of the first. Two additional features should be noted for the interpretation of this curious tumor. First, the fragments of the tumor of the second pattern are sometimes seen to be distinctly separable from the adjoining brain parenchyma, and the periphery of the tumor at that site shows a tangential condensation of fibrous connective tissue along its surface, such as would be expected to occur when a neuroepithelial tumor invades the subarachnoid space and, as a result, stimulates a conspicuous fibrous connective tissue reaction. Second, there is one focus of oligodendrogliomatous tumor adjacent to a moderately cellular area which, in reticulin preparations, is found to contain not only very abundant connective tissue but also a residual spicule of bone.

The histological interpretation of this tumor must take into account its location, as described clinically. This patient is stated to have had an erosion of the left posterior parietal region, which is demonstrated radiologically. At craniotomy, a large cystic mass causing bony destruction was found arising from the left parietal lobe. The erosion of the bone was described as originating in the inner table. The tumor was underlying the dura and measured 9 cm in its greatest diameter. Furthermore, this 3-year old girl first presented clinically with a fluctuant mass on the left side of the occipital region.

The above description indicates that a tumor apparently arising in the brain had transgressed the dura, eroded the skull and presented onto the scalp. This is a very unusual behavior for a primary glioma. Yet the appearances of much of the tumor are quite typical of an oligodendroglioma aside from the extraordinary des-

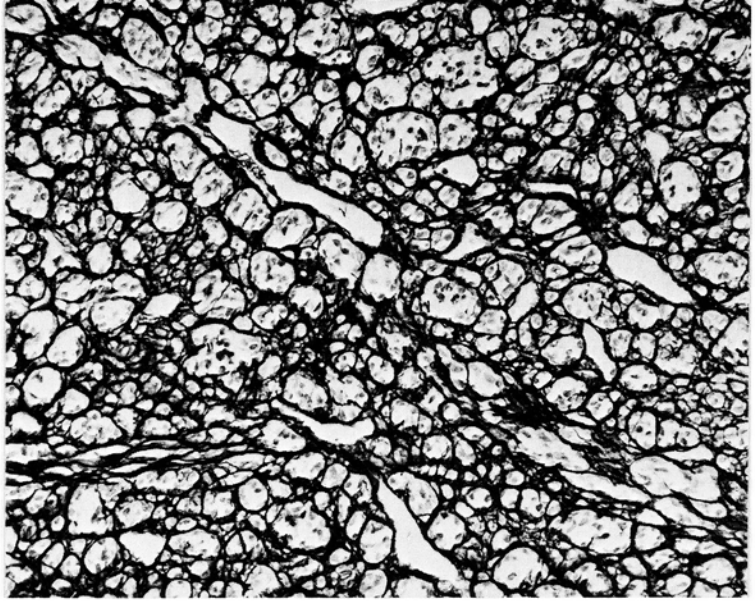


Fig. 3—Typical honeycomb pattern of oligodendroglioma with prominent perinuclear haloes, in tumor within cerebral substance. H & E x 300.

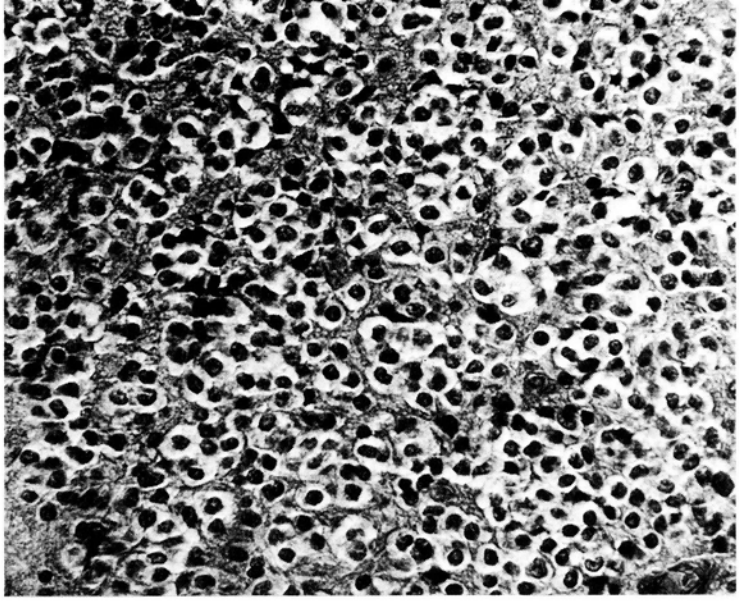


Fig. 4—Portion of tumor which had apparently transgressed the dura. Nests of oligodendroglial tumor cells are surrounded by a prominent connective tissue stroma. Gordon-Sweets' method for reticulin x 160.

moplastic reaction which is apparently present. The tumor showing the abundant connective tissue stroma does not appear to differ essentially in cytology from the intracerebral neoplasm. Furthermore, careful examination under the high power demonstrates that fibroblasts are present in abundance in the desmoplastic tumor. The most reasonable explanation therefore is that this is a primary oligodendroglioma, which, in this young child, grew spontaneously through the dura and into the bone, so that part of its mass became responsible for an intense desmoplastic reaction, the fibroblastic elements obviously arising from the dura, the periosteum, and the adjacent extracranial mesenchymal tissues. Such an event, extraordinary though it may be, would reasonably explain the curious "biphasic" microscopic appearances displayed by the tumor.

Dr. Rubinstein's diagnosis: OLIGODENDROGLIOMA of parieto-occipital region, transgressing dura and eroding parietal bone, with intense desmoplastic reaction.

Histopathologic diagnoses submitted by mail:

Oligodendroglioma	52
Ependymoma	24
Mixed glioma	16
Hemangioblastoma	12
Neuroblastoma	9
Medulloblastoma	9
*Astrocytoma	12
Others	29

Dr. Rubinstein: The pattern of the oligodendroglioma was obviously recognized by many pathologists in this case. I suppose that the "biphasic" pattern was responsible for the diagnosis of a mixed glioma. In certain areas the picture of rosettes or pseudorosettes formation might have suggested ependymoma. I would say that the rosettes here are not of the kind you do see in ependymomas, but I occasionally have seen such rosette arrangements in oligodendrogliomas. Neuroblastoma is another possibility, which I did entertain when I originally saw the preparation of this case, because the perinuclear halos

Fig. 5—Portion of oligodendroglioma outside the cerebral parenchyma, characterized by a pronounced desmoplastic reaction. Nests of oligodendroglioma tumor cells (lower half of photograph) are surrounded by a relatively acellular connective tissue stroma. In the upper half of the photograph, nests of tumor cells are very scanty, and the connective tissue extraordinarily abundant. H & E x 300.

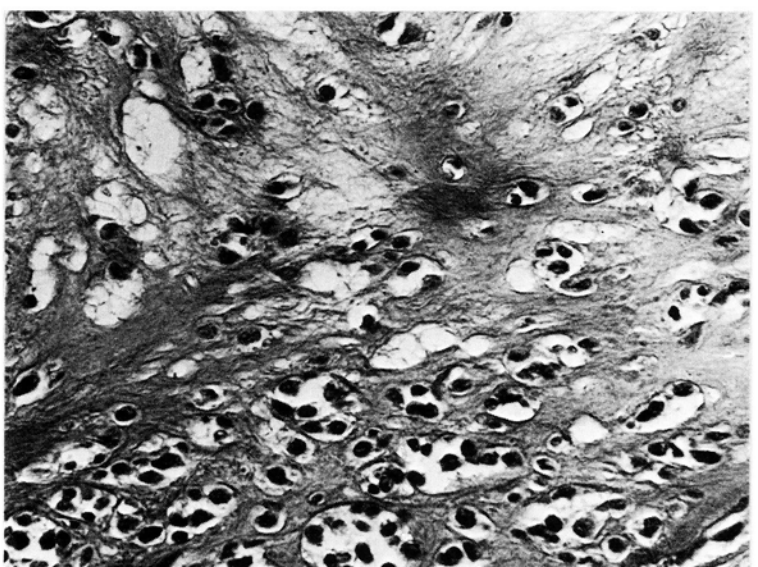
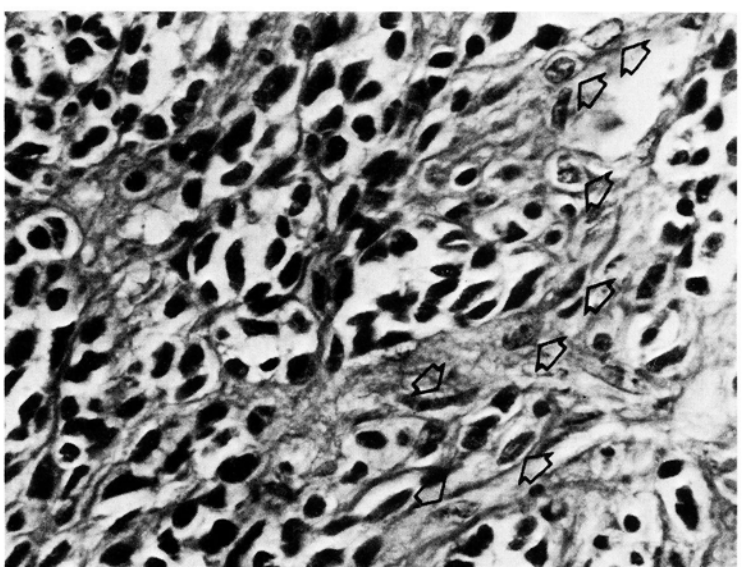


Fig. 6—High power of oligodendroglioma, with marked desmoplastic reaction. Amidst groups of darkly staining tumor cells, note pale elongated cells with a clear nucleoplasm and slightly irregular outlines (arrows). These cells, which are intimately related to connective tissue fibers, are interpreted as fibroblasts. H & E x 480.



were not very visible in the original section which was submitted to me, and the rosettes might well suggest a primary neuroblastoma. I entirely agree with Dr. Peterson's remarks on metastatic neuroblastoma, but there are very rare tumors in children that arise primarily in the central nervous system and that might be called neuroblastomas. It is the accepted convention to regard medulloblastoma as a primary cerebellar tumor; I suppose that the other features that I demonstrated are responsible for the suggestion that this might be a blood vessel tumor, a hemangioblastoma.

Dr. Regato: Dr. L. Lowbeer, of Tulsa, made a diagnosis of ependymoblastoma with oligodendroglial cell foci and questioned the possibility of this being a subependymal astrocytoma. Dr. W. J. Pepler, of Pretoria, offered a diagnosis of mixed glioma, oligodendroglioma with spongioblastoma. Dr. Samruay Shuangshoti, of Bangkok, preferred a mixed mesenchymal and neuroglial tumor, meningioma and glioma. Dr. H. M. Zimmerman, of New York, offered hemangioblastoma and oligodendroglioma.

Subsequent history: From May 25 to June 21, 1969 the patient was irradiated, receiving a calculated dose of 4000 rads in 26 days in "the region of the tumor". On July 7, 1970 she was reported to be doing well by Dr. Erickson.

Dr. French: This case was a bit confusing to me in that the patient had symptoms of short duration and had a fluctuant mass. I thought that it probably was some inflammatory lesion and I wondered if there was also redness and tenderness around it; one might aspirate it to see if it were an abscess. I've seen the angiogram and the huge porencephalic cyst in the occipital region bulging out with a hole through the bone and extending out a matter of 3, 4, or 5 centimeters at times. Other things that could occur would be a reticulum-cell sarcoma or hypernephroma. After doing an angiogram and an isotope scan, we would turn a craniotomy flap over this area and we would probably try to remove this lesion as extensively as we could, in the sense that we would attempt to do a total excision of it. I would suspect that this lesion might be moderately demarcated. I have seen lesions that were similar to this, oligodendrogliomas in young people which were well demarcated and in which event I would go along this line of cleavage and attempt to take this thing out.

Dr. Rubinstein: I have looked at the fragments very carefully and I must say many of them do show a very clear demarcation to adjacent tissue and this is both in the tissue of the first type, namely within the brain and also the tissue which seems to be desmoplastic. There is quite a good margin.

Dr. French: It surprises me that the fluid within the tumor was xanthochromic. Had this been bleeding? Is this why she had the temperature elevation? I would have tried to remove this tumor going along this line of demarcation. The patients I have run across have done reasonably well for a period of time, a matter of five years; we re-excise the lesion again in another five years, the patient eventually expiring of the lesion but doing so 15 years after the original diagnosis. It is hard for me to evaluate whether or not irradiation would be of benefit, but I tend not to do that at this age. It is a tough case.

J. Kepes, M.D., Kansas City, Kansas: This case could be very difficult if the round oligodendroglial cells were absent and only the spindle shaped cells, the captured cells with a clear halo would be present. A few years ago Dr. Zülch, in Germany, felt that maybe this group should be designated as a separate entity, the so-called polymorphous oligodendroglioma and they even convened a symposium, I think in Hamburg, to discuss it. I think the upshot was that this is indeed a form of oligodendroglioma and that it can give differential diagnostic problems. It wouldn't have surprised me too much if indeed this had invaded the bone because oligodendrogliomas occasionally do that. In Austria, Jellinger and Minauf published not long ago a case of oligodendroglioma in the spine involving the vertebrae rather extensively. Finally, Dr. Svoboda in the late 1950's published what I think is the earliest case of oligodendroglioma, in a 6 week old infant. I think in general when these tumors occur in the very young, they are somewhat different from the same tumor in an older age group and this is true for ependymomas, meningiomas and other neoplasms also.

J. F. Wilson, M. D., Salt Lake City, Utah: Despite the brevity of the patient's symptoms, the clinicians felt that this lesion was really chronic in nature. Dr. LaVerne Erickson was successful in completely removing this tumor. It was very well delineated from the surrounding brain tissue and had a very thin type of a pial membrane. Fluid from inside the tumor was not xanthochromic, but was clear and had, as I recall, around 2-1/2 grams percent of protein. We were impressed grossly by the marked variability and particularly the desmoplasia of this tumor. Dr. Erickson had seen her as recently as three weeks ago. She has no neurologic deficit, is doing very well, with no sign of recurrence.

L. Finney, M.D., Amarillo, Texas: If one did not live in the Continental United States and lived in an area where echinococcal disease is prevalent, the angiographic pattern would be almost pathognomonic of an echinococcal cyst in the parietal lobe.

Dr. Regato: I would like to ask this question from Dr. Rubinstein: There is, in the field of malignant tumors, some examples of tumors that are apparently combined, carcinosarcomas, and baso-squamous carcinomas, but these kind of things have been discredited for the most part as not being really true entities. In the field of neuropathology, this seems to be epidemic, you have a great deal of them. We have had some experiences with tumors that have been operated upon and then the patient was re-explored for some symptoms, no evidence of tumor was found, blind biopsies were taken just as a matter of thoroughness and then another tumor was reported, usually an astrocytoma. Is it possible that some of these other apparently combined features, morphologically interpreted as a tumor, are really reactive?

Dr. Rubinstein: The situation is a little easier in neuropathology, because one does have staining methods that, in reliable hands, make quite good distinction between mesodermal tissue, on one hand, and neuroglial tissue on another. These methods don't exist in general pathology. You can see reticulin and collagen, but there is no special tinctorial stain that will help you to identify epithelial cells. When you come to tumors of mixed cell populations, if you take tumors of the glioma group, it is generally accepted that these cells are often composed of mixed cells, of a mixed cell population which includes both oligodendroglial cells and astrocytomatous cells, and this has been confirmed extensively by experimental work of Dr. Zimmerman and his group and by others. We know from practical experience that mixed cell pop-

ulation within a neuroectodermal group is not infrequent, there is no difficulty in accepting this. This is no different than having, for instance, a carcinoma of the lung, which is partly squamoid and partially adenocarcinoma. The true mixed tumors, which you are concerned with, in which you have a mixture of mesodermal and neuroectodermal elements, I would say, by and large, are not very common. Quite common, and unfortunately, much neglected, is the concept of the desmoplastic reaction to invasive mesodermal tumor. In many cases I agree with you that the reaction is a desmoplastic one. I would be among those who tend to look first for desmoplastic reaction and need a lot of convincing that the mixed tumor population is really present.

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7. *Mixed Glioblastoma and Fibrosarcoma*

Contributed by **G. T. Hensley, M.D.,** Milwaukee, Wisconsin

THE PATIENT was a 47-year old man in January, 1970, when he complained of sudden loss of strength in his right hand and headaches of six months duration. At examination the muscular weakness was confirmed; it had extended to the entire right side of the body, with right facial paresis and drooping of the right shoulder. Babinski sign was present on the right. No papilledema and no sensory loss.

Dr. Peterson: Views of a left carotid arteriogram in the arterial phase without filling of the external carotid demonstrates a slight shift of the anterior cerebral vessels of a more distal type toward the right. In the region of the parietal lobe in the course of the distribution of the anterior cerebral artery there is an area about 8 cm in diameter where there is a relative avascularity and some straightening of vessels. The middle cerebral branches are not grossly abnormal, although there could be a slight pressure effect on the superior aspect of the sylvian triangle in its mid portion.

An avascular neoplastic process in the parietal lobe medially which could be either an astrocytoma or a falx meningioma.

Dr. Peterson's impression: Lesion of the medial side of the left parietal lobe, probably a FALX MENINGIOMA.

Roentgenologic impressions submitted by mail:

Astrocytoma	25
Glioblastoma	21
Meningioma	15
Tumor (frontal, parietal, intra-, supra-, retro-sylvian, pontine)	34
Others	15

Dr. Peterson: I don't see any reason for calling this pontine.

Dr. Regato: Drs. P. J. Hodes, of Philadelphia, and P. J. Roesler, of Colorado Springs, also suspected a meningioma in the supra-sylvian area. Dr. K. Hehman, of Cincinnati, preferred a fronto-parietal glioma and Dr. S. Sallaberry, of Colorado Springs, a pontine glioma.

Operative findings: The EEG showed an area of dysfunction, and the brain scan was consistent with a tumor of the left temporal area. On March 24, 1970, a craniotomy was carried out: the dura was opened revealing flattened gyri with intact pia and arachnoid. A soft tumor was found in the left hemisphere and "as far as possible" removed. The surgical specimen consisted of multiple friable fragments of whitish hemorrhagic tissue.

Dr. Rubinstein: This is a highly vascular and obviously malignant tumor with considerable cellular pleomorphism. Necroses are abundant, and there is a considerable degree of vascularity. The blood vessels are usually thin-walled. A very abundant connective tissue stroma is present, some of which appears relatively acellular and forms a band at the periphery of the fragments, suggesting therefore dura mater. The tumor abuts onto and in places presumably invades the dura.

The extremely abundant connective tissue stroma present throughout this tumor is confirmed with the reticulin preparation. Although extremely abundant, the connective tissue, however, varies. In most places, it forms numerous intersecting parallel strands, but in others it shows a number of confluent clear reticulin-free areas which, in cell stains, are seen to be highly cellular. These areas contain very anaplastic cell elements, with large hyperchromatic and frequently giant nuclei which have a dusky chromatin, usually an inconspicuous nuclear membrane, and rare nucleoli. The cytoplasm around these nuclei is usually fairly abundant and eosinophilic, and occasionally forms coarse processes, although fibrils are not elicited in these areas with the PTAH stain. These cells form therefore groups that are encompassed within a very prominent vascular connective tissue stroma. Their morphologic appearance is suggestive of highly anaplastic neuroglial tumor cells.

By contrast, the areas showing the parallel arrangement of intensely compact reticulin fibers show a different cytology. Here, the cells tend to be elongated, with nuclei

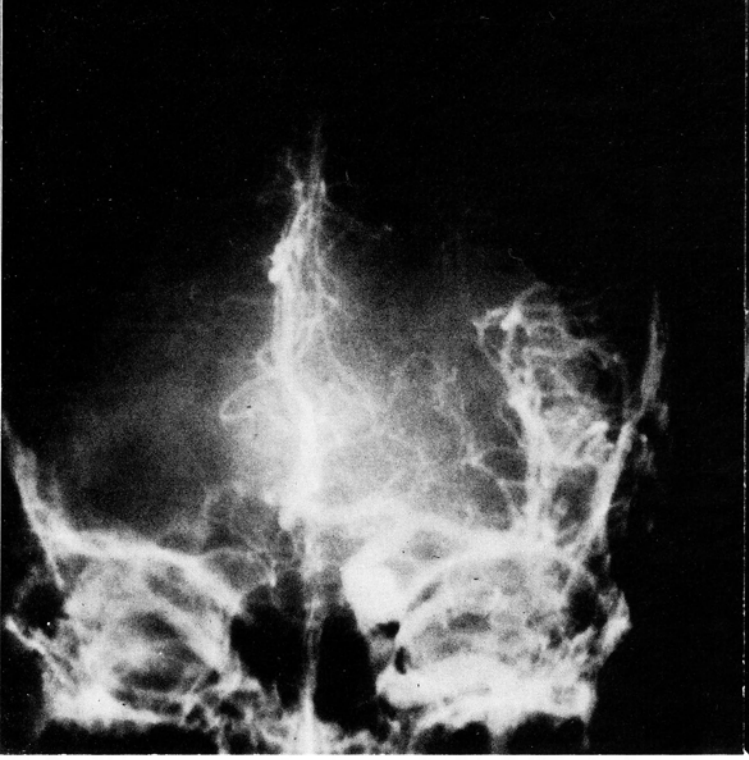


Fig. 1—Slight shift of anterior cerebral vessels toward the right.

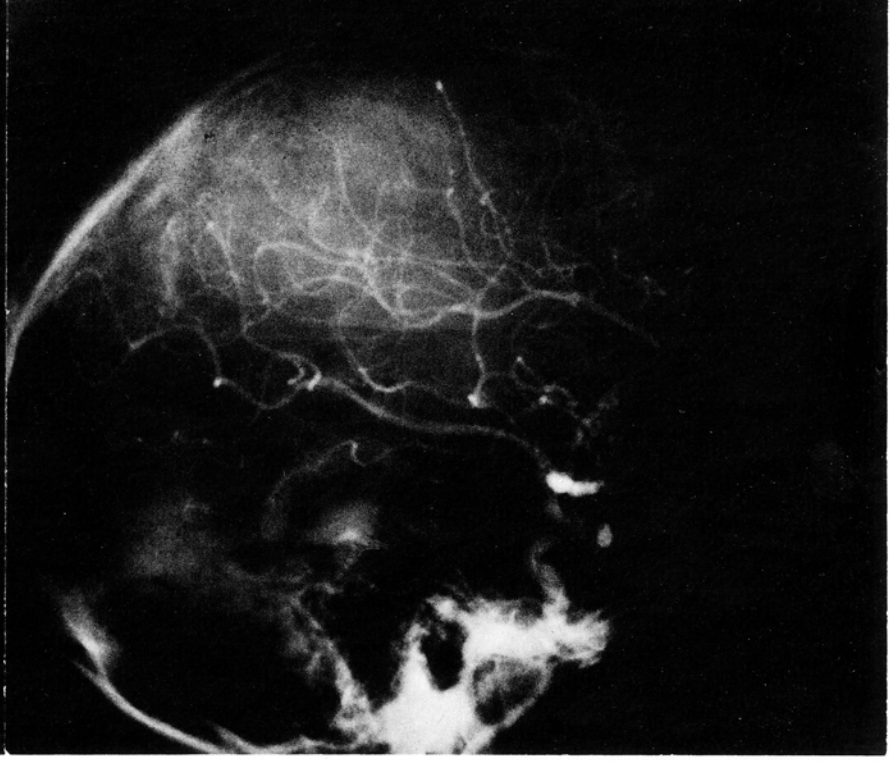


Fig. 2—Area of relative avascularity in the parietal lobe and some straightening of vessels.

which are spindle-shaped and sometimes notched, have a pale nucleoplasm, a delicate nuclear membrane, and often one or more prominent nucleoli. Atypical cells are seen among these elements, being occasionally giant and multinucleated, or with hyperchromatic nuclei. Mitotic figures are also present. In places these cells, though maintaining the same nuclear characteristic, become more stellate and arranged in a less compact manner; the reticulin preparation shows, however, very abundant connective tissue in these fields. This second type of neoplastic cellular tissue is interpreted as fibrosarcomatous. In many areas, however, the tumor cells have acquired extremely anaplastic malignant features, and it is not possible to decide with assurance whether they are gliomatous or sarcomatous. In a few areas, however, anaplastic tumor cells, presumably gliomatous, form compact masses surrounded by relatively acellular tissue, presumably originating from the dura, indicative therefore of dural invasion. One definite focus is seen which demonstrates invasion of a venous channel, presumably dural.

The contrasting cytology between the two types of tissue is somewhat better seen with the van Gieson preparation, in which the tumor cells of the first type tend to have a yellowish-golden cytoplasm, and those of the second type a more brownish or tan colored cytoplasm. Nevertheless, the very abundant fibrous tissue present throughout most of the tumor makes the distinctions very subtle, and for the diagnosis to be made in this case, one would prefer to see more clear-cut areas giving the diagnostic picture of the two kinds of neoplastic tissues encountered. The reticulin preparation shows in places the marmorate pattern which is so characteristic of this form of neoplasm.

The diagnosis of a mixed glioblastoma and fibrosarcoma is proposed for this case, the fibrosarcoma having presumably arisen from the marked vascular proliferation that is so characteristic a feature of glioblastoma multiforme. The diagnosis is offered largely on the morphologic and histologic resemblance of many of the areas of this case to other examples from one's personal experience that demonstrate in a much more convincing fashion the contiguous presence of obvious gliomatous and fibrosarcomatous elements. The diagnosis in such cases must obviously rest on the unequivocal recognition of these contiguous areas, and for this extensive sampling is often necessary. The recognition of these rare mixed tumors is complicated by the fact that, once a mixed tumor has begun to manifest itself, the sarcomatous element tends to overshadow the gliomatous, with the result that it may be very difficult to distinguish, in the terminal stages, the presence of an underlying malignant glioma. This event is particularly associated with temporal lobe tumors, and invasion of the dura, as in this case, is remarkably frequent. It is also possible that the fibrous connective tissue arising from the dura may itself participate to the neoplastic development of the sarcomatous element.

The gross appearances of the left frontoparietal cerebral tumor disclosed at postmortem is highly characteristic of the examples of mixed glioblastoma and fibrosarcoma I have seen. It is unusually well circumscribed, even lobulated, with a granular-looking, relatively homogeneous, pale greyish cut surface. The tumor reaches the surface over the parasagittal meninges and appears to be adherent to the falx. Grossly, it mimics somewhat a meningioma, except that areas of necrosis are present. This tumor is usually much better defined grossly than most glioblastomas.

Dr. Rubinstein's diagnosis: MIXED GLIOBLASTOMA and FIBROSARCOMA

Histopathologic diagnoses submitted by mail:

Glio (spongio)blastoma multiforme	32
Glioblastoma monstro (giganto)cellulare	21
Metastatic carcinoma	30
Sarcoma (meningeal, metastatic)	29
Ependymoma	5
*Astrocytoma	15
Others	12

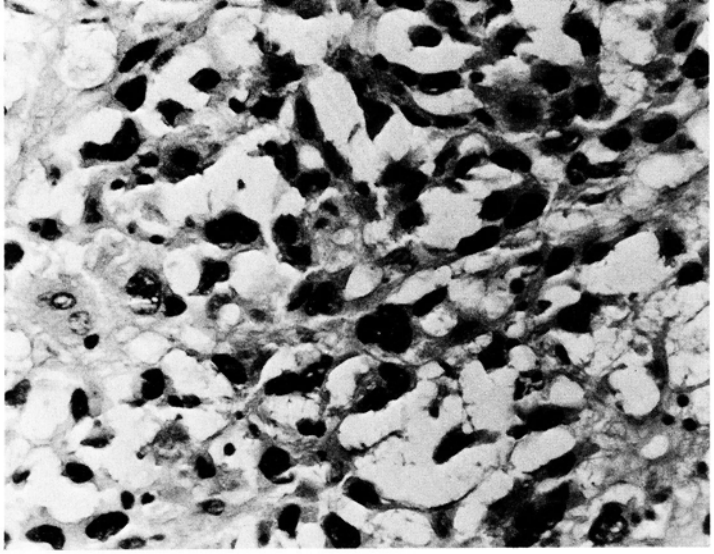


Fig. 3—Area of tumor composed of malignant astrocytes. van Gieson x 300.

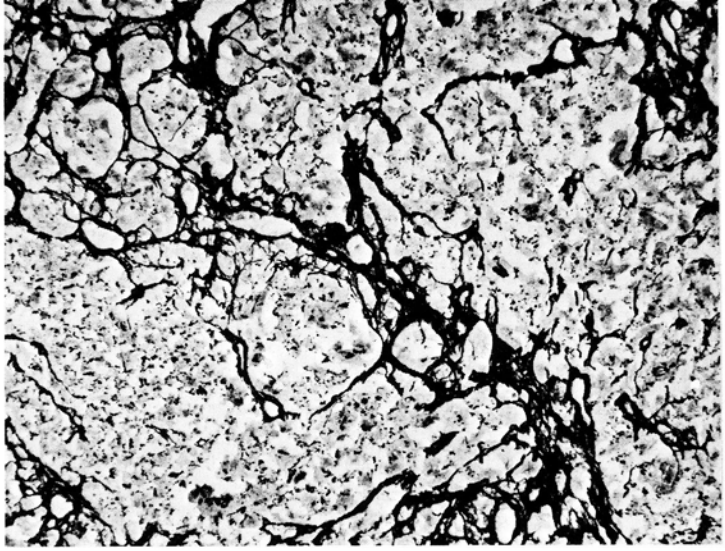


Fig. 4—Same area as in photomicrograph (1), stained for reticulin. This preparation shows that the fibrous connective tissue, though fairly abundant, is clearly supportive and not directly related topographically to the tumor cells. Gordon-Sweets' method for reticulin x 120.

Dr. Rubinstein: The diagnostic difficulties are very well illustrated by this table. Opinions are rather equally split between those who regard this as a form of glioblastoma, or a *monstro cellulare* one, and those who thought this was a sarcoma or a metastatic carcinoma. Obviously this case did present considerable diagnostic difficulties and it is not surprising with the H and E preparation. In this case special stains are very important to come to some sort of diagnostic conclusion; this supports the feeling I have that both elements are present. Those that are impressed by the gliomatous features regard this as a glioblastoma; those who are impressed by the sarcomatous features will call it a fibrosarcoma.

Dr. Regato: Drs. D.L. Dawson, and C.E. Berry, of Colorado Springs, made a diagnosis of glioblastoma multiforme. Drs. A. J. Zemel, of El Paso, and P. W. Gikas, of Ann Arbor, offered meningeal sarcoma. Dr. F.P. Bornstein, of El Paso, suggested giant-cell glioblastoma or sarcoma arising from the falx. Dr. Dorothy Russell, of Surrey, England, wrote: My slide shows a fairly large circumscribed area of polygonal cells that distinctly suggest carcinoma: deposits of secondary carcinoma can, of course, occur in pre-existing primary growths. Dr. Bornstein, attending this Cancer Seminar for the 18th time wrote: "The hope that age might bring wisdom is a sad illusion. . . I am flattered by the assumption. . that roentgenologists have *impressions* while pathologists make *diagnoses* . . . no pathologist in his right mind would dare to make a diagnosis without roentgenological help . . . A look at the gross specimen before the slide is often of some help. I am aware that these are weak excuses . . . "

Subsequent history: One month after operation the patient presented a hemiparesis, was on Dalantin and Librium and was considered totally disabled. On July 8, 1970 he expired. At autopsy there was residual tumor 6 cm in diameter, areas of necrosis and cystic degeneration with compression of the left ventricle. The mesencephalon, pons, medulla and cerebellum were free of tumor. No evidence of tumor was found in the kidneys, esophagus, stomach, gallbladder, duodenum, pancreas, liver, bladder, prostate, testes, adrenal or lungs.

Dr. Peterson: It would be nice on all of our cases if somehow we could get sections right through the brain and show us where the tumor was. This tumor came right up to the midline, which is the reason it was defacing or stretching those anterior cerebral vessels. The main trunk should have been displaced more than what we saw on the angiogram.

Fig. 5—Another field of this tumor, showing an arrangement of atypical cells in compact, intersecting streams. The cell nuclei are often elongated. The morphology of the cells is that of a fibrosarcoma. van Gieson x 160.

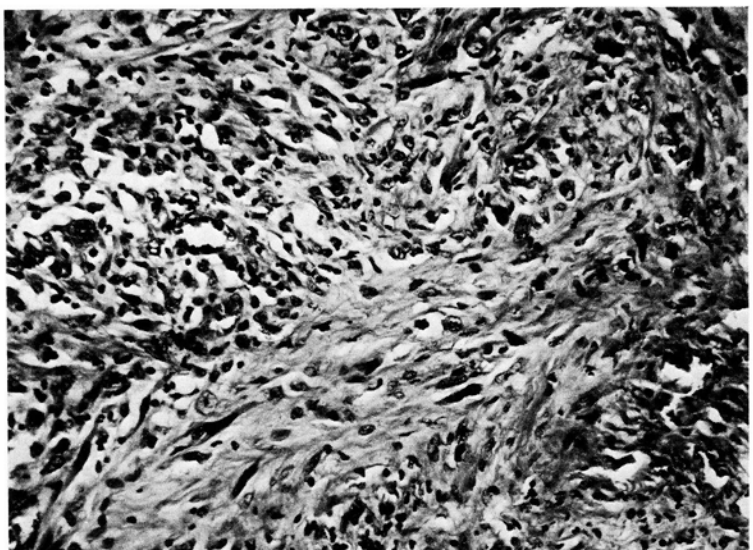
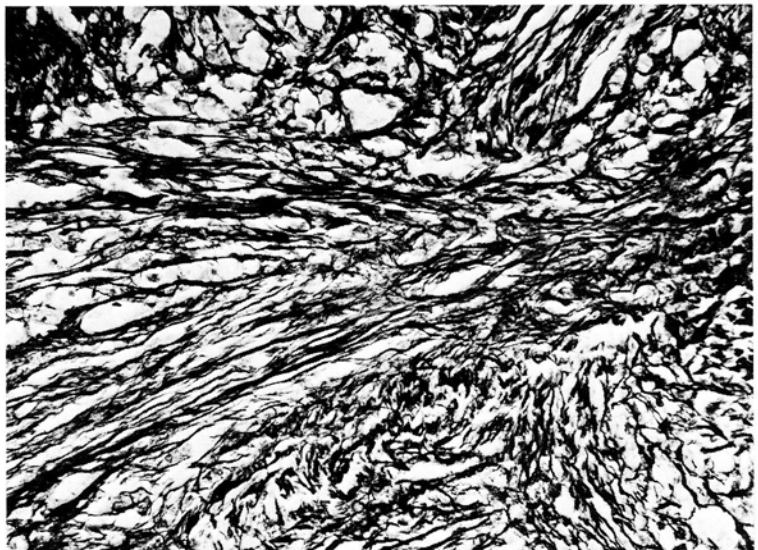


Fig. 6—Reticulin preparation from a field corresponding to that seen in photomicrograph (3). A compact meshwork of connective tissue fibers is arranged to form interlacing bundles similar to the alignment of the tumor cells seen in the previous photomicrograph. Gordon-Sweets' silver method for reticulin x 160.



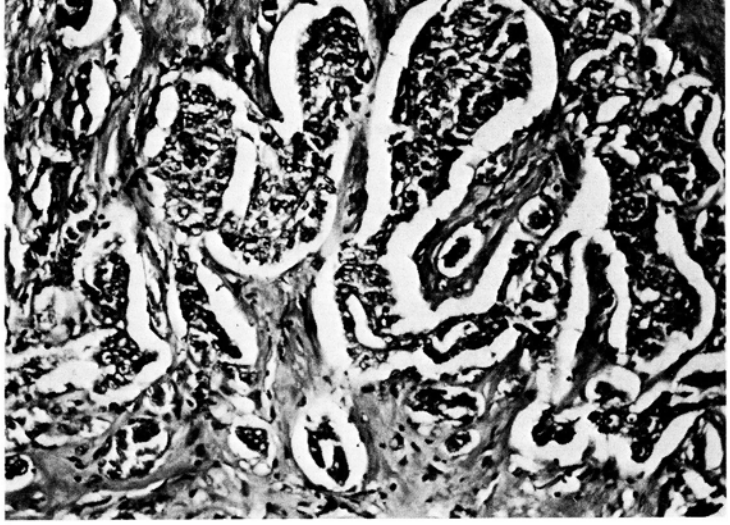


Fig. 7—Compact groups of anaplastic glioma tumor cells invading relatively acellular fibrous tissue, presumably dura. H & E x 120.

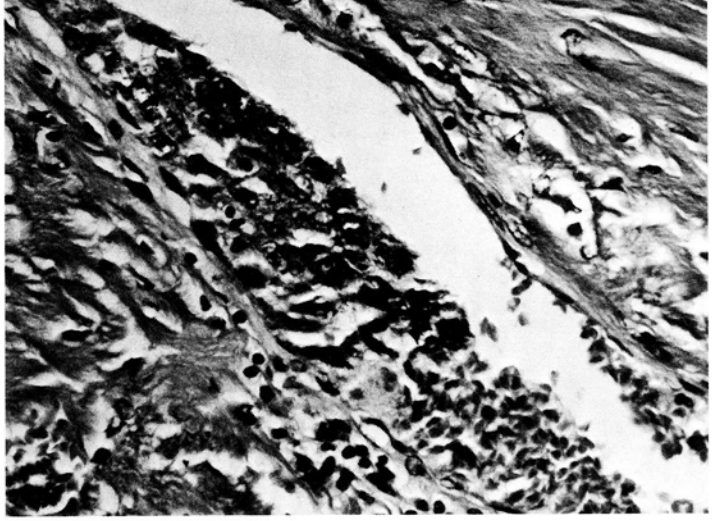


Fig. 8—Tumor cells permeating the lumen of a vein, presumably dural. van Gieson x 300.

Dr. French: The photograph of the post-mortem specimen shows a nice herniation beneath the falx. There is also a great deal of edema. This patient undoubtedly did not have such herniation of the cingulum beneath the falx at the time of radiologic examination. Clinically, it was a purely motor phenomenon involving the face, the arm, the shoulder, which would fit well with a posterior frontal lesion because there was no sensory impairment. The scan, unfortunately, was down the temporal lobe; that is the problem of getting too many tests. As long as you had the clinical and the radiographic evidence I think this is all one really needed here. In a situation like this, where the surgeon said 'I took it out as far as possible', he means as far as I possibly can without aggravating the neurological symptoms. When a term is used, it depends how it is meant: if she just says Hmmmm that's one thing, if she says *no* is another.

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8. *Anaplastic (Malignant) Astrocytoma*

Contributed by **F. R. Dutra, M.D.** and **J. J. Protass, M.D.,** Castro Valley, California

THE PATIENT was a 49-year old woman in October, 1969, when she was hospitalized with a history of headaches, vomiting and disorientation for the past month. Examination revealed marked aphasia, right Babinski response and slight bilateral papilledema.

Dr. Peterson: Views of a left carotid angiogram with injection into the common carotid shows filling of the internal and external carotid arteries. The AP view is in the early arterial phase and the lateral view in a late arterial, early capillary phase. There is an extreme shift of the anterior cerebral vessels to the right of a rather square type which indicates a rather larger lesion located at some distance from the major part of the anterior cerebral artery. In the AP projection, the sylvian point is depressed somewhat. Otherwise the middle cerebral vessels are normal. In the lateral projection, none of the major vessels are visualized inasmuch as the film is made in a later phase demonstrating the more peripheral branches of both the anterior and middle cerebral arteries. In the frontal and anterior temporal area the vessels appear normal. There is evidence of a large mass in the posterior parietal, occipital and posterior temporal region producing stretching of vessels with what appear to be a few abnormal or tumor vessels in the posterior temporal and inferior parietal area.

These findings indicate a large mass, neoplastic in type, occupying the parieto-occipital, temporal region, possibly associated with considerable edema. A primary intracranial neoplasm would be more likely than a metastatic tumor. Because of the appearance of the few tumor vessels which are visualized it would seem that a malignant tumor would be more likely than a meningioma.

Dr. Peterson's impression: Large mass in the left parieto-occipital-temporal area, most likely a GLIOBLASTOMA.

Roentgenologic impressions submitted by mail:

Meningioma	25
Glioma	33
Metastatic tumor	18
Tumor (temporal, parietal, parieto-occipital, occipito-temporal, anterosylvian)	24
Others	16

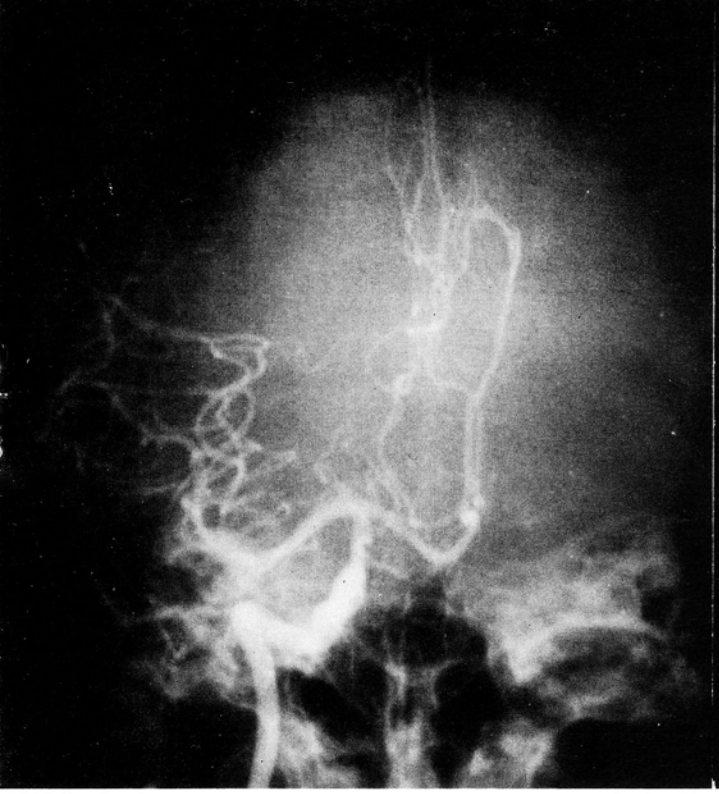


Fig. 1—Extreme shift to the right of anterior cerebral vessels.

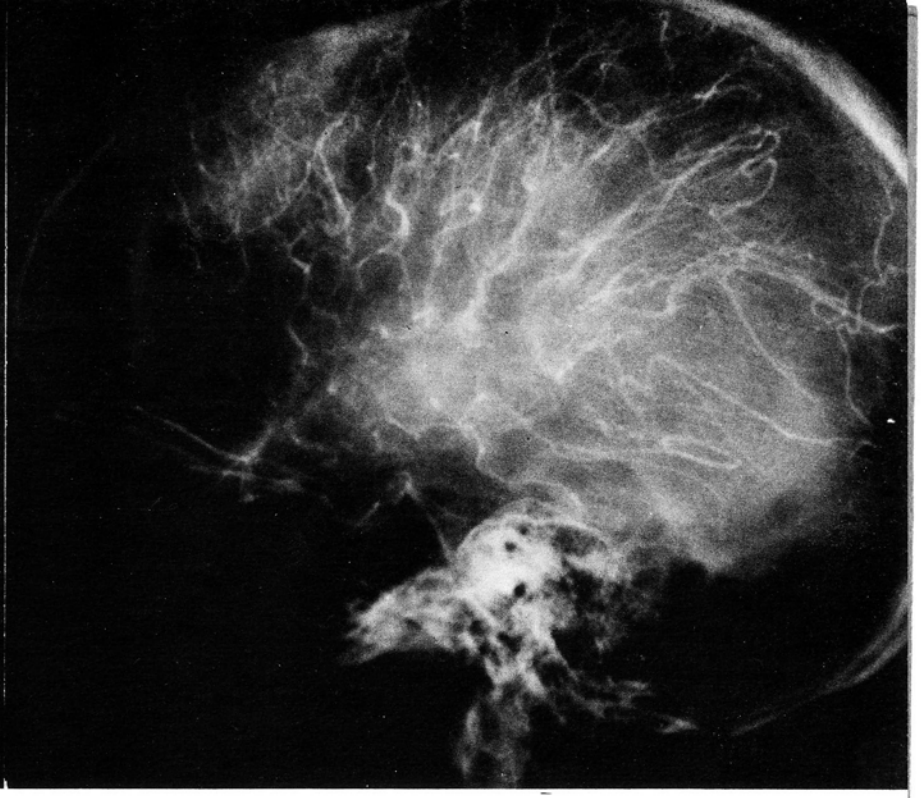


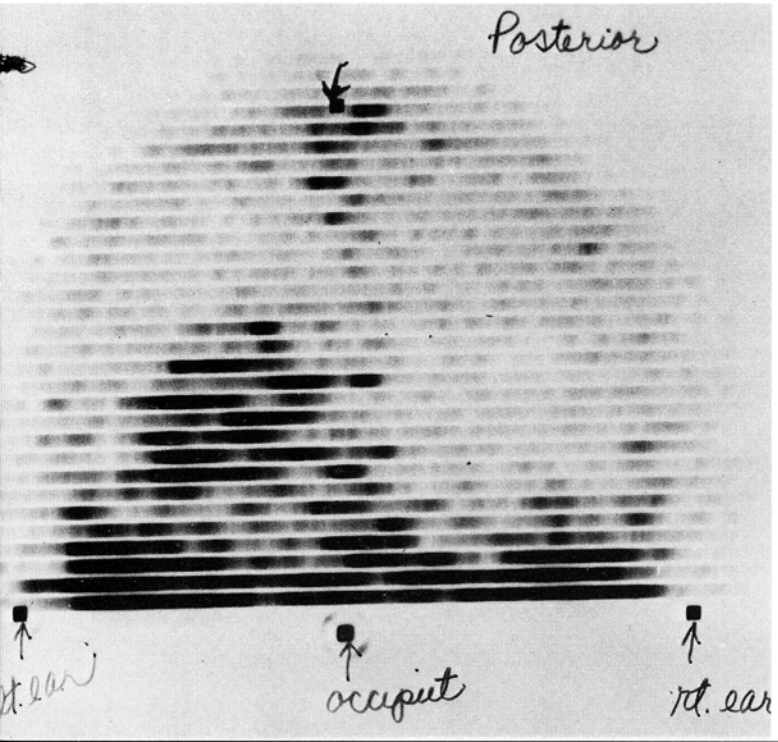
Fig. 2—None of the major vessels are visualized. Evidence of mass in posterior parietal region.

Dr. Peterson: We know that metastatic tumors are associated with a fair amount of edema; in metastatic tumors, there is a rounded cluster of tumor vessels, or else you have not too much to guess on. The amount of tumor vessels here were not great so we are guessing the difference in histology and I guessed glioma.

Dr. Regato: Drs. J. M. Sala, of Springfield, Missouri, A. Schlessinger, of Cincinnati, and P. H. Riemenschneider, of Santa Barbara, concurred in their impression of parieto-occipital glioma.

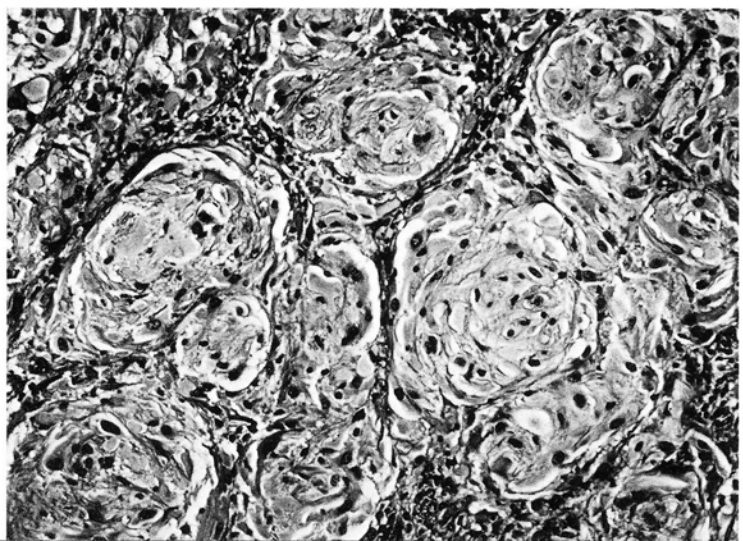
Operative findings: The brain scan showed increased activity in the parietal area. On October 28, 1969, a craniotomy was done; a left occipital lobectomy was done, tumor was cut across but later additional removal was done.

Fig. 3—Radioisotope scanning showing area of increased activity in the parietal lobe.



Dr. Rubinstein: These are fragments of partly necrotic and partly viable tumor. The architecture of the viable fragments is somewhat unusual in that it shows an arrangement in which areas composed of compact cellular formations are separated by a more loosely textured arrangement. In other areas, the tumor cells form compact nests with a rounded outline, apparently separated by a regular vascular stroma, among which chronic inflammatory cells are present. The cytology of the tumor cells is quite pleomorphic, some of the cells being stellate, others elongated and pilocytic, and others again rounded and bloated, with an eosinophilic cytoplasm and almost no cell processes. The nuclei too vary in size and in shape. These are frequently atypical and hyperchromatic. Multinucleated giant cells are present. Intranuclear inclusion bodies are occasionally seen. Mitotic figures are found. Other features include, in addition to the necrosis already mentioned, foci of obvious prominent vascular endothelial proliferation.

Fig. 4—Compact nests of tumor cells separated by a supporting stroma in which chronic inflammatory cells are present. H & E x 160.



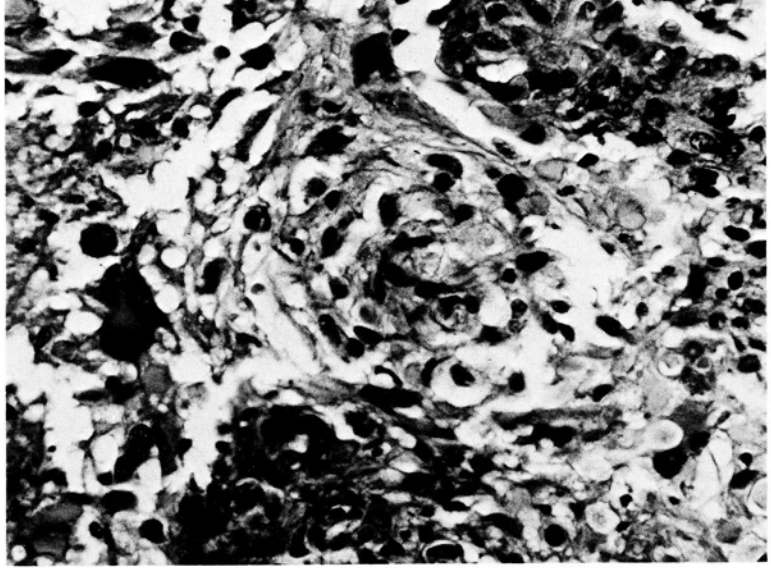


Fig. 5—High power of loosely textured nest of fibrillated neuroglial cells. Foci of vascular endothelial proliferation are present in the right upper corner and along the central lower edge of the photograph. Note hyperchromatic nuclei, and one multinucleated giant cell (left of center). H & E x 300.

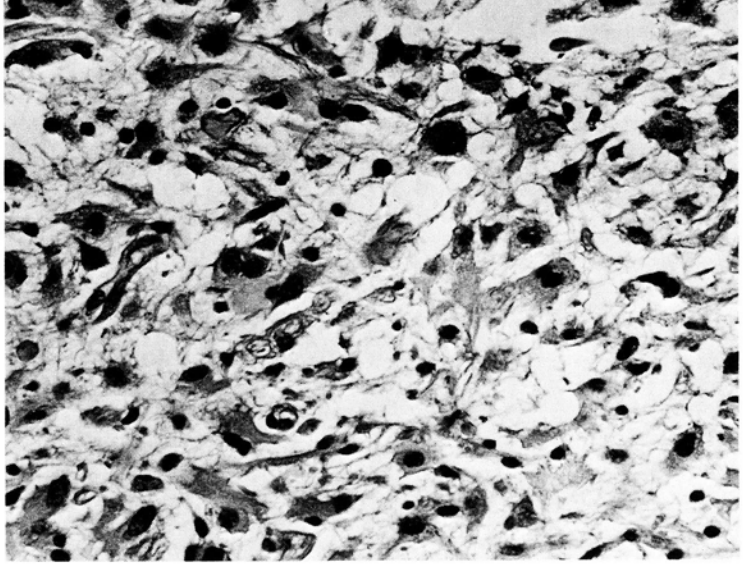


Fig. 6—Area of tumor showing typical malignant astrocytoma cells. H & E x 300.

The cells frequently have coarse or finer fibrillary processes. A PTAH preparation confirms the presence of both fine and coarse neuroglial fibers in places, thus indicating the astrocytic nature of the tumor. The reticulin preparation confirms that the tumor cells are not associated with any reticulin fibers, which are entirely confined to the rather rich vascular stroma.

The picture is therefore essentially that of an anaplastic, malignant neuroglial tumor, many of the cells of which are of astrocytic lineage. There is marked cellular pleomorphism. Giant cells are numerous in places, and in a few appear to dominate the picture. Necrosis and vascular endothelial proliferation are present. In some areas the tumor cells are rich in neuroglial fibers, in others neuroglial fibers cannot be demonstrated. The unusual feature about this tumor is the curious pattern of cell nests forming almost a whorling arrangement. The differential diagnosis lies between a malignant astrocytoma, or a glioblastoma multiforme. The cytological and architectural features that determine the microscopic entity of glioblastoma, except pseudo palisades, can be demonstrated in this case, but I feel that the term anaplastic, or malignant, astrocytoma more correctly designates this case.

Dr. Rubinstein's diagnosis: ANAPLASTIC (Malignant) ASTROCYTOMA

Histopathologic diagnoses submitted by mail:

*Astrocytoma	33
Meningioma	32
Meningiosarcoma	18
Giant Cell glioblastoma	17
Glioblastoma multiforme	18
Sarcoma	9
Chordoma	5
Others	27

Dr. Rubinstein: Now the wide scatter of opinion on this case emphasizes the diagnostic difficulties that were met. Some were obviously impressed by the swirling pattern, so there is quite a large number who thought about a meningeal tumor or, because of the malignant element, meningiosarcoma. In opposition to that there is quite a large group who thought of a glial tumor, either astrocytoma or giant-cell glioblastoma or glioblastoma multiforme. If the diagnosis of astrocytoma is entertained here, the qualification of malignant astrocytoma is necessary.

Dr. Regato: Drs. F.R. Dutra, of Castro Valley, California, and P. Cooper, of Los Angeles, offered a diagnosis of magnocellular glioblastoma. Dr. K. Jollinger, of Vienna, fusi-and monstro-cellular glioblastoma. Dr. M.H. Sulak, of San Antonio, made a diagnosis of glio-sarcoma. Dr. G. Gricouroff, of Paris, offered malignant glio-schwannoma. Dr. J. A. Carney, of Rochester, Minnesota, astrocytoma. Dr. R. Reicher, of Sofia, saw two lesions, astrocytoma and meningeal blastoma.

Subsequent history: In December, 1969, the patient was irradiated and was well for several months afterwards. In July, 1970, he complained of blurred vision. He was to receive chemotherapy.

Dr. French: We have increased intracranial pressure and an aphasia and no visual field changes, so that the probabilities of having involvement of only the occipito-temporal lobe are not great. The angiograms indicate a lesion in and around the angular gyrus just above this. The approach that I would have taken would have been to turn a large craniotomy flap in that region and remove the tumor out to the point that you think you were reaching reasonably normal tissue, but not do a lobectomy because this would leave the patient with a hemianopsia. You are quite certain, even pre-operatively, that you are not going to cure this patient. Nothing is going to cure this patient, including irradiation. But it is necessary to reduce the pressure as much as possible and that can be best done by removing the content of the tumor. I don't think the outlook would have been any different, if it had been done my way or as it was actually done. I think by the time she was operated upon the tumor had crossed the corpus callosum and it was inoperable.

F. R. Dutra, M.D., Castro Valley, California: The patient did receive chemotherapy, vincristine plus a new substance known as BCNU. Six weeks after the therapy was completed she had deteriorated. She then received CCNU, also without improvement.

Dr. Regato: Dr. Peterson I would like to ask you to comment on this: it is obvious that in a good number, perhaps a majority, of the cases of these intracranial lesions, the clinical information even at its best, may not be sufficient to point out the location of the tumor; with the present day methods of arteriography, ventri-

culography, and pneumoencephalography, a considerable contribution may be made by the roentgenologist, and beyond that, because of the character of the vessels, etc., he may be able to say that this is actually a tumor and that in his impression it might be benign or malignant. But, am I correct in saying that when the roentgenologist goes to the point of stating that this is a glioma multiforme, he is really capitalizing on his experience of another such case that he saw in that same region, and really not as strong grounds as he would otherwise be. In other words, must the radiographic examination necessarily lead to a histologic diagnosis or should it confine itself to add valuable secondary information?

Dr. Peterson: Your question has to do with whether or not radiologically we can make a histologic diagnosis. I think that there is no question that in many cases you can make a diagnosis of a malignant tumor and be very accurate. And after that it becomes less accurate as to whether it is a glioblastoma or a metastasis or some other malignant tumor. There are certain patterns that are quite good for glioblastoma and probably do not fail more than 10-15 percent of the time. Then it comes down to what is the final criteria. I am shaken here, more than I thought I would be, by the multiple reports of pathologists; it could be that the radiologic diagnosis, poor as it is, is as good as that of most pathologists.

Editor's Note: Patient expired January 5, 1971.

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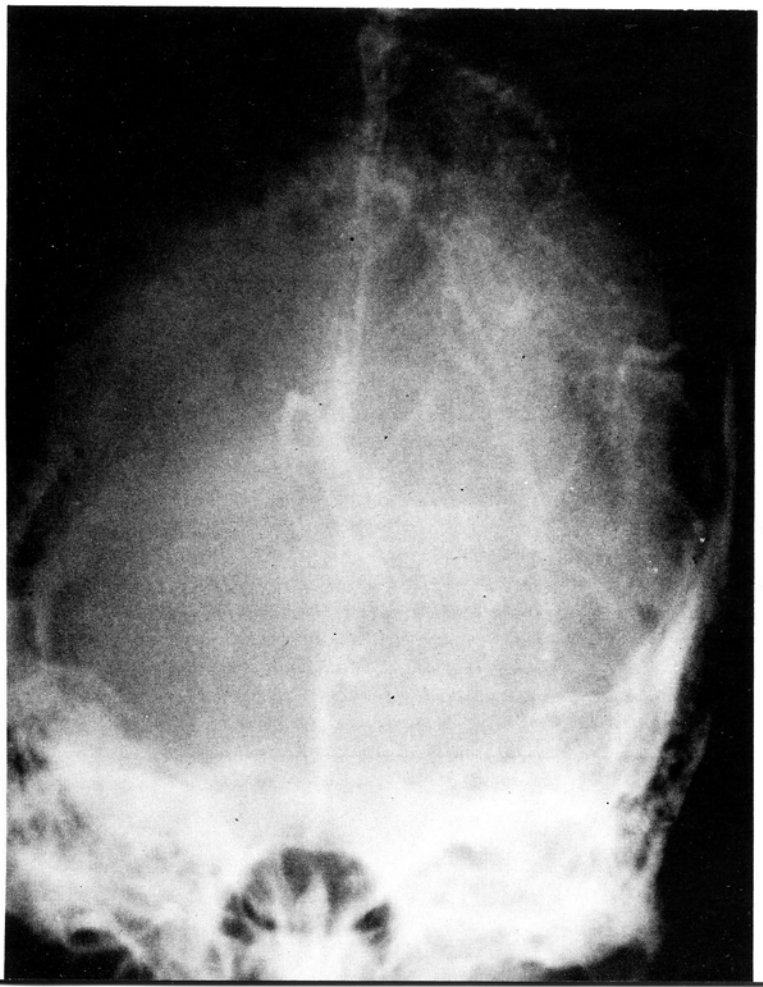
9. *Metastatic Cerebral Adenocarcinoma*

Contributed by **A. O. Severance, M.D.** and **H. F. Elmendorf, M.D.,** San Antonio, Texas

THE PATIENT was a 39-year old woman in March, 1970, when she presented with mental confusion, headaches and vomiting; seven months previously a "tumor" had been resected from her right lung. Examination revealed flattening of the optic disks, right facial and hypoglosse paralyses.

Fig. 1—Marked right displacement of the internal cerebral vein and medial displacement of the basal vein.



Dr. Peterson: A lateral carotid arteriogram in a perhaps late arterial phase, as far as timing is concerned, and a venogram demonstrate rather marked displacement of the internal cerebral vein to the right and a marked medial displacement of the basal vein which would be compatible with herniation of the uncal region. In the lateral projection, there is filling of the middle cerebral vessels and almost no contrast medium in the anterior cerebral. There is also filling of external carotid branches indicating a relatively late phase in the circulation cycle but still moderately early filling of the intracranial vessels is present. The middle cerebral is markedly shifted superiorly and forward. The entire area is relatively avascular, although there is one small cluster of what are probably tumor vessels in the temporal region just posterior to the level of the dorsum sellae and perhaps another group of abnormal vessels posterior and superior to this. Otherwise, the vessels over the temporal lobe are stretched, consistent with an intratemporal mass. The anterior coronal artery appears to be elevated.

The findings indicate increased intracranial pressure, a mass lesion in the temporal area perhaps associated with much edema extending into the parieto-occipital region and with some tumor vessels present. A glioblastoma or metastatic malignancy are the most likely.

Dr. Peterson's impression: METASTATIC MALIGNANT TUMOR temporoparietal.

Roentgenologic impressions submitted by mail:

Metastatic tumor	30
Tumor (fronto-parietal, posterior temporal, infra-, supra-sylvian)	36
Glioblastoma	7
Others	5

Dr. Peterson: A number of radiologists also felt this was metastatic tumor. I suspect this is that old monkey business of looking at the history: this patient had a lung tumor, then you guess this other lesion is metastatic. This is all right for guessing games and it is all right for con-

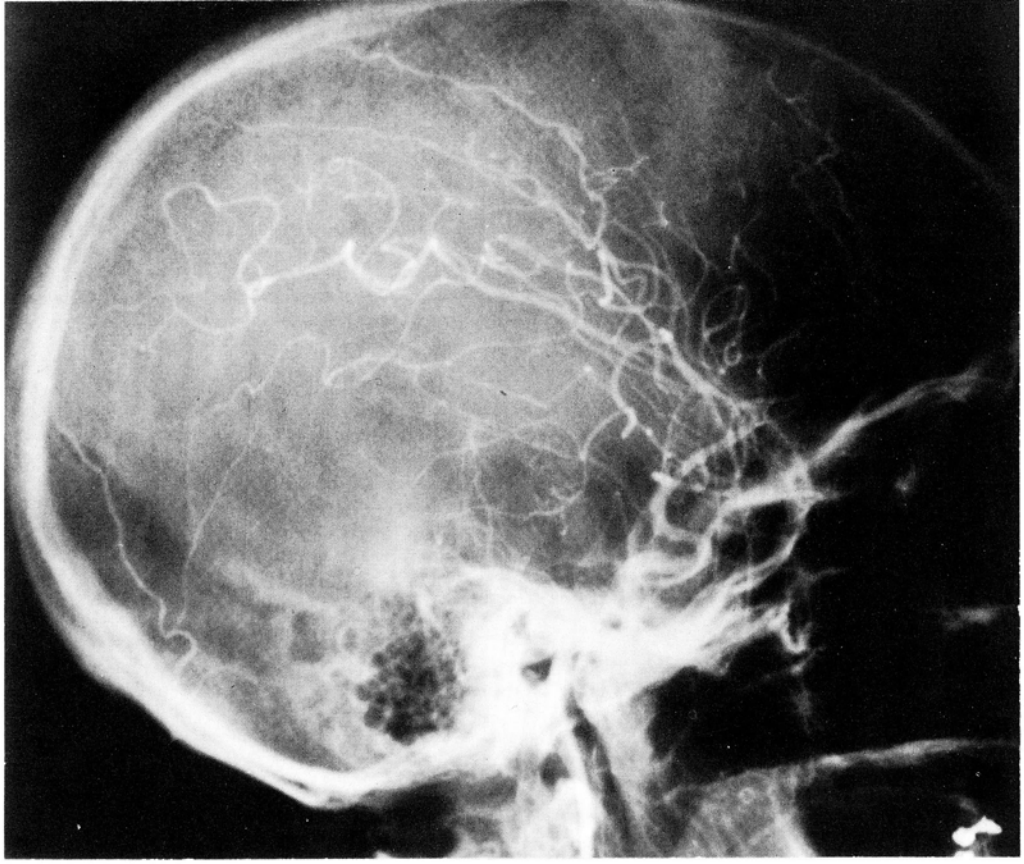


Fig. 2—Moderately early filling of middle cerebral vessels in spite of late phase of circulating cycle, with superior and forward shift.

ferences, but it really is not on the film. Now if the patient had not had a lung tumor my guess is that these same radiologists would have knocked off most of these and jumped to the diagnosis of glioblastoma.

Dr. Regato: Trusting that the details provided in the history were not a "red herring", the radiologic experts concurred on the probability of a cerebral metastasis from a carcinoma of the lung.

Operative findings: On March 24, 1970, a craniotomy was done. An incision about the middle temporal gyrus exposed a firm discrete mass 5 mm from the surface: it was enucleated. The surgical specimen weighed 11 grams and contained a soft, yellow-orange tumor 3.5 x 2.2 x 2 cm. We obtained from Dr. Severance, slides of the pulmonary surgical specimen which showed an adenocarcinoma. These slides were submitted to Dr. Rubinstein.

Dr. Rubinstein: A highly cellular and anaplastic neoplasm, in places relatively well defined from the adjacent brain, but not encapsulated. A marked chronic inflammatory reaction is present, especially at the periphery of the tumor. Extensive necroses are present. In most places, the picture is that of uniform masses of large polyhedral cells with a high nucleo cytoplasmic ratio, large nuclei with prominent nucleoli, and frequent anaplastic cell forms. Mitotic figures are numerous.

The appearances are of a highly malignant epithelial neoplasm, the picture being characteristic of metastatic carcinoma. Occasionally, the tumor cells are arranged not only in trabeculae but also in a faintly papillary pattern, which suggests a poorly differentiated adenocarcinoma.

The reticulin pattern shows a moderately abundant connective tissue stroma, tending to separate the tumor cells into well defined lobules. The adjacent brain is markedly hypercellular, and shows a microcystic appearance characteristic of the edematous reaction at the periphery of a metastatic tumor. The increase of cellularity is due to an increase of neuroglial cells, of microglial cells and activated macrophages, and of diffuse infiltrating chronic inflammatory cell elements.

This patient had a previous resection of the lung, which was diagnosed as adenocarcinoma. The microscopic appearances of the tumor in the brain are compatible with this sequence of events.

Slides from the primary lesion removed from this patient 7 months before the craniotomy show a poorly differentiated low-columnar and cuboidal celled tubular adenocarcinoma, the picture of which is identical with the cerebral tumor. It is impossible, from the microscopic preparations of the lung tumor, to decide whether the pulmonary neoplasm is primary or secondary. Microscopically, the cerebral metastatic growth is quite compatible with a metastatic adenocarcinoma that originated in the pulmonary tree.

Dr. Rubinstein's diagnosis: Poorly differentiated METASTATIC ADENOCARCINOMA

Histopathologic diagnoses submitted by mail:

Metastatic carcinoma (adeno, chorio, squamous, etc.)	114
Metastatic melanoma	17
Pinealoma	12
Ependymoma	3
*Astrocytoma	5
Others	3

Dr. Rubinstein: There was an overwhelming support for the view that this is a metastatic tumor; I think there is some evidence of adenocarcinoma. A diagnosis of pinealoma is understandable because of the marked inflammatory reaction present; in many of the tumor cells there is at first glance some resemblance to the germinoma type which forms the majority of pineal tumors, but the picture is much more anaplastic than what you see in a pineal germinoma.

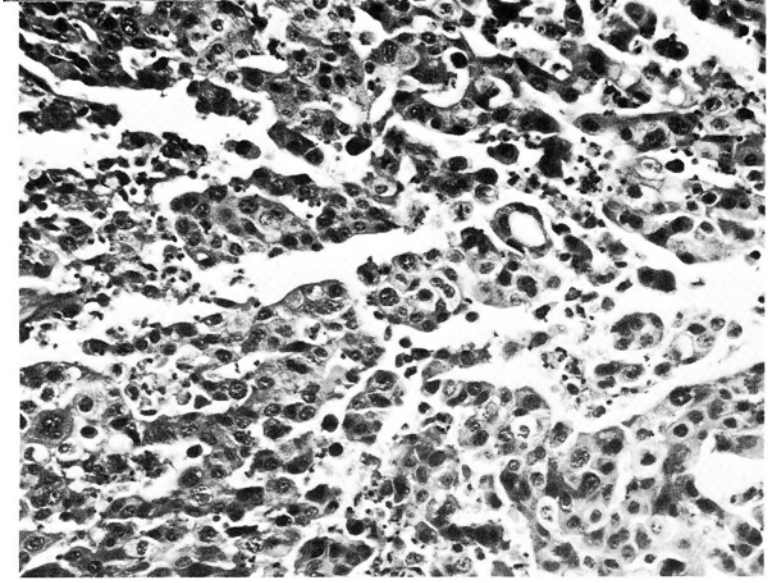


Fig. 3—Low power view of anaplastic epithelial tumor cells, arranged in trabeculae, with a faintly papillary pattern. The appearances are those of a metastatic carcinoma and suggest a poorly differentiated adenocarcinoma. H & E x 120.

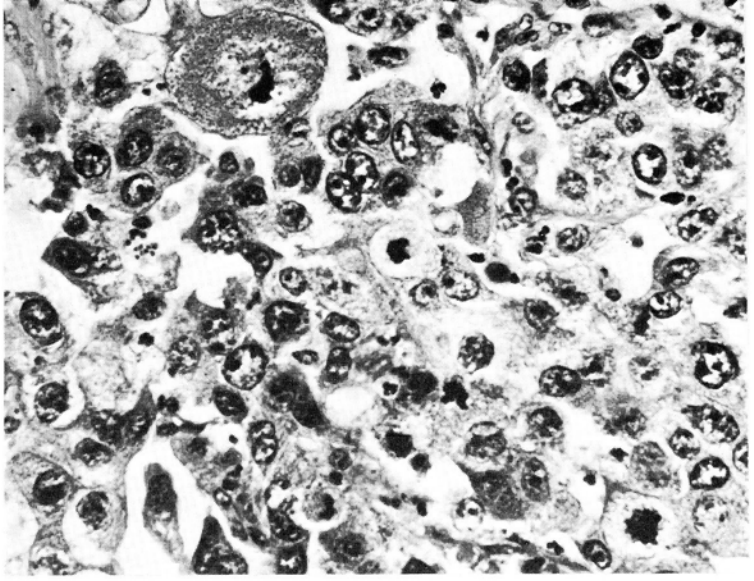


Fig. 4—High power view of anaplastic metastatic carcinoma. H & E x 300.

Dr. Regato: Differing only as to whether the origin was testicular, bronchial, renal, etc., the experts agreed on a diagnosis of metastatic carcinoma.

Subsequent history: Following operation the patient did not do well and three months later, in June, 1970, she expired. No autopsy was done.

Dr. French: This patient had a hypoglossal nerve involvement and a right facial nerve involvement which should be due to a lesion down in the brain stem or out in the cerebello-pontine angle. Having an angiogram like this showing a lesion we agree that it is most likely metastatic. I suppose one could do a spinal puncture and test the cerebro-spinal fluid for cells, for confirmation. How to treat the patient? I would probably operate on the patient to try to decompress him and then any other form of therapy, be it irradiation or chemotherapy, is not going to make too much difference to him.

Dr. Regato: In other words, there is nothing to do for the patient, so he might as well have radiotherapy?

Dr. French: No, I don't mean it that way. One should do everything possible as long as the individual is surviving with any degree of comfort for him.

Dr. Regato: Since the advent of Cobalt and Supervoltage roentgentherapy, we have treated quite a number of patients with metastatic lesions of the brain to considerable advantage to them. We have even those in which we have irradiated the metastatic brain lesions without knowing where the primary was, the patients have done well for quite some time until the primary lesion was found and then was treated. Of course, in most of these instances the eventual result is not cure, but in metastatic lesions from the breast and from the lung, the thorough and skillful irradiation of the brain for metastasis is of a considerable palliative value in many instances.

F.R. Dutra, M.D., Castro Valley, California: I would like to ask Dr. del Regato whether in all of these cases where it is clearly evident beyond all reasonable doubt that it is metastatic carcinoma in the brain, he has required tissue confirmation before proceeding with radiotherapy to the brain?

Dr. Regato: That is exactly the difficulty involved, particularly when no primary lesion is suspected; irradiating them without that confirmation is something that we do reluctantly. But in the presence of a patient that is fast becoming worse and for whom there is no other treatment, we have done it and we have been pleased to have done it. More often, this is a metastatic lesion from a known primary that is already present, cancer of the lung, or cancer of the breast. The irradiation of the entire skull implies epilation; this is of particular significance to ladies and we usually humor them about the fact that their husband should buy them wigs of different colors, but the hair eventually comes back after irradiation with Cobalt-60 or supervoltage.

Dr. Rubinstein: Is this not the kind of circumstance where it would be justifiable to start rigorously controlled clinical trials using controls? If, in fact these cases do respond to irradiation, as you are claiming they are, it seems to me that it is perfectly ethical to do so in this kind of case; since it is by no means universally accepted that metastatic carcinoma should be irradiated, a very carefully controlled clinical trial could be set up. What is your reaction to that?

Dr. Regato: I am, in principle, opposed to the administration of radical radiotherapy to patients in whom the diagnosis is not verified. But in the overwhelming majority of the patients with brain metastases, either by the previous existence of a primary lesion, or because the patient has been explored in the belief that there was a primary lesion, we do have histopathologic confirmation. I do not think that this is the kind of problem that will require a randomized experiment. Anyone would be convinced of the considerable palliative value of radiotherapy in the presence of cases in which there is unquestionable histopathologic proof.

Dr. Rubinstein: I must say, on the contrary, that this should be established; proper randomization and proper clinical trial is in fact a perfectly proper way of investigating therapy. I think that we ought to know for certain how effective is irradiation.

Dr. Regato: The obvious answer to that is that we do know. No, not being facetious, the fact is, we have patients that were bedridden and in bad state who have walked out of our hospital after recovering from considerable bothersome symptoms and really patients in bad shape that have

recovered. I am not saying any more than what is already self evident, that radiotherapy is an excellent means of palliation of metastatic carcinoma of the brain. These patients do die of their tumor eventually, because if they have brain metastasis, usually they have other forms of metastasis also.

Dr. Rubinstein: Did each patient have operative intervention and removal of the tumor before hand?

Dr. Regato: Some of them have because they were thought to have primary brain lesion; in others the brain metastases are part of a widespread dissemination of cancer that would not warrant a craniotomy for histologic confirmation.

Dr. Rubinstein: I was raising this question for the sake of discussion. I would like to ask Dr. French, a neurosurgeon, whether it is not a very well known fact clinically, that operation for any form of tumor, whether malignant or benign, is often followed by a remarkable clinical recovery.

Dr. French: Indeed they are often followed by improvement. I would like to put in a plea not to indiscriminately irradiate patients just because they had a primary lesion some place and they show on angiogram or clinically, an intracranial lesion. I think this is very bad. I firmly believe that validation of the lesion should be obtained under any circumstances.

Dr. Regato: In the cases that I am talking about any neurosurgeon would properly refuse to do a craniotomy just for histologic confirmation.

Dr. French: Not necessarily. If there is some question of the character of the lesion, it should be biopsied. It should be taken out if it can.

Dr. Regato: Oh, it is not only a biopsy that you propose; you mean that the lesion should be resected.

Dr. French: I think one of the easiest lesions for a surgeon to remove is a metastatic lesion.

F.R. Dutra, M.D., Castro Valley, California: I think that there are patients being unnecessarily operated upon; not just minor operations, but craniotomies which I regard as quite a bit of surgery, in patients with tumors that are well known to have a predisposition to metastasize to the brain. When the metastases appear and are recognized in the brain, I think it is superfluous and extremely traumatizing to the patient and devastating to the patient's family; also in some cases, financially, to subject them to a craniotomy in order to obtain a piece of tissue before they go to radiotherapy.

Dr. French: This is a lack of understanding of what we do at the time of surgery; we don't biopsy a metastatic nodule, we take it out. It is the easiest tumor to remove; if you have a patient that is aphasic and hemiplegic with increased intracranial pressure, who has had a carcinoma of the lung, you better take the lesion out rather than irradiate him, because he can recover.

E. Chobot, Jr., M.D., Grand Junction, Colorado: I have had, in my practice, a patient operated for a metastatic carcinoma of the lung to the brain, still playing golf 12 years after operation.

J. Kepes, M.D., Kansas City, Kansas: I feel very strongly that in most instances you just cannot know whether or not you are dealing with metastatic carcinoma until you look at it under the microscope.

Dr. Rubinstein: I have the impression that many pathologists would agree with this view.

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10. *Reticulum-Cell Sarcoma (Microglioma) of the Cerebellum*

Contributed by **R. L. Wahl, Jr., M.D.** and **M. J. McNally, M.D.,**
Colorado Springs, Colorado

THE PATIENT was a 29-year old woman in March, 1970, when she complained of progressive bilateral temporal pains and vomiting. On examination there was bilateral nystagmus and papilledema and a large area of hemorrhage above the left optic disk. Spinal fluid showed 59 mgm % protein and 38 I.U. of LDH.

Dr. Peterson: Angiograms which were apparently done by the retrograde brachial method on the right side or by catheter injection into the innominate artery on the right side show filling of the internal and external carotid and the vertebral system. There is a trace of contrast medium in the left internal carotid artery in the neck and no major displacement of the intracranial vessels. All of the intracranial vessels are on the small side, although this could be normal. There are no recognizable tumor vessels, although in the AP projection there are some vessels on the right side in the region of the U loop which are disturbing but are not recognizable in the lateral view. In the lateral projection there is a lack of vasculature in the distribution of the posterior frontal branch of the middle cerebral artery with one vessel in this area which has a rather hazy, ragged appearance. This raises the possibility of some vascular abnormality, such as an arteritis, with occlusion of some vessels in this area.

There are no findings which would definitely indicate a neoplasm. There are also no areas which would suggest an aneurysm. An area of vascular pathology in the posterior frontal branches of the middle cerebral artery is suggested possibly with occlusion of some branches in this region.

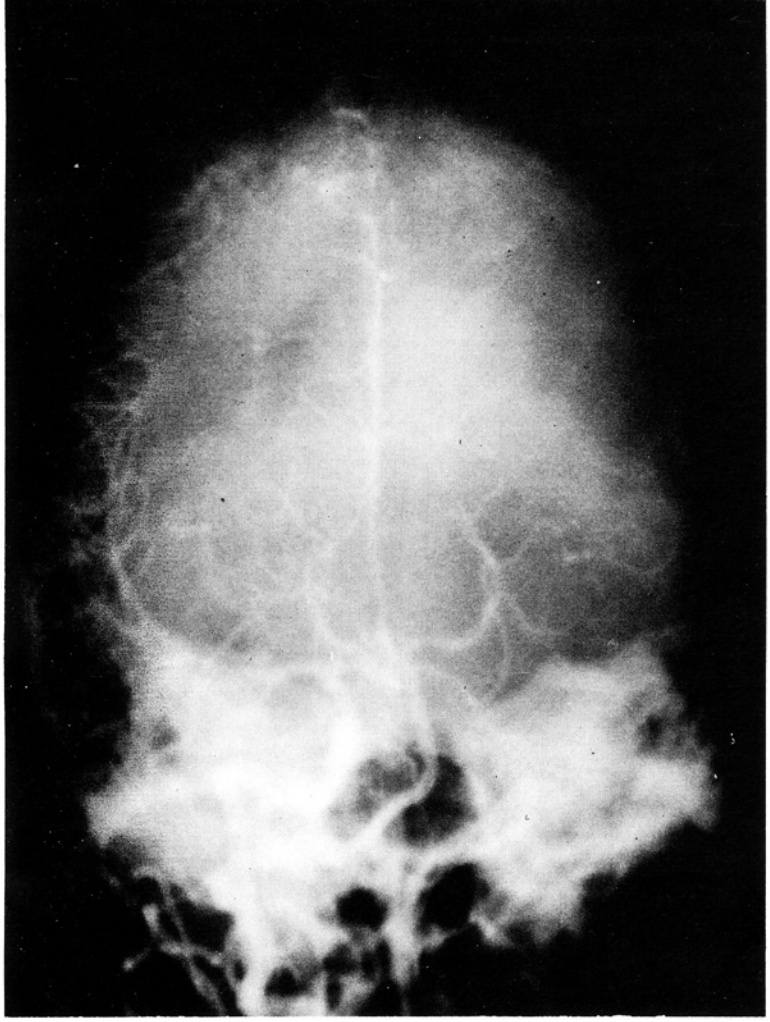


Fig. 1—No recognizable tumor vessels and no major displacement.

Dr. Peterson's impression: Some evidence for a primary vascular abnormality, such as an ARTERITIS.

Roentgenologic impressions submitted by mail:

Hydrocephalus	21
Tumor (posterior frontal, posterior occipital, thalamic, in 4th ventricle, cerebello-pontine, cerebellar, in posterior fossa)	36
Various tumors	25
Non neoplastic	15
Lymphoma	1
Others	15

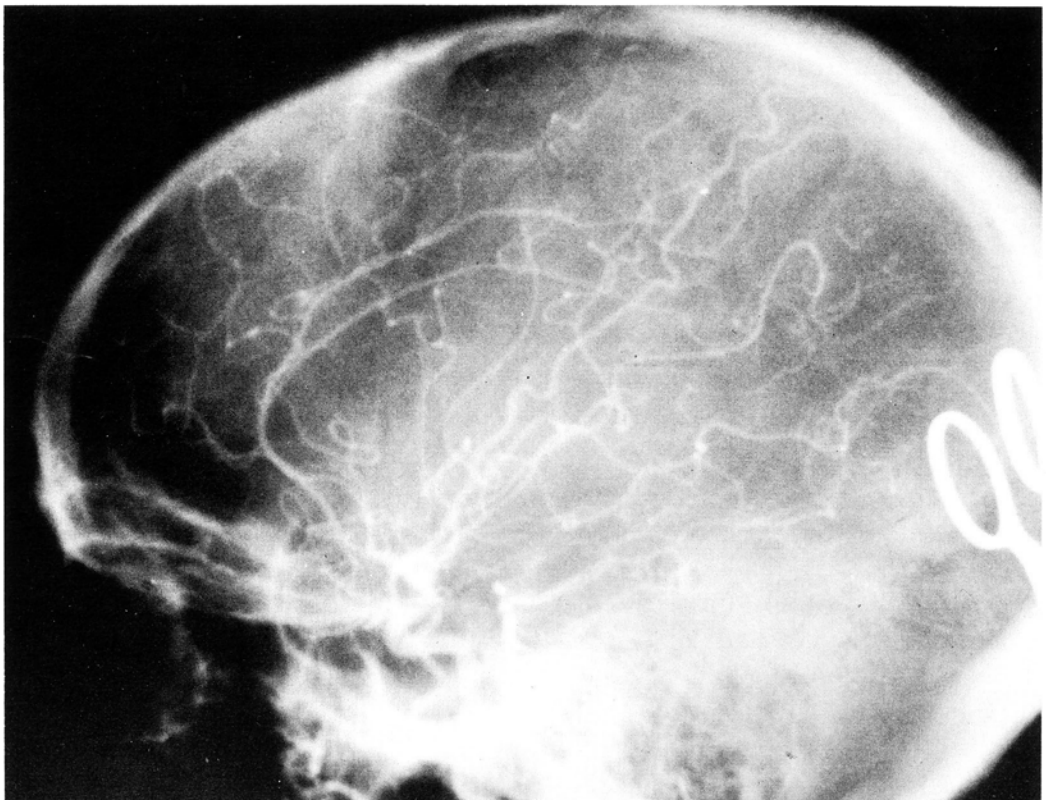
Dr. Peterson: A number of radiologists felt there was hydrocephalus; if you thought there was hydrocephalus, you would look in the posterior fossa or you could go to the 3rd ventricle or the 4th ventricle and seek anything that might obstruct things. If we had had a venous phase AP view we might have been able to make a statement about hydrocephalus.

Dr. Regato: Drs. L.O. Martinez and J. Sheldon, of Miami, offered an impression of cerebellar tumor. Dr. J. W. Barber, of Cheyenne, preferred a thalamic tumor or hematoma.

Operative findings: On March 19, 1970 a sub-occipital craniotomy was done along the posterior midline overlying the inion and extending to the laminae of the first two cervical vertebrae. The dura was opened and there was obvious herniation of the tonsils with a reddish-gray mass underlying the left vertex and lying on the vermis. Piecemeal removal was done with good control of bleeding. The aggregate fragments, yellow-tan in color, weighed 6.5 grams and measured 3.5 cm in their greatest diameter.

Dr. Rubinstein: This piece of tumor is obviously related to the cerebellum, which, in one place, appears to be diffusely invaded by tumor cells. The tumor is highly cellular and has on the whole a remarkably homogeneous appearance. The cells tend to be rather large, spheroidal or notched, with a clear nucleoplasm and coarse chromatin nodes, with frequently small conspicuous nucleoli. The cytoplasm is extremely ill-defined. There is a mixture of other cells of inflammatory nature in places, especially at the periphery. These are mostly lymphocytes, especially around the blood vessels which feed the tumor.

Fig. 2—Lack of vasculature in the distribution of the posterior frontal branches of the middle cerebral artery.



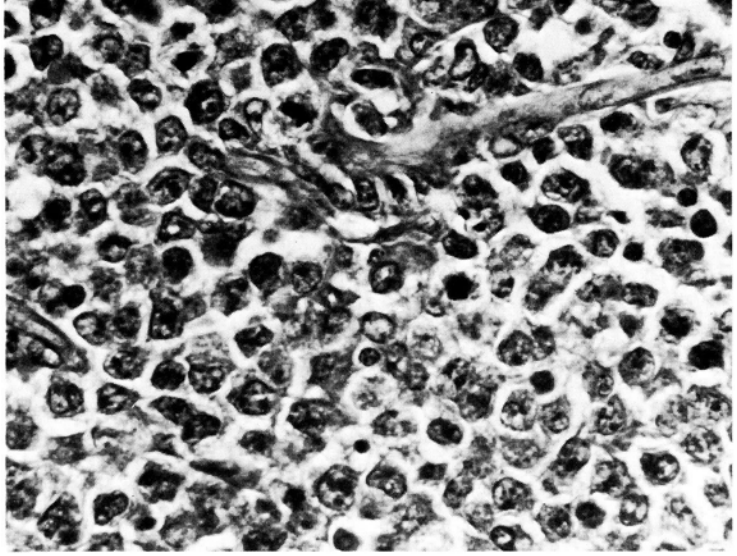


Fig. 3—Relatively uniform cytology of tumor cells, with large spheroidal or notched nuclei containing coarse chromatin nodes and, occasionally, small conspicuous nucleoli. The cytoplasm is ill-defined. Note mitotic figures. H & E x 480.

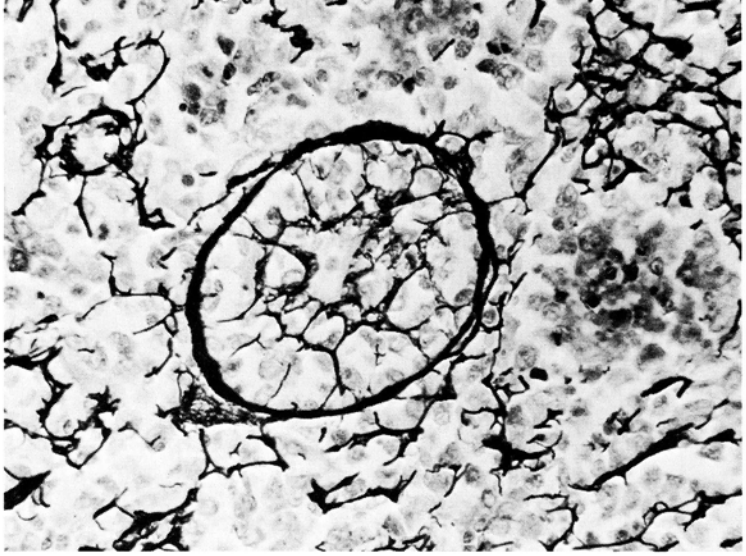


Fig. 4—Characteristic reticulin pattern in tumor, with increase of reticulin fibers in perivascular space and along outer margin of Virchow-Robin space. Gordon-Sweets' silver method for reticulin x 300.

Under the high power, the tumor cells are suggestive of primitive cells of the reticulo-endothelial system. Small multinucleated giant cells are occasionally present. Mitotic figures are numerous, amounting frequently to two or three per high-power field.

The PTAH shows a complete absence of neuroglial fibers. The reticulin preparation shows a rather variable connective tissue stroma throughout. In places, it is rather scanty and confined to the blood vessels, in others it is more abundant, forming a rather loose pattern. In a few there is a conspicuous arrangement of reticulin fibers with a hoop-like architecture around blood vessels, characteristic of tumors of the reticulum-cell sarcoma-microglioma group.

The differential diagnosis in this case lies, in the case of a tumor of uniform cytology originating in the posterior fossa, between a medulloblastoma, possibly of the desmoplastic type, a pleomorphic cell sarcoma, a tumor of the reticulum-cell sarcoma-microglioma group, and an undifferentiated metastatic neoplasm. The microscopic picture is unlike that of a medulloblastoma. Neither the H & E nor the PTAH suggests a primary tumor of neuroectodermal origin. Nor does it have any resemblance to the desmoplastic form of medulloblastoma, sometimes interpreted, erroneously in my view, as a primary "sarcoma" of the cerebellum. The cytology is also somewhat different from a polymorphic cell sarcoma. It consists of large cells with inconspicuous cytoplasm, prominent notched and vesiculated nuclei mixed with inflammatory cells. These features are all in favor of a tumor of the reticulum-cell sarcoma-microglioma group. This interpretation is supported by the characteristic reticulin picture that is found in places. It is unlikely to be a metastatic epithelial tumor.

For the diagnosis of microglioma, silver impregnations are necessary. In the absence of these, it is impossible to decide whether this tumor should be placed among the microgliomas or the reticulum-cell sarcomas. In the absence of this information, it is less committal to place it among the reticulum-cell sarcoma-microglioma group.

Dr. Rubinstein's diagnosis: CEREBELLAR TUMOR OF THE RETICULUM-CELL SARCOMA (MICROGLIOMA) GROUP.

Histopathologic diagnoses submitted by mail:

Reticulum-cell sarcoma (histiocytic lymphoma)	96
Microgliomatosis	14
Pinealoma	9
Ependymoma	5
Metastatic tumor	9
Seminoma! (dysgerminoma)	5
*Astrocytoma	1 !
Others	11

Dr. Rubinstein: Pinealoma was proposed, I suppose, again, because of this juxtaposition of large cells and lymphocytes which is characteristic of the germinoma; it is indeed quite true that the differential diagnosis especially in the floor of the 3rd ventricle does lie between an ectopic, so called ectopic pinealoma or, as it should really be called, a suprasellar germinoma, and tumors of the microgliomatosis group. This is why the diagnosis of seminoma (dysgerminoma) was offered. I would interpret this as analogous to what is called pinealoma. Metastatic tumor is not unreasonable considering the well defined character of this tumor.

Dr. Regato: Dr. A.O. Severance, of San Antonio, and Dr. G. H. Moore, of Colorado Springs, made a diagnosis of lymphosarcoma, reticulum-cell type. Dr. Samruay Shuangshoti, of Bangkok, and Dr. P. Cooper, of Los Angeles, suggested microgliomatosis. Dr. Yvon LeGal, of Strasbourg, preferred malignant pinealoma. Drs. C.R. Vest, of Fort Sam Houston, Texas, and Dr. L.B. Henley, of San Antonio, offered anaplastic ependymoma.

Subsequent history: A diagnosis of primary pleomorphic sarcoma was rendered. Post operatively she was quadreplegic and in response to questions she became agitated, made grimaces and cried. From March 31 to May 5, 1970, her entire cranial contents were irradiated through 2 lateral fields; a total calculated dose of 4200 rads in 35 days was received in the mid-sagittal plane. Her condition did not improve, she had some hematuria and gastrointestinal bleeding, her temperature was markedly elevated and on May 30, 1970, she expired.

Autopsy revealed no residual lesion on the skull, but lesions of histocytic type were identified in the lymph nodes of the mesentery and retroperitoneal regions, and in the liver, small intestine, ovaries, lung, myometrium, bladder, pericardium, heart and kidneys. The bone mar-

row was entirely replaced by cells of the same character.

D. L. Dawson, M.D., Colorado Springs: The patient actually died of peritonitis because of perforation of the ilium where it had been invaded by the tumor. The bone marrow showed total replacement by reticulum-cell sarcoma. The endocardium and myocardium showed a leukemic like infiltrate and the infiltration of the kidney accounted for the hematuri. The bone marrow slides from several sites, the femur, the ribs and vertebrae, showed complete replacement by reticulum-cell sarcoma.

Dr. Regato: Was there any evidence of residual tumor in the brain?

Dr. Dawson: In the brain we found no tumor.

Dr. French: This is a bad disease. Whenever you get a lady, 25 to 50 years of age with a posterior fossa lesion it is going to be a bad disease unless it is an angioblastoma; this is comparatively infrequent in ladies as compared to men. In a patient with a history like this, which is non-localizing except to the posterior fossa, we might well not have done an angiogram. Dr. Peterson would have advised other studies; a ventriculogram was indicated because of the increased pressure. A craniotomy is the procedure of choice and after that radiation therapy; it behooves us all, whenever there is even a question of this type of lesion, to consult with a radiotherapist.

R. M. Sherwin, M.D., Fort Huachuca, Arizona: I was a resident in pathology at the Penrose Hospital when this patient presented with just headaches; during the spinal fluid examination, electrophoresis and enzymes were investigated. I had a chance to extend Dr. Rice's observations on electrophoresis of unconcentrated spinal fluid using the microsome technique. We studied 300 patients, 5 of which had a malignant neoplasm primary in the brain and all 5 of these showed an elevated beta-globulin, as did this patient. Following surgery, in two of them, a repeat spinal fluid examination revealed a beta-globulin back down to a normal range. It may be that this may offer some clinical help in some patients. These observations have been accepted for publication in the American Journal of Clinical Pathology.

Dr. Peterson: Did we find out how the diagnosis was established? Was it a clinical diagnosis and then surgery or were there more radiologic studies?

Dr. Dawson: There were ventriculograms taken just before surgery.

Dr. Peterson: I would like to ask Dr. French would you operate on the posterior fossa without an air study here?

Dr. French: No I would not operate on the posterior fossa without an air study because I think one can do a ventriculogram without appreciable danger; it could benefit the approach to the posterior fossa a great deal. I did not bring up the LDH because doing a spinal fluid test in a patient with bilateral papilledema is not, as a general rule, worth what you gain from it.

W. O. Smith, Jr., M.D., Denver, Colorado: I wonder if Dr. Rubinstein would discuss briefly medulloblastoma in adults. Is it a different entity, how does it present?

Dr. Rubinstein: The medulloblastoma in adults presents the same way as many medulloblastomas in children, except that there is a definite tendency for medulloblastoma presenting in children to occur in the midline whereas many of those that occur in adults, particularly young adults, tend to be in the lateral lobes. Because they arise in the lateral lobe these tumors very frequently tend to invade the leptomeninges very early and may form a rather well-defined mass which may mimic a primary mesodermal tumor. When the pathologist gets the specimen, he too may think in terms of a primary mesodermal tumor because it can be unusually firm and almost woody hard. It is only the microscopic examination that demonstrates, in these adult cases, a very classical pattern of reticulin free areas adjacent to areas showing an intensive reticulin connective tissue network. I am quite convinced from an extensive study of these cases that these tumors all belong to the medulloblastoma group, but the medulloblastoma group is a rather complex entity composed of very anaplastic cells that may occur in children or in young adults. These are probably a truly embryonal tumor composed of cells which are very primitive. Recently we have had an interesting experience in coming across a neonatal cerebellar medulloblastoma which had in fact many other features of the adult type of medulloblastoma, namely, these areas of reticulin free tumor surrounded by areas of large amount of connective tissue. In addition, the case that we observed, and which was reported to Dr. Kadin recently, showed areas which unquestionably merged with a marked neoplastic proliferation of the external fetal granulare. This patient was a neonate who therefore had still its preserved fetal external granulare, so it is quite possible that some of these tumors do arise from remnants, although up to now it has been very difficult to prove this.

Dr. Regato: Regardless of the histogenetic controversy, there is no controversy as to how to best treat medulloblastomas: by means of radiotherapy.

Dr. Rubinstein: It is very important to make this point because there have been patients deprived of the proper treatment because a diagnosis of cerebellar-sarcoma has been made. These patients have not been given the kind of standard treatment they ought to be given, namely irradiation of the entire neuraxis. This is why, I think, this controversy is not simply a semantic one, is not simply a matter of histogenesis, although that is important enough. If you wish to call it sarcoma, it is fine, but the patient better be given the right treatment, which is irradiation of the entire neuraxis.

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11. *Glioblastoma Multiforme*

Contributed by **M. Presti, M.D.** and **M. J. McNally, M.D.,**
Colorado Springs, Colorado

THE PATIENT was a 47-year old woman in April, 1970, when she complained of nausea and right sided headaches. There was a history of "tumor" removed from the arm several years previously; in the past 12 months she had experienced a "crawling" sensation in the right cervical region. On examination there was a papilledema but no neurological deficit; there was a palpable mass on the right side of the thyroid gland which had been present for 3 years.

Dr. Peterson: A single, lateral view in a late arterial phase of a carotid angiogram is available. There are definite tumor vessels occupying an area about 5 to 6 cm in diameter in the mid temporal region superiorly, probably extending into the parietal area and causing elevation of some of the middle cerebral branches as well as stretching and draping of the surface branches of the middle cerebral over the mass. The lesion is relatively round and reasonably well circumscribed.

This lesion could be either a primary glioma, such as a glioblastoma multiforme or a metastatic malignancy.

Dr. Peterson's impression: METASTATIC TUMOR left superior temporal area.

Roentgenologic impressions submitted by mail:

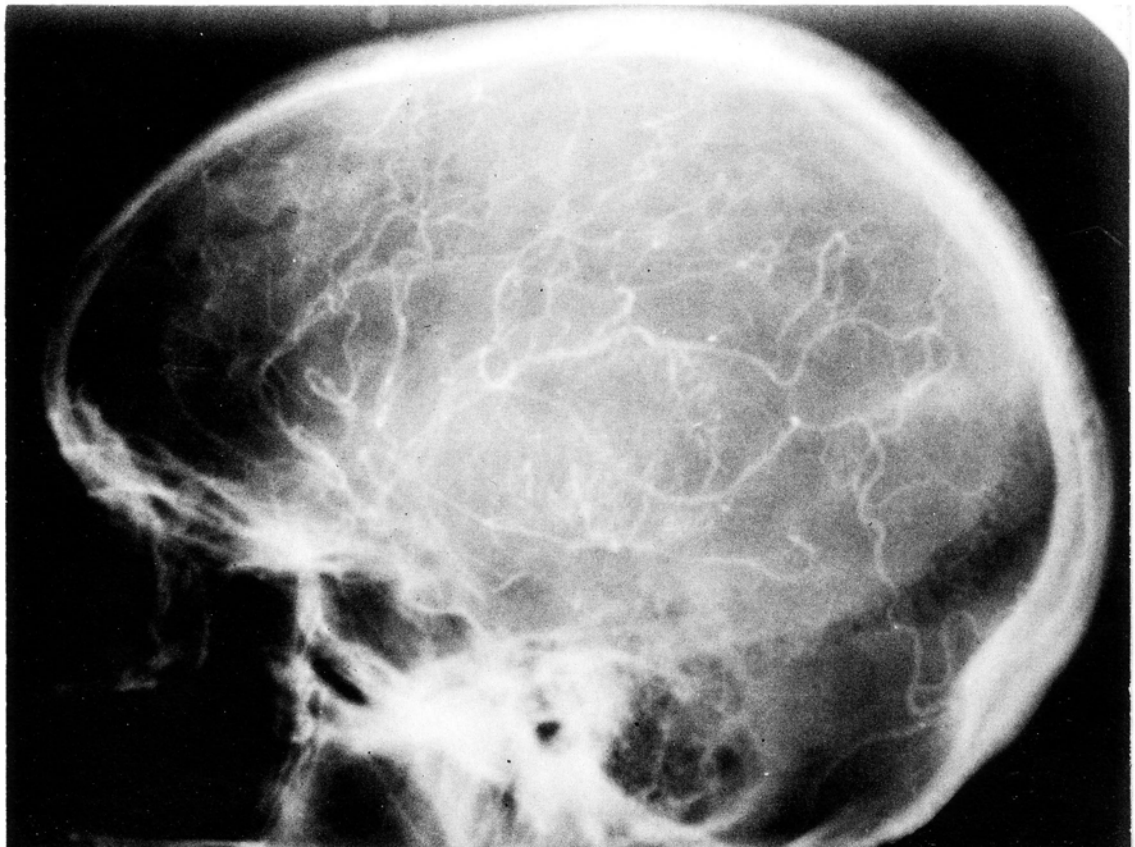
Metastatic tumor	70
Tumor (temporal, posterior temporal, infra-, retro-sylvian, choroid)	34
Others	21

Dr. Regato: Dr. P.H. Riemenschneider, of Santa Barbara, offered an impression of metastatic tumor of the temporal lobe; Dr. K. Hehman, of Cincinnati placed the metastasis in the postero-temporal area and Dr. P. J. Hodes, of Philadelphia, in the infrasylvian area.

Operative findings: On April 20, 1970, a craniotomy was carried out but only internal decompression and biopsy were done. Within several hours she had to be reoperated for further decompression. On June 9, 1960, this patient had a tumor of the soft tissues of the left arm removed by Dr. C.B. Nitka, of Colorado Springs. A slide of this tumor (St. Francis Hospital, 60P-2018) could not be located and the blocks were not found. We inquired from the A.F.I.P. and learned that they had been consulted (Accession No. 963644). Their diagnoses varied from benign mixed tumor to extraskeletal chondrosarcoma; whatever the case it was thought to be tumor with a low degree of malignancy. Dr. F.M. Enzinger was kind enough to loan us their slide which was only recently submitted to Dr. Rubinstein.

Dr. Rubinstein: This is a highly cellular tumor, showing necrosis in places. The microscopic picture is as a rule homogeneous, the tumor cells showing in most places no special architectural features and presenting as darkly staining, usually oval slightly irregular nuclei with a dusky chromatin nuclei. Nucleoli are not conspicuous. Mitotic figures are frequent. The tumor shows abundant vascul-

Fig. 1—Tumor vessels occupying an area in the mid-temporal region, superiorly.



arity, the vessels being usually thin-walled. Vascular endothelial proliferation is present in places. In a few areas, the tumor cells begin to be arranged in a pseudopalisading fashion around small central areas of necrosis.

The reticulin pattern shows that reticulin fibers are not present amidst the tumor cells, but the impregnation outlines the considerable vascularity of this neoplasm.

The microscopic appearances are characteristic of those of a glioblastoma multiforme.

The tumor removed from the arm several years previously is entirely different histologically from the intracerebral tumor, and appears to be a distinct, unrelated lesion.

Dr. Rubinstein's diagnosis: GLIOBLASTOMA MULTIFORME

Histopathologic diagnoses submitted by mail:

Hemangio (sarcoma, pericytoma, Kaposi's)	36
Metastatic (neuro, fibro, leio) sarcoma	25
Malignant (Schwann, neurin, neurilem) oma	24
*Astrocytoma	23
Glioblastoma multiforme	12
Metastatic melanoma	11
Ependymoma	10
Others	18

Dr. Rubinstein: I am really at a loss to explain the wide variety of diagnoses and I, therefore, find it very difficult to comment. I suppose that the spindle shaped cells, the high cellularity, and, of course, the absence of special stainings, to exclude a sarcomatous tumor, was responsible for the diagnoses of sarcoma. The presence of diffuse infiltration at the periphery, I think, would have been in favor of a primary tumor. The suggestion of a malignant Schwannoma or neurilemoma, within the central nervous system, it a somewhat unusual diagnosis; in fact, it is peculiar, although it is possible that such cases do exist and it should be made with the greatest caution. I find it difficult to explain this discrepancy and I really have sort of got to leave it at that.

Dr. Regato: Dr. Samruay Shuangshoti, of Bangkok, and Dr. C. E. Berry, of Colorado Springs, also made a diagnosis of glioblastoma multiforme. Dr. A.O.Severance, of San Antonio, and Dr. H.M. Zimmerman, of New York, offered an unequivocal diagnosis of metastatic malignant melanoma. Dr. J.A. Carney, of Rochester, Minnesota, and Dr. W.J. Pepler, of Pretoria, preferred perivascular fibrosarcoma. Dr. C. Maso, of Chicago, made a diagnosis of hemangiosarcoma.

Subsequent history: On April 21 the patient expired. An autopsy was done. The entire right temporal lobe was found to contain a large hemorrhagic cavity 5 cm in diameter and considerable additional necrosis. There was also some evidence of hemorrhage in the occipital lobe and in the pons. There was no gross evidence of residual tumor but on microscopic examination, foci of residual tumor were found within the extensive necrosis. There was massive cerebral edema. There was no evidence of tumor anywhere else in the body except for the cortical adenoma of the left adrenal and a ganglioneuroma of the cauda equina.

Dr. French: On a 47-year old lady who is really quite normal neurologically and psychologically, after validating the lesion and decompressing her, we would then treat her with radiation therapy. If it seemed to benefit her but for a very short time, we would then give her chemotherapy. We have gone through most all the chemotherapeutic agents and none of them have been really very beneficial as far as we are concerned. We wrote a paper on Mithramicin because we had one patient who did tremendously well but then the next five did quite poorly. We have gone through CCNU, BCNU and so on, I don't think we have an ideal chemotherapeutic agent, but it seems to me that some day that is going to be the treatment of choice for this type of lesion. I presume radiotherapy also might some day become the treatment of choice. I understand that with various types of linear accelerators great things can be done, but I don't know if enough of this has been done around the world yet to validate the results.

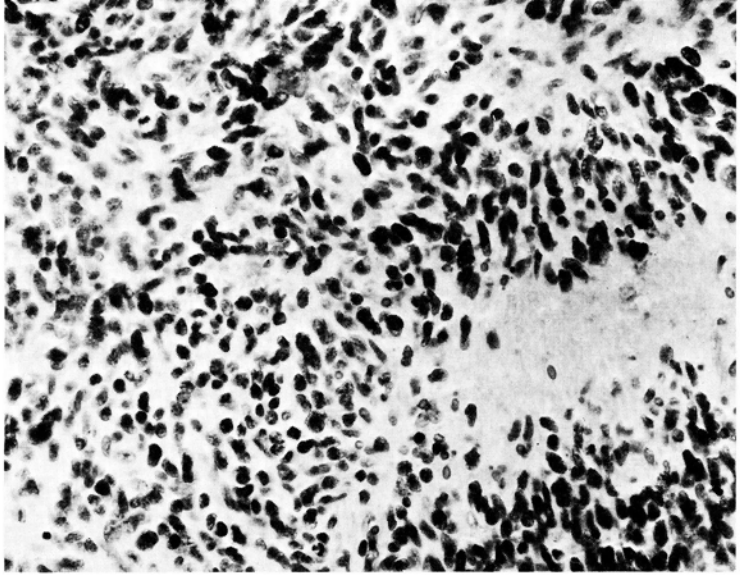


Fig. 2—Closely packed, homogeneous, darkly staining tumor nuclei, showing characteristic pseudopalisades on the right. V. G. x 300.

Dr. Regato: There are few, even among the finest radiotherapists who have a sufficient experience in the treatment of intracranial tumors to claim expertise, but this is not their fault. The fact is that the cases are not being referred to them. It is a matter of the prevailing disbelief, if I can call it so respectfully.

F. P. Bornstein, M.D., El Paso, Texas: The great diversity of pathological diagnoses in this case have perhaps an explanation, because when I looked at the slides that were projected, there was only a very faint similarity to the slides that I received. The areas of mitotic figures were not there. We know that in glioblastoma multiforme you can get perfectly harmless areas that look like astrocytoma without malignant areas. I think that explains much of the diversity, but I just didn't have any areas that looked malignant enough to deserve to be called that. If you cut 500 slides you get variation.

Dr. Rubinstein: I think Dr. Berthrong can reply to that.

M. Berthrong, M.D., Colorado Springs: In this case we used 6 or 7 blocks. Dr. Rubinstein got a slide of all 7 blocks. I think that probably explains it. We diagnosed this tumor as a poorly differentiated glioma. We questioned whether it was a spongioblastoma or a glioblastoma multiforme. In spite of time involved, we look at every tenth slide in the boxes that contain nearly 400 slides; I go down the line and as I looked at it, the tumor blended gradually from one picture to another, as Dr. Rubinstein showed.

Dr. Rubinstein: What about this palpable mass on the right side of the thyroid gland which had been present for three years; was this confirmed pathologically?

Dr. Berthrong: This was a chondroid nodule.

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12. *Metastasizing Malignant Organoid Granular-Cell Myoblastoma (Malignant non-chromaffin paraganglioma or alveolar soft part sarcoma)*

Contributed by **M. R. Abell, M.D.** and **T. O. Gabrielsen, M.D.,** Ann Arbor, Michigan

THE PATIENT was a 36-year old woman in October, 1969, when she complained of headache, dizziness, vomiting and progressive loss of visual acuity over a period of 14 months. Eight years previously she had an 8 cm "tumor" removed from the left leg. On examination there was marked bilateral papilledema, loss of vision of the right eye and left hemianopsia; reflexes were normal.

Dr. Peterson: This is a carotid angiogram in the late arterial phase. There is a rather large lesion about 6 x 10 cm in size in the parieto-occipital area reaching from the midline laterally to the lateral aspect of the brain. This lesion is reasonably well circumscribed and consists of a number of large, tortuous, vascular structures which are very well defined in addition to some smaller, very hazy and abnormal vessels. There are also some larger aneurysmal appearing dilated vessels. There is rapid flow through this vascular lesion with considerable contrast medium recognizable down in the sigmoid sinus during this arterial phase. No films are available when the larger intracranial vessels were filled making it difficult or impossible to judge the amount of displacement of vessels which may be present. The vessels in the immediate vicinity of the lesion superiorly in the parietal area are curved modestly around the lesion. There is some evidence to suggest a slight zone of edema in this area.

The differential diagnosis lies between a neoplasm and an arterial malformation. Many of the rather well formed vessels would fit with an arterial malformation but there are also a number of small, poorly developed vessels which fit better with a neoplasm. The type of neoplasm would be difficult to determine but the possibilities would be a glioblastoma multiforme and metastatic malignancy. The lesion is unusually large for metastasis but it is rather well circumscribed as a metastasis might be.

Dr. Peterson's impression: GLIOBLASTOMA, right parieto-occipital area.

Roentgenologic impressions submitted by mail:

Metastatic tumor	31
Parieto-supra-retro-sylvian	24
Glioblastoma	12
Hemangioma	12
A-V malformation	19
Meningioma	6
Others	18

Dr. Peterson: If one means by hemangioma an arteriovenous malformation, that has some validity, the usual hemangioma does not look like this. Meningioma doesn't seem very likely. I would stick with the metastatic tumor or glioblastoma multiforme.

Dr. Regato: Dr. J.J. Senyszyn, of New York, also suggested a glioblastoma which Dr. P.J. Hodes, of Philadelphia, placed in the post-, supra-, and retrosylvian area. Drs. J. Lemon, of Denver, and A. Schlessinger, of Cincinnati, preferred an A-V malformation.

Operative findings: On October 6, 1969, a right parieto-occipital craniotomy was done. Upon opening the dura a large reddish-purple tumor was seen adhering to the dura; it was very vascular. A cleavage plain was found and the 12 x 6 x 6 cm tumor was separated from the edematons brain. The surgical specimen consisted of two fragments 6 x 3 x 2 and 4 x 2 x 2 cm in diameter; the tumor was lobulated apparently circumscribed, hemorrhagic and in part necrotic but gray-yellow in color in other areas. In July, 1961, the patient, a Japanese national, had been operated at the Tokyo Sanitarium, a Seventh-Day Adventist Hospital, for a tumor of the left leg. An inquiry made by us revealed that she was operated by Dr. Richard A. Nelson, now of Corona, California. He removed the tumor with one-third of the gastrocnemius and part of the soleus muscle. The tumor measured 8 cm in diameter and was firm, homogeneously grayish and very vascular. A histopathologic diagnosis of *granular-cell myoblastoma* was made by Dr. K. Kumegaki who indicated that this was "synonymous" with alveolar soft part tumor or paraganglioma. In spite of numerous efforts a slide of this tumor could not be obtained from the Tokyo Sanitarium; the Tumor Board of the White Memorial Hospital has no record of having been consulted or of receiving the slides from Tokyo. The A.F.I.P. has no record of receiving the slide.

Dr. Rubinstein: This tumor forms a well-defined mass clearly separated from the adjacent brain by a moderately thick fibrous connective tissue capsule. The histological appearance is distinctive. It is composed of collections of large rounded and polyhedral cells with a voluminous, usually eosinophilic cytoplasm, and eccentric nuclei which almost always contain a large prominent central nucleolus. Occasionally, the nuclei are somewhat irregular and hyperchromatic. Mitotic figures are not found. In many fields, a characteristic arrangement is found, the tumor being partitioned by a delicate vas-

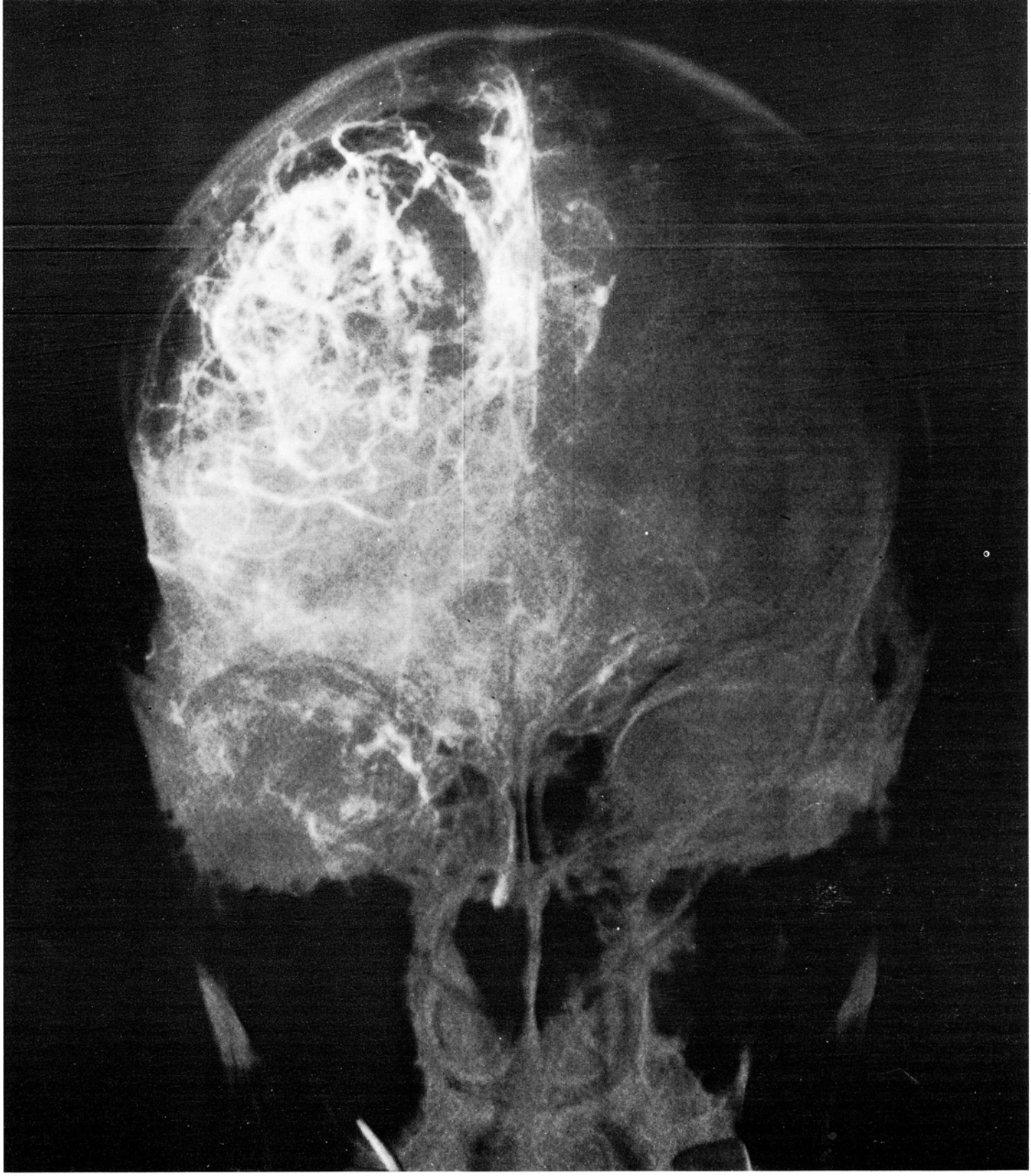

Fig. 1—Substraction roentgenogram of carotid angiogram in arterial phase showing large tortuous vascular structures in parietal area.

cular connective tissue stroma. The tumor cells tend to be attached along one side of their cytoplasm to these fine intersecting partitions, the center of the lobules so formed being sometimes empty of tumor cells. In places, cystic degeneration is present, and the tumor parenchyma is found to contain pale eosinophilic material. The tumor is abundantly vascular, the blood vessels, usually veins, showing a focal mural thrombosis in places.

Under the high power, the cytoplasm of the tumor cells is often incompletely eosinophilic. In places, it is finely granular, in others it contains a central "core" which stains less intensely. In others, it has a finely reticulated or a ground-glass appearance, or is definitely foamy in appearance. Multinucleated giant cells are very occasionally seen.

In places, the tumor shows focal infiltration by chronic

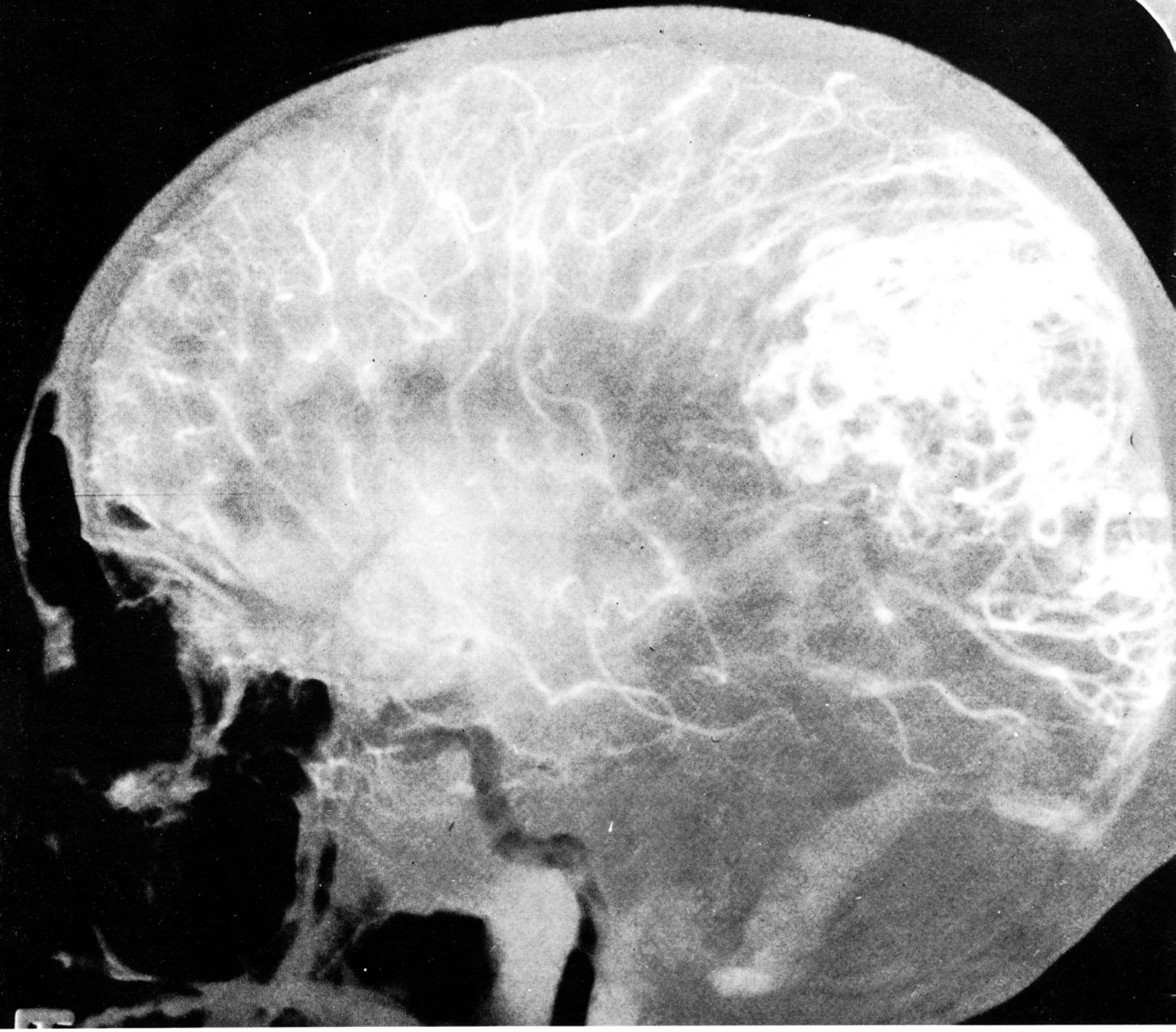

Fig. 2—Substraction roentgenogram showing dilated vessels in parietal region.

inflammatory cells, especially lymphocytes, plasma cells and eosinophils. The PTAH stain provides no additional information. No striations can be demonstrated. The reticulin preparation demonstrates the striking partitioning of the tumor by delicate fibrous connective tissue into large numbers of closely packed lobules. The PAS stain demonstrates the marked PAS-positivity of cytoplasmic granules in the tumor cells in places. In a number of cells, needle-shaped PAS-positive material is also demonstrated, suggestive of a crystalline structure.

This tumor does not appear to arise from the central nervous system parenchyma. Its circumscribed nature, and its subdural location in the parieto-occipital lobe are suggestive of metastatic neoplasm.

The history of this patient having had a tumor diagnosed as "granular cell myoblastoma" removed from the left leg 8 years previously, and the subsequent information that she had a lobectomy of the right lung for what was diagnosed as alveolar soft part sarcoma, are helpful in the histological diagnosis of this neoplasm. From the microscopic point of view, this tumor corresponds faithfully to what has been called a "malignant organoid granular cell myoblastoma," or alternatively "alveolar soft part sarcoma," or again "non-chromaffin paraganglioma." This mysterious neoplasm, originally included among the somewhat nebulous group of the "granular cell myoblastomas" is well discussed in the references quoted.

The differential diagnosis lies with a metastatic car-

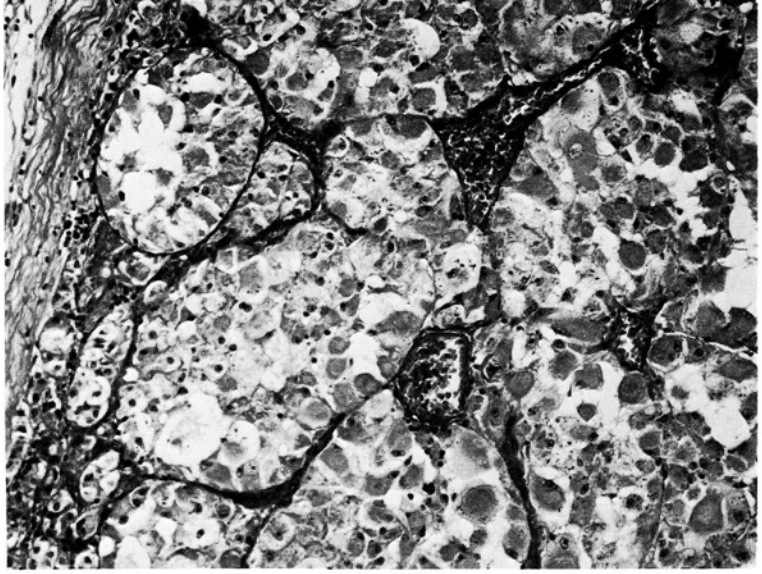

Fig. 3—Low power of tumor, showing lobular formations separated by a delicate vascular connective tissue stroma. Part of the capsule of the neoplasm is seen on the left. The tumor cells are large, rounded or polyhedral, with a voluminous eosinophilic cytoplasm and eccentric nuclei. H & E x 120.

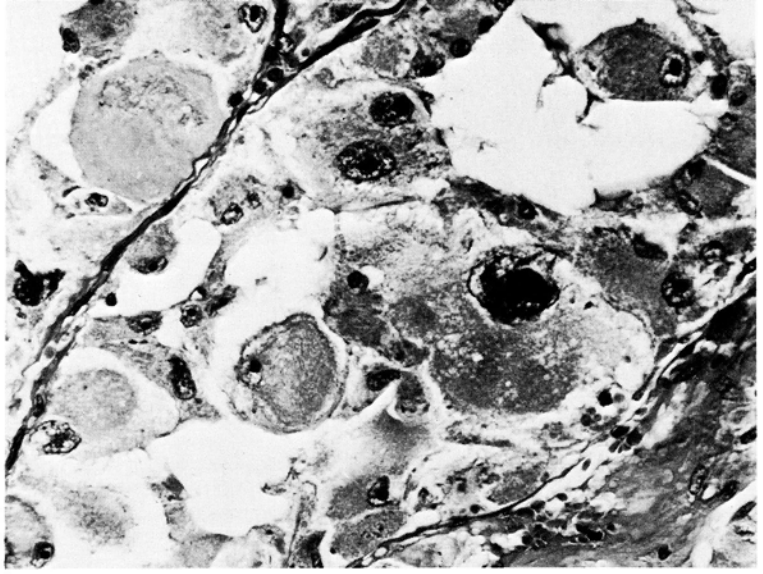

Fig. 4—High power view of large rounded eosinophilic tumor cells, with eccentric nuclei and prominent nucleoli. An occasional binucleate cell is present. Note also an occasional large atypical hyperchromatic nucleus. H & E x 300.

cinoma of the kidney, an undifferentiated carcinoma, a liposarcoma, and even a chordoma.

The malignant behavior of this tumor is well recognized. Widespread metastases, including cerebral, have been repeatedly reported. Intracranial secondary deposits have been listed by Meredith et al., Christopherson et al, and by Smetana and Scott (3 cases).

Dr. Rubinstein's diagnosis: Metastasizing MALIGNANT ORGANOID GRANULAR-CELL MYOBLASTOMA (Malignant non-chromaffin paraganglioma, or alveolar soft-part sarcoma).

Histopathologic diagnoses submitted by mail:

Metastatic alveolar soft-part sarcoma	75
Metastatic granular-cell myoblastoma	17
Metastatic melanoma	6
*Astrocytoma	20
Others	30

Dr. Rubinstein: Alveolar soft-part sarcoma is obviously a fashionable diagnosis and granular-cell myoblastoma is synonymous in this case. Metastatic melanoma should certainly be considered. I understand the diagnosis of astrocytoma because of the superficial resemblance of some of these cells with large gemistocytic astrocytes.

Dr. Regato: Dr. P. B. Putong, of Chicago, and Dr. H. M. Zimmerman, of New York, and Dr. J. M. Loizaga, of Seville, Spain, made a diagnosis of metastatic alveolar rhabdomyosarcoma. Drs. K. Jollinger, of Vienna, J. B. Frerichs, of El Paso, and F. R. Dutra, of Castro Valley, California, worded their diagnosis as metastatic alveolar soft-part sarcoma. Drs. P. W. Gikas, of Ann Arbor, L. Lowbeer, of Tulsa, Felicia Slowik, of Budapest, and R. M. Sherwin, of Fort Huachuca, Arizona, made a clear diagnosis of metastatic granular-cell myoblastoma.

Subsequent history: In January, 1970, a metastatic nodule was found in the right lower pulmonary lobe and in May, 1970, a lobectomy was done and the patient recovered. She had then no other evidence of disease.

Dr. French: This was a metastatic lesion and in spite of the vascularity it is really not too difficult to remove because you really stay out of the tumor. You go around the edge of it and shovel the thing out; even though it looks frightening, the surgical excision of it is not all that bad.

T. O. Gabrielsen, M.D., Ann Arbor, Michigan: This tumor really bled, 14 units of blood were replaced. But it was removed in toto: the patient did improve a lot after the operation and has really done remarkably well. We had, of course, other films and there was no problem for us to see that there was a lot of vascular displacement; we did not consider seriously arterio-venous malformation.

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13. *Intraspinal Malignant Melanoma*

Contributed by **J. H. Clifford, M.D., H. McClintock, M.D.** and **A. Lubchenco, M.D.**
Denver, Colorado

THE PATIENT was a 64-year old man in September, 1964, when he complained of pain in the left arm and shoulder, of 4 months duration. Examination revealed only pain to percussion of cervical vertebrae. The spinal fluid showed 9 lymphocytes per mm^3, sugar 68 mgm% and protein 82 mgm%.

Dr. Peterson: Cervical myelogram demonstrates a mass lesion at the fourth cervical level primarily on the left side. This mass is rather round, but 2 to 2½ cm in diameter and seems to be rather intimately related to the shadow of the spinal cord. There is, however, widening of the subarachnoid space on the left side as compared to the right. There is not the classical recognition of displacement of the cord to the right as one would usually expect to see with an intradural extramedullary tumor. There is no obstruction. There is questionable evidence of an abnormality of the pedicle of the fourth cervical vertebra on the left side.

The differential diagnosis would lie between an intradural extra-medullary lesion, such as a neurofibroma, as contrasted with an unusual intramedullary tumor, which could be either a primary cord tumor or a metastatic tumor to the cord. It would be difficult to clearly separate or differentiate one of these lesions from the other in unusual circumstances. If there is truly an abnormality of the pedicle on the left side, this would favor a dumbbell type of neurofibroma with an intradural component. On the basis of the rarity of intramedullary cord tumors with exophytic projections as well as the rarity of metastatic tumors to the cord it might be well to favor an extramedullary tumor. If there is a pedicle erosion it would be well to favor a neurofibroma.

Dr. Peterson's impression: DUMBELL NEUROFIBROMA at level of 4th cervical.

Roentgenologic impressions submitted by mail:

Neurofibroma, neuroma, neurilemoma, neurinoma	33
Tumor (extramedullary, intramedullary, intradural)	30
Ependymoma	15
Meningioma	22
Others	30

Dr. Peterson: Most of the observers thought of neurofibroma. It is conceivable for a cord tumor to have a portion of it sticking out but I think that would be very rare. Meningioma or neurofibroma could give much the same appearance.

Dr. Regato: Drs. P.H. Riemschneider, of Santa Barbara, K. Hehman, of Cincinnati, and J. C. Lemon, of Denver, also suggested a neurofibroma.

Operative findings: On September 1, 1964, a laminectomy was done from the 3rd to the 5th cervical vertebrae: a brown nodular tumor was found in the subdural space, adhering to the cord, along the left postero-lateral aspect of the cord about the level of the fourth cervical vertebra. The tumor was totally removed with a dorsal nerve root.

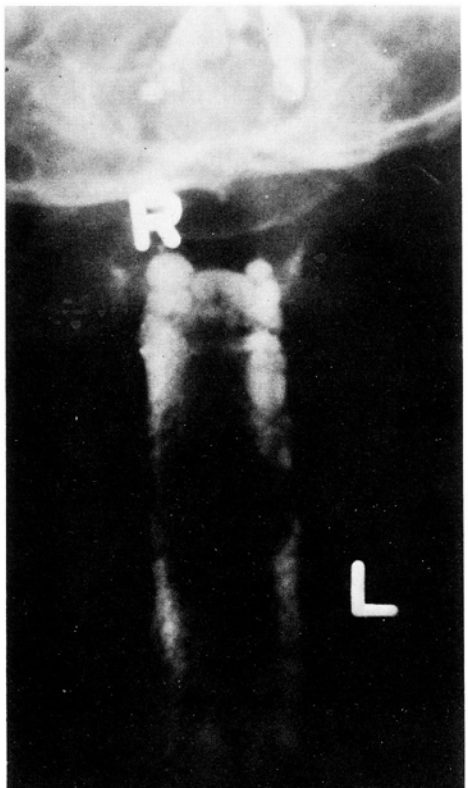
Dr. Rubinstein: This is a highly cellular tumor with a somewhat varying appearance in different fields. In some areas, the cells are arranged in compact intersecting drifts and streams and present elongated nuclei with conspicuous central nucleoli and very indistinct cytoplasmic outlines. In other fields, the cytology is more pleomorphic, the cells being more globular and sometimes multinucleated. Again the nuclei very frequently contain prominent nucleoli. The cytoplasm is often highly eosinophilic. Mitotic figures are present. In some areas, the cells appear to form nests surrounded by a thin layer composed of small flattened cells. The cells within these nests are a little less densely cellular than those outside it. Their cytological features are the same.

A reticulin preparation confirms that there is a very abundant reticulin network which tends to encompass the tumor cells with nests of various sizes. The nests are reticulin-free. These appearances therefore are similar to those of other tumors that metastasize in the subarachnoid space, such as metastatic carcinomas, gliomas, especially medulloblastoma. This is interpreted as a desmoplastic reaction on the part of the meningeal fibroblasts resulting from tumor invasion.

A prominent feature is the presence of a considerable amount of brown pigment in the tumor cells. This pigment is argentaphilic with the Fontana silver preparation.

The microscopic appearances are those of a milignant melanoma in the subarachnoid space. Whether this is a metastasis from a focus elsewhere in the body, or from a primary within the central nervous system cannot be

Fig. 1—Myelogram showing rounded mass in cervical region.



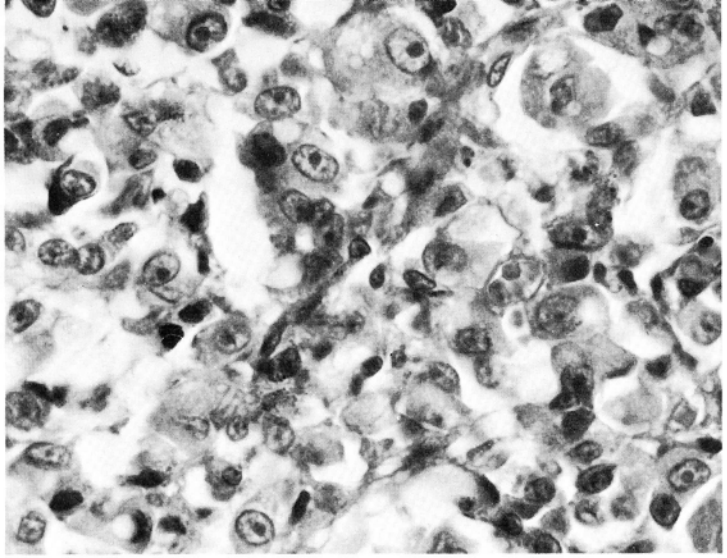


Fig. 2—High power of tumor cells with globular cytoplasm and conspicuous, occasionally eccentric, nuclei with prominent nucleoli. Some of these cells contain melanin pigment. H & E x 640.

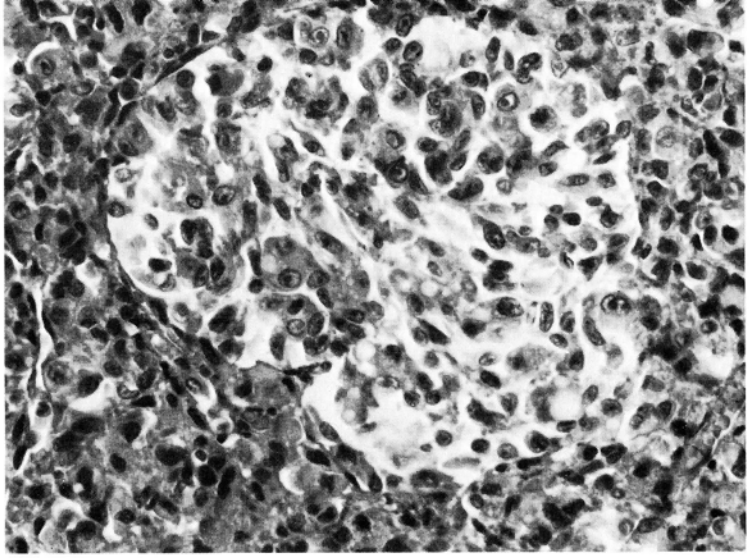


Fig. 3—Frequently, the cells appear to form nests of lesser density, separated from the remainder of the tumor by a delicate membrane. H & E x 300.

stated from the microscopic preparations. Melanomas are known to occur occasionally as primary malignant tumors within the central nervous system. They then usually arise from the leptomeninges. They may originate both from the brain or, rarely, within the spinal cord.

Dr. Rubinstein's diagnosis: INTRASPINAL MALIGNANT MELANOMA

Histopathologic diagnoses submitted by mail:

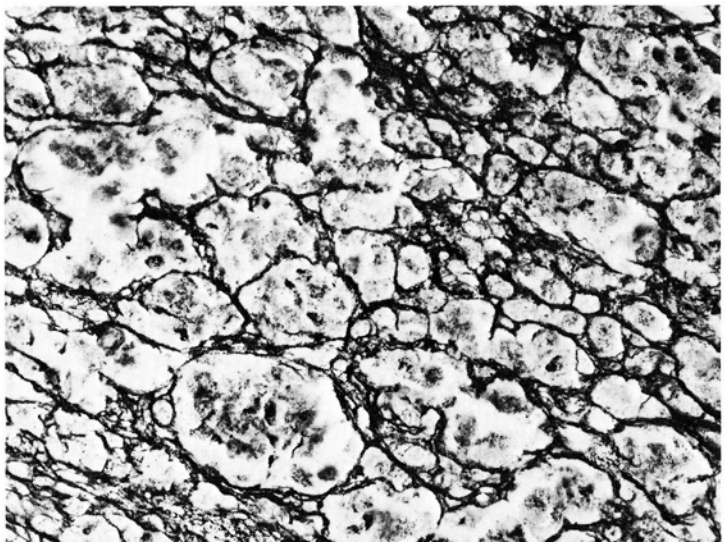
Malignant melanoma	90
*Astrocytoma	15
Meningioma	12
Metastatic carcinoma	5
Others	22

Dr. Rubinstein: There is little evidence, from a cytologic point of view, that these cells look like astrocytic cells. I am curious as to the other diagnoses.

Dr. Regato: I will list them for you: Ependymoma, malignant neurinoma, meningioma, hemangioblastoma, ganglioneuroblastoma, myeloma, metastatic carcinoma, rhabdomyosarcoma, chromaffinoma, sarcoma, periangioma, chordoma and xanthoma.

The observed pigment must have appeared unequivocal evidence of malignant melanoma to the experts: practically none dissented.

Fig. 4—A reticulin preparation confirms the presence of an abundant reticulin network which separates tumor cells into nests of various sizes. This is the result of infiltration of the subarachnoid space by melanoma, with the production of a desmoplastic reaction on the part of the meningeal fibroblasts. Gordon-Sweets' silver method for reticulin x 300.



Subsequent history: Eighteen months after the surgical intervention the patient presented memory deficits, mental confusion, blurred vision, headaches and weakness of the lower extremities; he developed pneumonia and on August 4, 1966, he expired. At autopsy numerous black nodules were found in the frontal and parietal cerebral lobes, in the cerebellum, the meninges, the pituitary, the liver and spinal cord.

Dr. French: Doing the myelogram certainly was appropriate in an individual with this symptomatology. One seldom has any evidence that the lesion is going to be melanoma, unless they have had a previous melanoma. One should consider very strongly going ahead with the laminectomy shortly after the myelogram, that is the same day. Those I am speaking about are primarily those with a total block. I thought this was probably a neurofibroma and most likely a dumbbell type of neurofibroma. I think that Dr. McClintock, if he operated on the patient, probably suspected this was a melanoma at the time of surgery by its appearance and by its adherence.

Dr. Rubinstein: Numerous nodules were found scattered throughout the central nervous system, at autopsy, and we are also informed that deposits were found in the pituitary and in the liver. It is not impossible, of course, for a primary melanoma in the central nervous system to metastasize extracranially; I know of one really well authenticated case published in the literature, the one by Salm, where an extremely meticulous examination was made to exclude a primary elsewhere. Knowing how frequently small primary lesions may be missed, I would ask whether in fact the autopsy was preformed in this case with sufficient care and thoroughness to exclude a possibility of a small primary elsewhere than in the central nervous system, because of the presence of metastatic deposits in the liver. One should exclude the possibility of a small primary in the skin, scalp, various internal organs, including the adrenal, and the rectum, and, of course, the eyes and the choroid.

J. H. Clifford, M.D., Denver, Colorado: I performed the autopsy, there were about 30 or more nevi on the skin and I did not obtain any samples from these. On gross examination they all looked benign, but that is the best I could do. The optic fundi were examined carefully by an ophthalmologist when the patient was alive and his opinion was that they were negative.

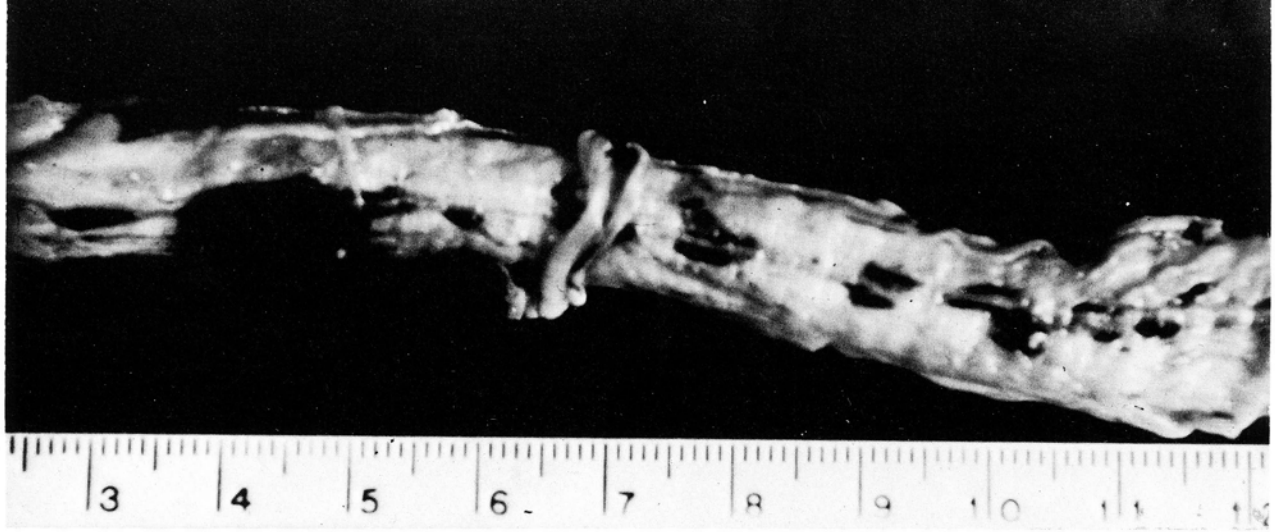


Fig. 5—Autopsy photograph of spinal cord.

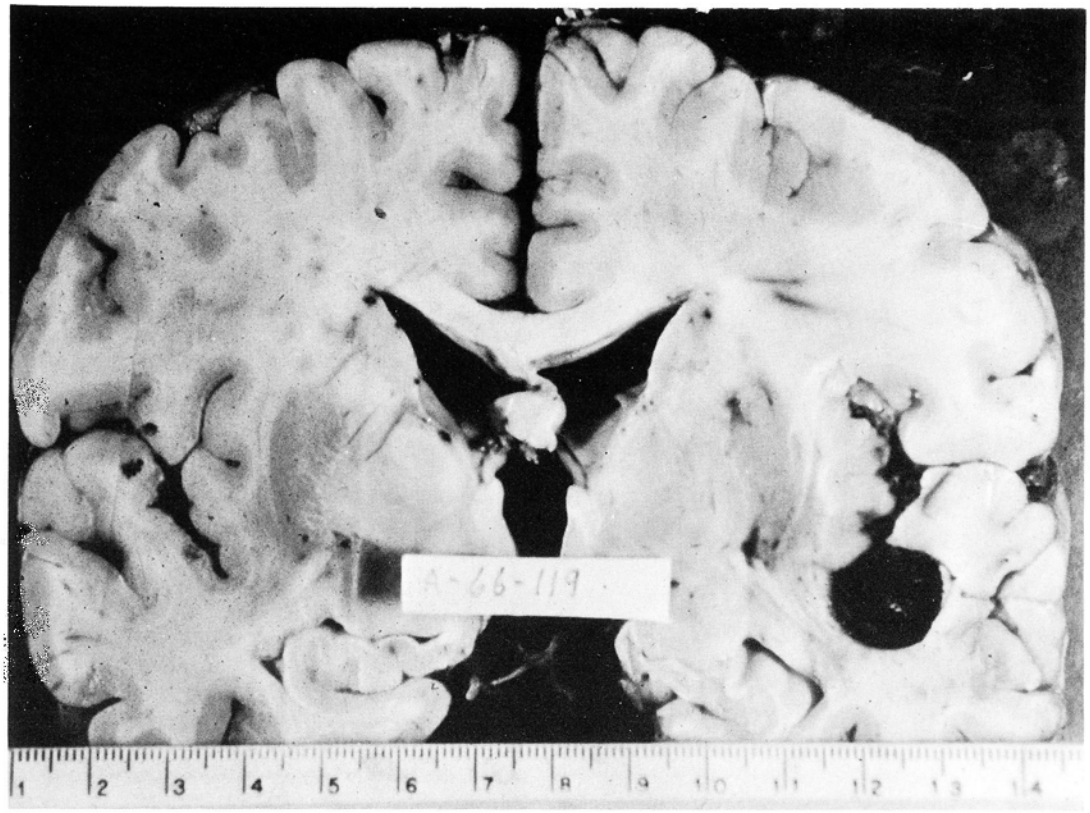
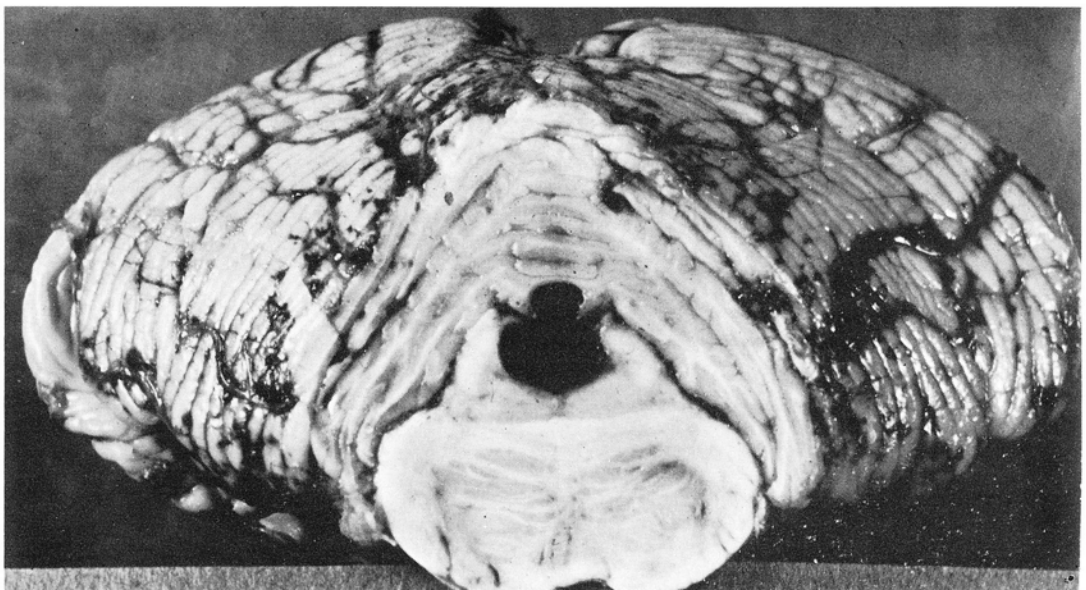


Fig. 6—Autopsy section of brain.

Fig. 7—Autopsy photograph of cerebellum.



Dr. Rubinstein: It is not impossible theoretically that primary melanoma should metastasize extracranially. Do you have any further evidence of a path where it spread? Could you find for instance, vascular invasion by the primary in the central nervous system that might give you an idea as to how it spread to the liver?

Dr. Clifford: I didn't find any evidence of intravascular spread in the sections, but I examined those several years ago; it would be interesting to go back and look at those again for that.

Dr. Regato: In a very large number of cases of melanoma that came to autopsy, 15 percent had no identifiable primary.

L. Lowbeer, M.D., Tulsa, Oklahoma: We had a case where there was extensive metastasis to the liver and there was no history of previous removal of a tumor. At autopsy I stripped off the foreskin and the glans penis looked as if painted with a black brush. This had escaped every physician who had catheterized this patient.

Dr. Regato: If it is rare, Dr. Lowbeer has seen it.

V. Lopez, M.D., Columbia, Missouri: At the Roswell Park Institute we saw one case of melanoma of the cervix; there are many others reported.

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14. *Polymorphic-Cell Sarcoma of Bone Invading the Spinal Cord*

Contributed by **Leo Lowbeer, M.D.,** Tulsa, Oklahoma

THE PATIENT was a 10-year old boy in July, 1966, when he suddenly presented paralysis of the lower extremities and bladder, accompanied by fever. On examination he appeared emaciated; the spinal fluid showed 1125 mgm % of proteins.

Dr. Peterson: Myelogram shows a complete obstruction of the opaque column at the level of the second lumbar vertebra. At the area of obstruction the column comes to a tapered point which is most compatible with an extradural compression of the entire dural sac at this level. There are no recognizable bony abnormalities in the lumbar spine as seen on the myelogram films. There is also a single film of an intravenous urogram which shows contrast medium in kidneys and ureters and in the bladder. The bladder is elongated and displaced toward the left side and indented on the right side by a pelvic mass which is probably related to a very extensive bony lesion involving the right ilium. The right ilium demonstrates a mottled increased density with new bone production and spicule formation on the lateral margin of the ilium just above the acetabulum. The mass lesion which is indenting the pelvis also has a mottled appearance suggesting calcification or ossification within the soft tissues. There is increased density of the right ischium and pubic bone but this could be related to technique and not represent any actual pathology in this area. The lesion in the right ilium is compatible with a malignant tumor, such as a Ewing's tumor, osteogenic sarcoma or neuroblastoma. There is no evidence to suggest a primary tumor of the kidneys. The upper poles of the kidneys are not well visualized, particularly the right one, and the right kidney appears to be tilted a little outwards which raises the possibility of a primary tumor in the right adrenal. Most likely there is a relationship between the malignant tumor involving the right side of the pelvis and the lesion obstructing the spinal canal at the second lumbar level.

Dr. Peterson's impression: Malignant tumor of the right ilium with extension of the soft tissue mass into the true pelvis displacing the bladder, possibly an OSTEOGENIC SARCOMA. Extradural compression of the dural sac at the second lumbar vertebral level representing extradural metastases from the tumor in the pelvis or possibly metastases from other primary which has also metastasized to the pelvis.

Roentgenologic impressions submitted by mail:

Metastatic tumor	15
Malignant "lymphoma"	30
Ewing's tumor	10
Various neurogenous tumors	24
Inflammatory lesion	18
Others	30

Dr. Peterson: Lymphoma can mimic almost any bone lesion and some kind of metastatic tumor is certainly possible. I should have mentioned Ewing's tumor. This is not an uncommon site for a Ewing's tumor in the ilium. The Ewing's tumors that I have seen have had a more destructive element than this one has and not so much of that dense new bone formation. These various neurogenous tumors don't seem to me to fit at all. I suppose it is barely possible to have an osteomyelitis. I don't think it fits very well. But the others here are certainly possibilities.

Dr. Regato: Dr. A. Schlessinger, of Cincinnati, offered Ewing's sarcoma of bone. Drs. J.W. Barber, of Cheyenne, and B.A. Zickerman, of New York, considered this an extradural tumor.

Operative findings: In July, 1966, a laminectomy was carried out from the 12th dorsal to the 2nd lumbar vertebra: an extradural tumor was found filling the intervertebral foraminae on the left side. Several tan colored and firm fragments, measuring in the aggregate 3 x 3 x 2 cm were removed.

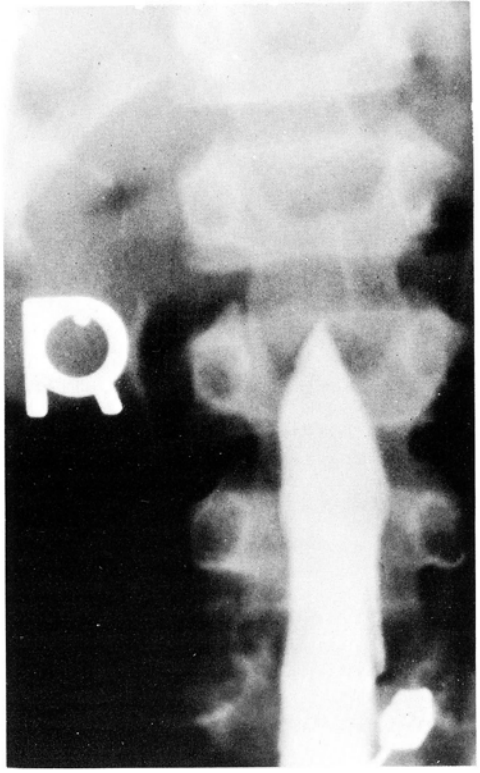


Fig. 1—Myelogram showing complete obstruction at level of second lumbar vertebra.

Dr. Rubinstein: These are multiple fragments, some of which contain viable tumor and others highly necrotic tissue. In a few places it is possible to recognize the main architecture of the tumor, namely that it is lobulated and surrounded by a fibrous connective tissue capsule which sends intersecting partitions into its parenchyma, dividing it into nodules. The cellularity varies from field to field. In some areas, it is scant, and consists of elongated darkly staining cells that send their cytoplasmic extensions into a rather loose and delicately reticulated matrix, possibly composed of mucin or pseudomucin. The denser areas show cells in which the nuclei are round or oval, hyperchromatic, frequently with rather prominent nucleoli, and a cytoplasm which is ill-defined and eosinophilic. Throughout this more cellular part of cytoplasm contains vacuoles of different sizes, some of which relatively small and others quite large, suggesting a somewhat "bubbly" appearance. The cells show a good deal of anaplasia, consisting of irregularity in shape, nuclear hyperchromatism, occasional giant cells, and many mitotic figures. The cytology is therefore definitely suggestive of a malignant neoplasm.

The tumor shows a marked vascularity in places. Some areas are composed largely of young vascular spaces and even resemble a hemangioendothelioma. Large tumor cells are also occasionally aligned to border cleft-like spaces which are covered by very thin endothelial-like cells. Considerable hemorrhage with thrombotic material is present.

A van Gieson preparation confirms that parts of the tumor are surrounded and intersected by collagen. In places, the amorphous strands in the rarified matrix surrounding the tumor cells is moderately PAS-positive.

The gross, histologic and cytologic features are more in favor of a chordoma than any other possibility. A second alternative, well below the first, is some form of teratoma, but there is little in support of this diagnosis.

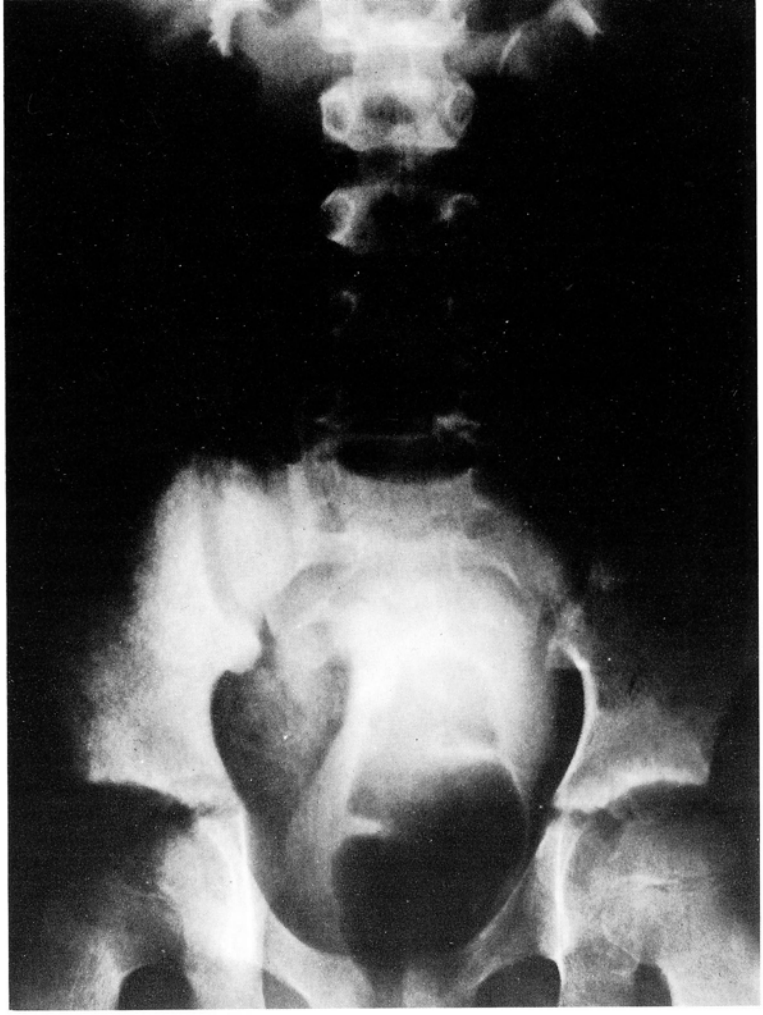


Fig. 2—Increased density of the right ilium.

The presence of extensive necroses, the atypical appearance of the tumor cells and the many mitoses indicate that this should be regarded as a malignant chordoma.

Dr. Rubinstein's diagnosis: MALIGNANT CHORDOMA

Histopathologic diagnoses submitted by mail:

Chordoma	59
Metastatic rhabdomyosarcoma	21
Chondrosarcoma (myxo, osteo)	25
Malignant mesenchymoma	11
Lowbeer's sarcoma	1
*Astrocytoma	8
Others	9

Dr. Rubinstein: On the whole I was fairly well supported. There is not much evidence in the preparation we received of cartilaginous change. Mesenchymoma, presumably due to a somewhat pleomorphic picture, there are areas suggesting a blood vessel tumor.

Dr. Regato: Drs. C.F. Farinacci, of San Antonio, and H.M. Zimmerman, of New York, also made a diagnosis of chordoma. Drs. F.R. Dutra, of Castro Valley, California, Y. LeGal, of Strasbourg, and C.E. Berry, of Colorado Springs, submitted malignant mesenchymoma. Drs. G. Gricouroff, of Paris, and R. Reicher, of Sofia, offered myxochondrosarcoma. Drs. S.W. Kowierschke, of Bryan, Texas, and V.F. Lopez, of Columbia, Missouri, preferred chondrosarcoma, plain. Dr. Dorothy S. Russell, of Surrey, England, submitted a diagnosis of probable polymorphic-cell sarcoma of bone. Dr. L. Lowbeer, of Tulsa, whose case this is, made a diagnosis of anaplastic chondroblastic osteosarcoma.

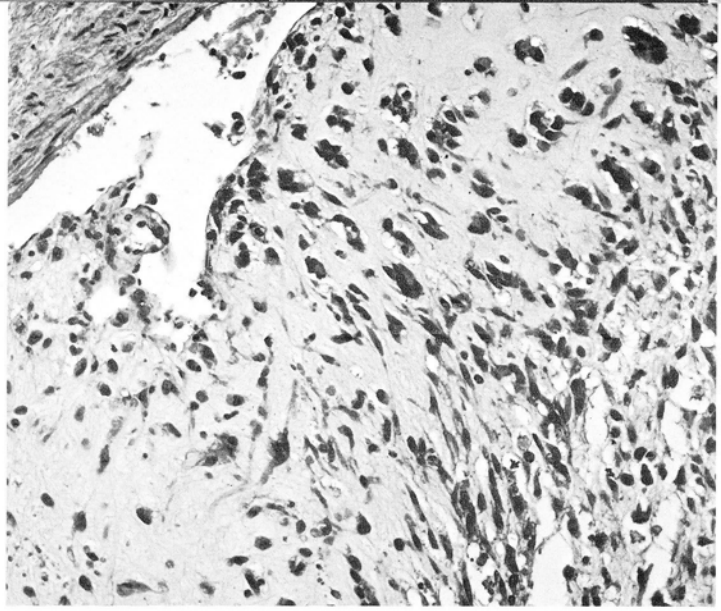


Fig. 3—Low power view of relatively poorly cellular tumor, consisting of elongated and darkly staining cells extending into a loose amorphous matrix. Part of the connective tissue capsule is seen in the left upper corner. H & E x 160.

Subsequent history: Following operation the dense bony area of the pelvic bone became larger and eburnation of the 4th lumbar vertebra became apparent. The liver became enlarged and lung metastases appeared.

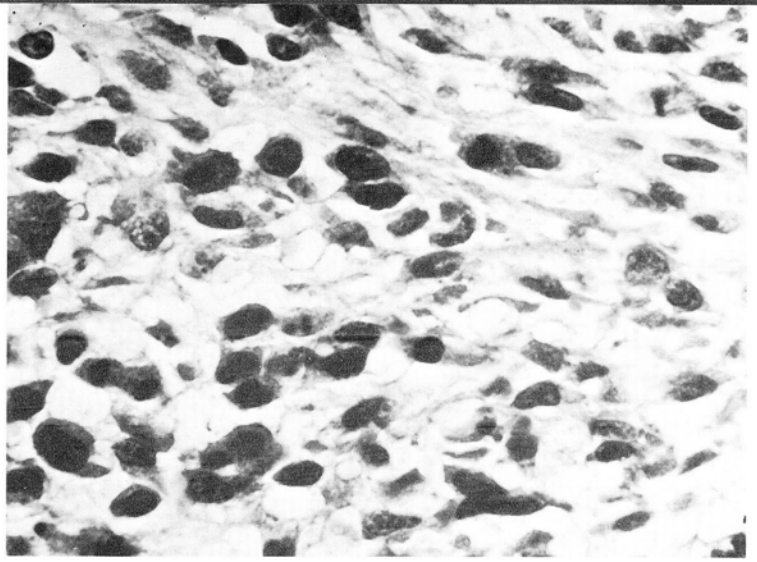


Fig. 4—High power of anaplastic tumor cells, with hyperchromatic nuclei and mitotic figures. H & E x 480.

The patient expired on September 6, 1966. Autopsy revealed extensive infiltration of the skin and muscles in the operative area. There was eburnation of numerous dorsal and all lumbar vertebrae as well as sacral and pelvic bones; sclerotic nodules were found in both femurs and metaphyses of tibias. Numerous tumor thrombosis of the subdiaphragmatic portion of the inferior

Fig. 5—Autopsy photograph of section of the spine.

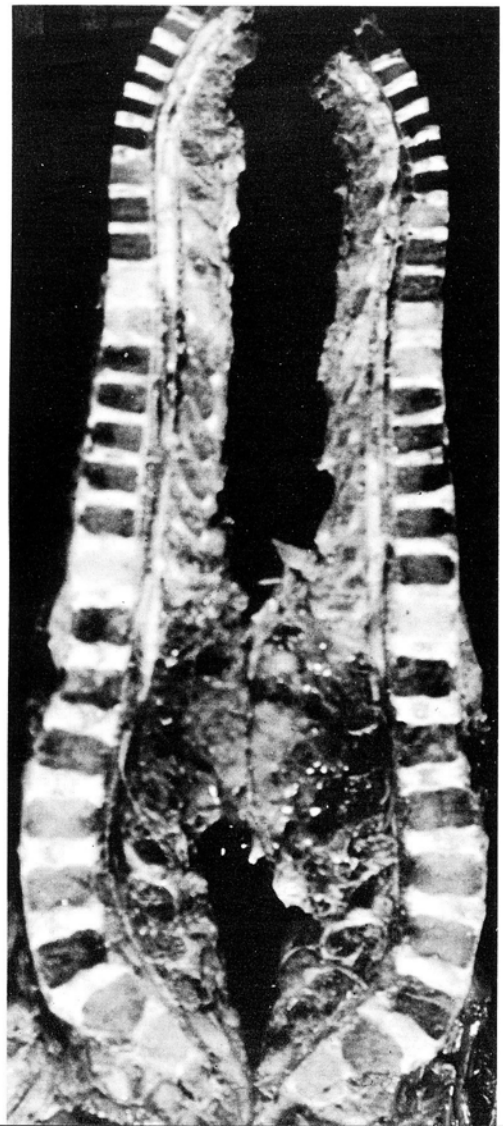
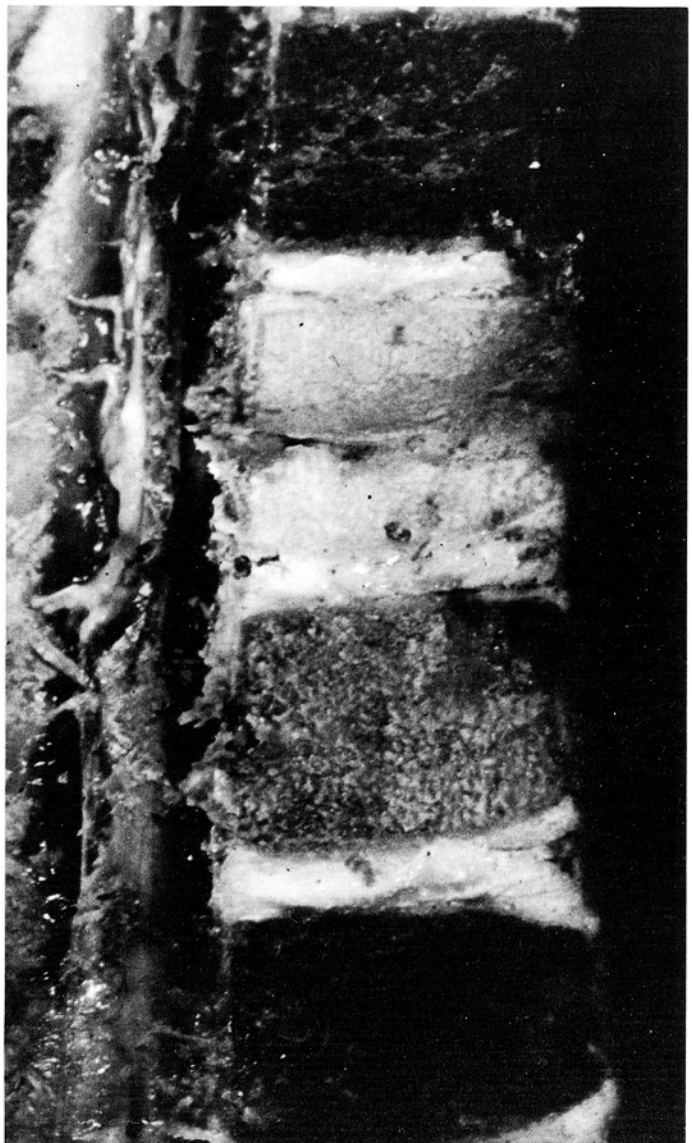


Fig. 6—Detail of vertebral eburnation.



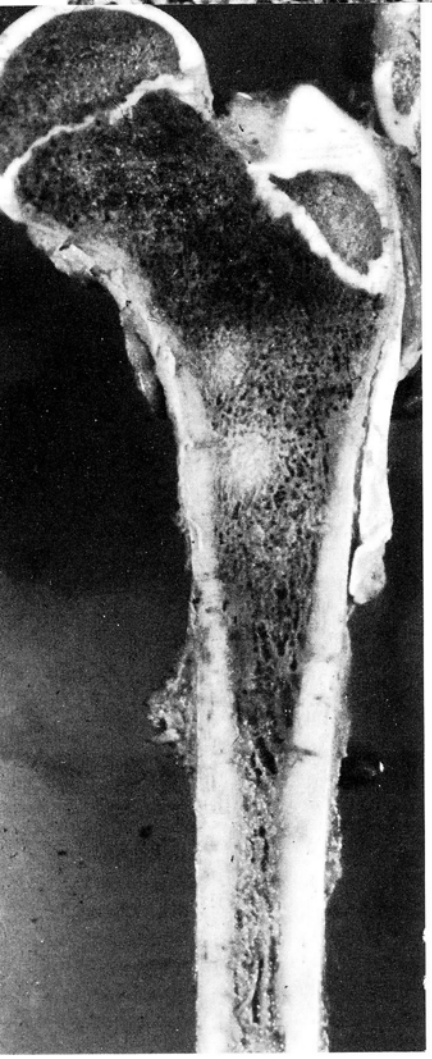


Fig. 7—Section of proximal femur.

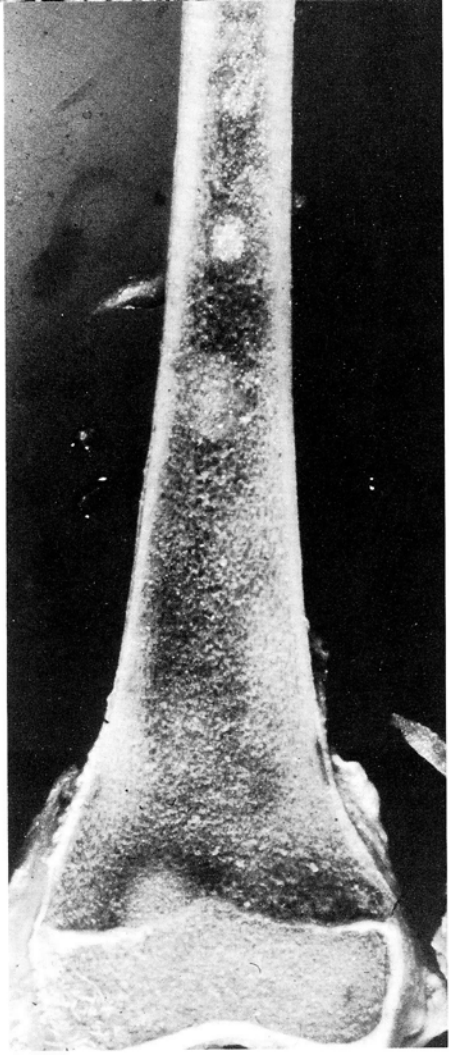


Fig. 8—Section of distal femur.

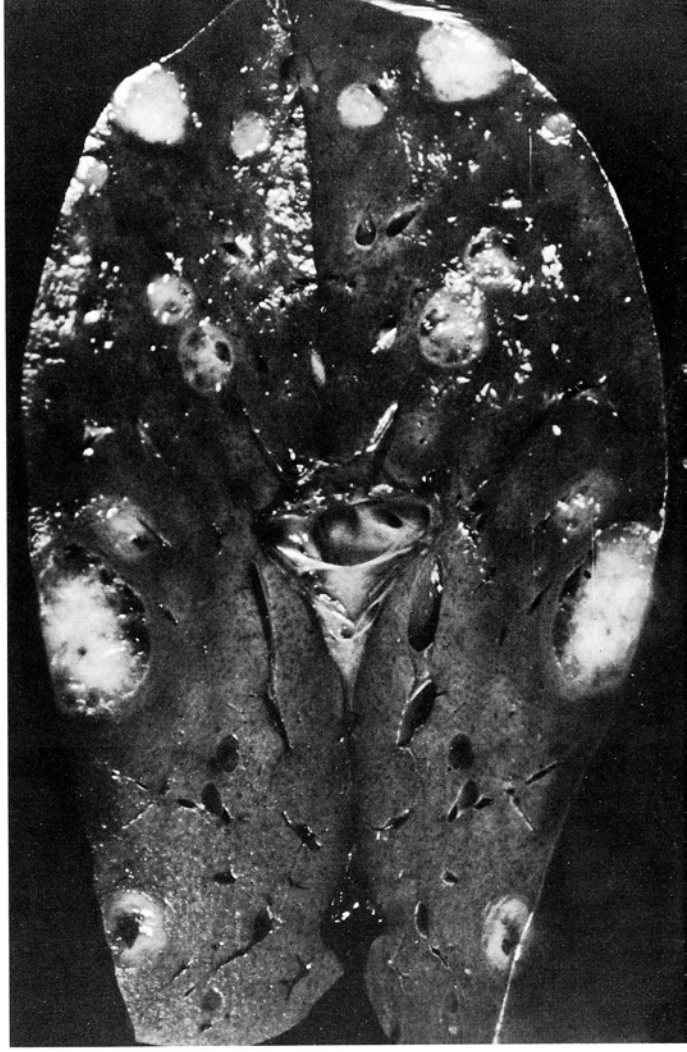


Fig. 9—Metastases to liver.

vena cava and the entire thoracic duct. There were metastates in the retroperitoneal and mediastinal lymph nodes, some of which were grossly cartilaginous; there were also multiple hepatic and pulmonary metastases.

Dr. Regato: Dr. Lowbeer presented 50 beautiful color photographs. I have chosen ten of them and I would like for him to comment as they are projected.

L. Lowbeer, M.D., Tulsa, Oklahoma: This case shows an unusual phenomenon for an osteogenic sarcoma, namely destruction of the disc. Outside the bone the tumor has the histologic character of a chondrosarcoma. There are characteristic metaphyseal foci of osteogenic sarcoma in this type of osteosarcoma. There were metastases to the lungs and one could see their cartilaginous character outside the skeleton. There were similar cartilaginous appearing metastases in the liver. In first biopsy there was an enormous invasion of veins; in addition, there was invasion of many capillaries. If one stains it with trichrome, this substance is found to be osteoid. Chondrosarcomas do not act this way, they do not show the same radiologic picture, which has been so well demonstrated as being characteristic of sclerosing osteosarcoma. There were characteristic foci of osteoid which are best demonstrated in the trichrome stain.

Now one of the pitfalls of this particular tumor is that (a) it looks like chondrosarcoma extraskeletally; (b) some areas look so acellular that one doesn't realize that they are malignant. In 1960 in this Cancer Seminar there was a case presented which was diagnosed as a melorheostosis, but two years later when the patient died in England, his case was published as one of these cases of multicentric osteosarcoma. The question is, was this a multicentric tumor or a tumor with a tendency to metastasize to bones? This particular tumor is extraordinarily aggressive and has a tendency to be multicentric and at the same time it tends to metastasize; it also has a tendency to strangle itself by osteoid. Therefore, the contention that this is multicentric is correct, but it is also correct that it has a tendency to metastasize. The average duration of life is not more than eight months.

Dr. French: When one loses neurological function so suddenly the prognosis is always very poor, because it probably implies a vascular component to the loss. Regaining functions is not likely. I think Dr. Lowbeer should be congratulated.

Dr. Rubinstein: Upon seeing the slides Dr. Lowbeer has projected, I would be inclined to agree with his diagnosis. I take it that from his pictures that he certainly has excluded what seems to be a primary tumor arising in the notochordal region. I was not entirely convinced of the chondromatous element, histologically, but I am sure that this is present in the sections that you looked at. The osteoid tissue is certainly very convincing. Do you base the diagnosis of multicentric osteosarcomatosis on the evidence of venous invasion?

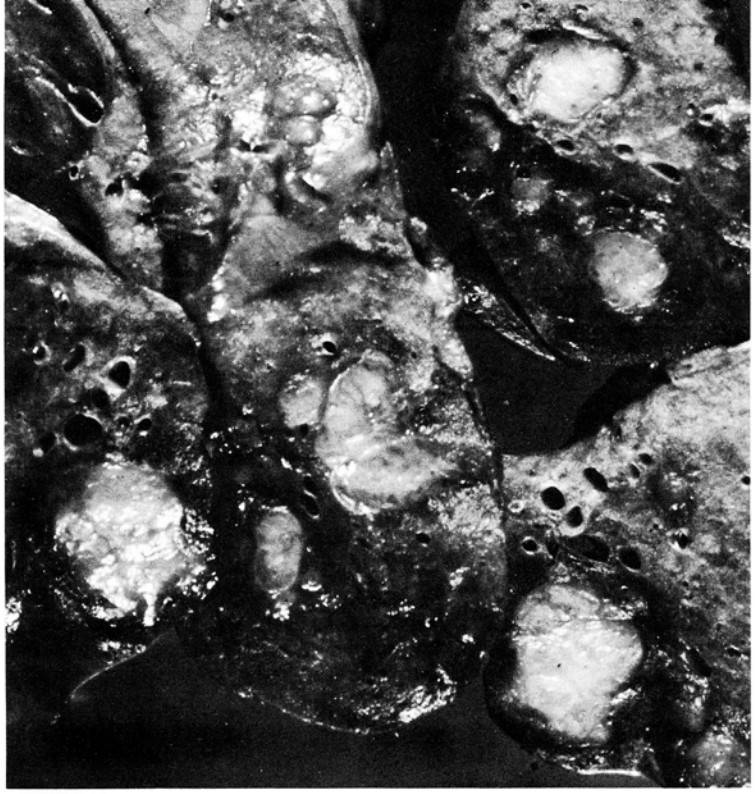


Fig. 10—Metastases to lung.

Dr. Lowbeer: Our idea is that this would be multicentric osteosarcoma due to multiplicity of lesions, the fact that it looked radiologically like a sclerotic variant of osteosarcoma, and that in the biopsy one could find in a predominantly chondroblastic type of sarcoma, areas of osteoid. It was on that basis, and not on the basis of capillary invasion, that I made the diagnosis.

Editor's Note: On reconsideration of the presented evidence and discussion, Dr. Rubinstein changed his diagnosis to that of POLYMORPHIC—CELL SARCOMA OF BONE as suggested by Dr. Dorothy Russell.

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End Case 14

15. *Myxopapillary Ependymoma of the Cauda Equina*

Contributed by **E. Jenis, Maj., M.C., L. Kemp, Col., M.C., J. C. Slaughter, Maj., M.C.** and **D. R. Smith, Maj., M.C.,** U. S. Army, Washington, D.C.

THE PATIENT was a 35-year old man in September, 1969, when he complained of progressive weakness of both lower extremities of three years duration plus recently acquired urinary incontinence. Examination revealed severely lessened strength of all muscles and decreased sensory response plus areflexia of the lower extremities. The spinal fluid showed 230 mgm % proteins.

Dr. Peterson: Myelogram demonstrates an almost complete obstruction at the first lumbar vertebral level. The end of the obstructed column of Pantopaque is concave and rounded with a tongue of contrast medium extending along the left side of the canal with a few droplets reaching above the lesion at the level of the upper border of the first lumbar vertebra. On the right side the contrast extends up for only a short distance and the entire picture of the lower end of the lesion is one of a "capping" effect such as one obtains when the contrast medium is in direct contact with the tumor which usually means the tumor is in the subarachnoid space and extramedullary. There are no definite bony abnormalities.

The appearance of the lesion would fit better with an extramedullary than an intramedullary tumor, although the location corresponds with that might be the tip of the spinal cord. Any of the tumors which might occur in the subarachnoid space probably should be considered, such as neurofibroma, meningioma, ependymoma, cholesteatoma, lipoma or some rare type of cyst. Most likely the tumor is of a relatively benign type.

Dr. Peterson's impression: EPENDYMOMA OF FILUM TERMINALE.

Roentgenologic impressions submitted by mail:

Ependymoma	42
Meningioma	22
Neurofibroma	15
Lipoma	9
Others	40

Dr. Peterson: I think it could be a meningioma, it could be a neurofibroma, it could be a lipoma, it could be others. As long as it is not placed extradurally, it could be any of those.

Dr. Regato: Dr. P. H. Riemenschneider, of Santa Barbara, offered an impression of intradural ependymoma. Dr. B. A. Zickerman, of New York, called it an intramedullary ependymoma and Dr. K. Hehman, of Cincinnati, an ependymoma of the conus medullaris.

Operative findings: On October 15, 1969, a decompression laminectomy was done from the 12th dorsal to the 3rd lumbar vertebra. After opening the dura a sausage-shaped tumor was found in the dural canal, free from the nerve roots but attached to the filum terminale; it was red and hemorrhagic. A complete resection of the tumor and the filum terminale was done. The specimen measured 3 x 1.8 x 1 cm; the tumor appeared encapsulated, hemorrhagic and gray-white in color.

Dr. Rubinstein: This is an apparently circumscribed, slightly lobulated and in most places encapsulated tumor of moderate cellular density and very loose texture. Much

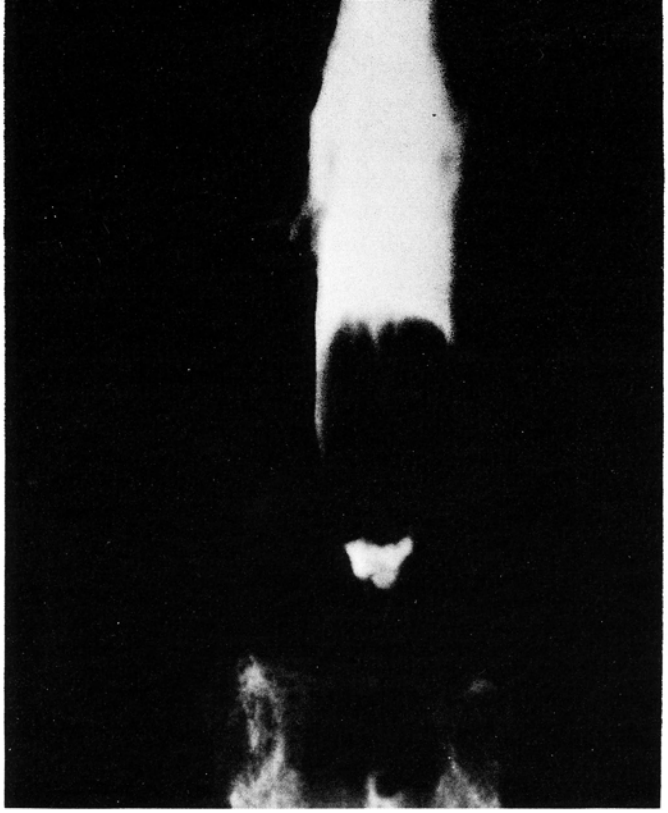

Fig. 1—Myelogram showing almost complete obstruction at level of first lumbar vertebra.

Fig. 2—Gross appearance of tumor and cross section.

of the pattern consists in an arrangement of numerous fairly closely packed microcystic spaces containing pale eosiniphilic or faintly basophilic morphous material and surrounded by a network of highly fibrillated and frequently stellate cells. In some areas, these spaces are lined by cells which appear low cuboidal. At the periphery the tumor cells form strongly fibrillated tapering processes which are attached to the external fibrous capsule of the growth. Here the picture is almost papillary. Within the substance of the tumor a fairly abundant vascular connective tissue is found, onto the blood vessels of which tumor cells again tend to be attached by long fibrillated processes. These processes all taper to a point and do not show any foot plate expansions. The nuclei are usually remote from these cytoplasmic attachments. In a few areas, the architecture is more solid, consisting of closely packed groups of fibrillated cells without other distinctive features. Many of the blood vessels show considerable hyalined thickening of their walls; some are filled with red blood cells, others are empty.

The cytology of the tumor is benign, the nuclei being on the whole ovoid and regular, moderately hyperchromatic, and only rarely atypical. Large hyperchromatic nuclei are, however, occasionally found. Mitotic figures are not encountered.

The PTAH preparation confirms the glial fibrillary nature of the tumor cells.

The microscopic appearances of this lower intraspinal tumor is so characteristic that a differential diagnosis hardly exists. This neoplasm belongs to the group of ependymomas arising in the region of the cauda equina which is included within the designation of "myxopapillary ependymoma." This is known to form a distinct clinicopathological entity associated with fairly typical and easily recognizable histological picture. Stains for mucicarmine were not performed on this case, and the papillary pattern is, admittedly, not very prominent. However, the histological picture is so characteristic that the entity of "myxopapillary ependymoma of the cauda equina" can reasonably be made to include this particular example. The presence of an abundant vascular connective tissue stroma recalls the normal structure of the filum terminale, in which the connective tissue is a continuation of the pia mater. The cells are obviously neuroglial and highly fibrillated. Their recognition as ependymal cells should hinge on the finding of (a) typical ependymal rosettes or canals; and (b) the demonstration of cilia and blepharoplasts in the cytoplasm of the tumor cells. However, neither of these criteria can always be fulfilled, although a more extensive examination in this case might do so. A personal example of my experience with the identical histological picture produced remote metastases in which the characteristic hallmarks indicative of the ependymal nature of these cells, namely the formation of ependymal canals and the demonstration of blepharoplasts, could be demonstrated.

Dr. Rubinstein's diagnosis: MYXOPAPILLARY EPENDYMOMA.

Histopathologic diagnoses submitted by mail:

Myxopapillary enpendymoma	41
Hemangi-, hemangioblast- oma	27
Neurin-, Neurilem-, Schwann- oma	32
Chordoma	15
*Astrocytoma	14
Others	15

Dr. Rubinstein: Quite a number of pathologists thought of a neurilemoma, of Schwannoma, possibly because of the very loose texture of the tumor and because other areas presumably were rather more compact, reminiscent of a palisading arrangement, but a reticulin preparation would show the complete absence of reticulin except in the blood vascular stroma. The picture of chordoma is understandable because of these large vacuolar areas, which mimic it. Astrocytoma is quite a reasonable diag-

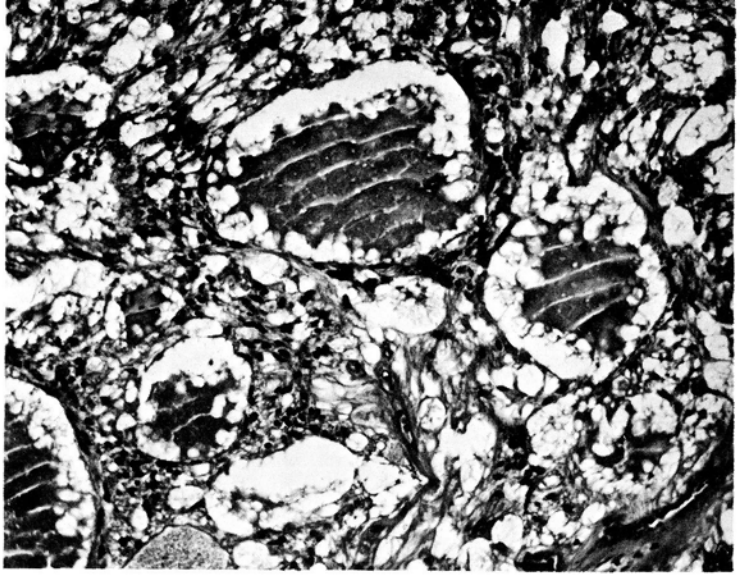

Fig. 3—Microcystic spaces containing eosinophilic material, presumably protein, surrounded by fibrillated, frequently stellate cells. H & E x 120.

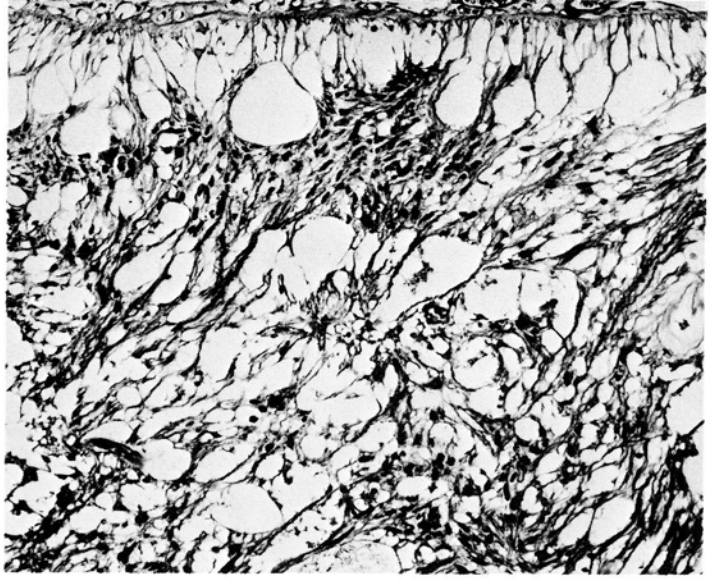

Fig. 4—At the periphery of the tumor, the cells have strongly tapering processes which are attached to its fibrous capsule. Microcystic spaces, which are frequently confluent, are present. PTAH x 120.

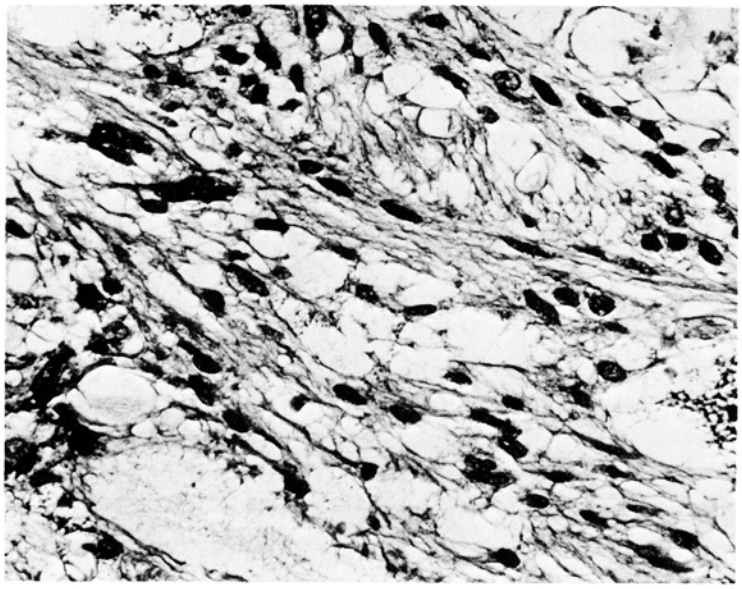

Fig. 5—Groups of delicately fibrillated cells. The fibers are strongly positive with PTAH. It is not possible to say from this micrograph whether the cells are astrocytic or ependymal, but ependymal cells are frequently fibrillated. PTAH x 300.

nosis, because many of these cells do look like astrocytic cells, they are stellate and they have neuroglial fibrils.

Dr. Regato: Dr. Felicia Slowik, of Budapest, also made a diagnosis of myxopapillary ependymoma. Dr. P. W. Gikas, of Ann Arbor, submitted neurilemoma. Dr. G. Gricouroff, of Paris, offered angiomatous neurilemoma. Dr. P. Cooper, of Los Angeles, preferred hemangioblastoma. Dr. H. M. Zimmerman, of New York, hemangioma.

Subsequent history: In January, 1970, the patient had symmetrical ambulatory weakness and sensory loss.

Dr. French: Occasionally a myelogram that does not quite go up to the L-2 or L-1 level will be done for low back pain and the tumor is missed. But, of course, with this profound neurological loss, this would never occur. If you take out an ependymoma of the filum terminale, you ought to remove the filum as far distally as well as proximally. These tumors are radiosensitive also and if I ever operated on a patient such as this and it were not well defined and I thought I could not take it out, I would certainly irradiate that patient. I have followed one patient that I operated on in 1940 and at the present time she has recurrence of her tumor, but she has remained quite stable during these past 30 years.

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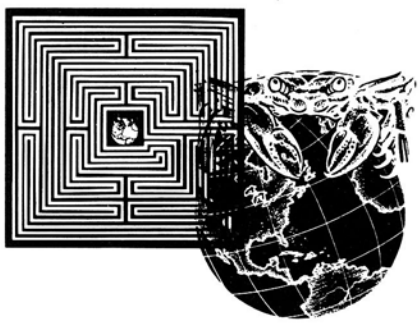


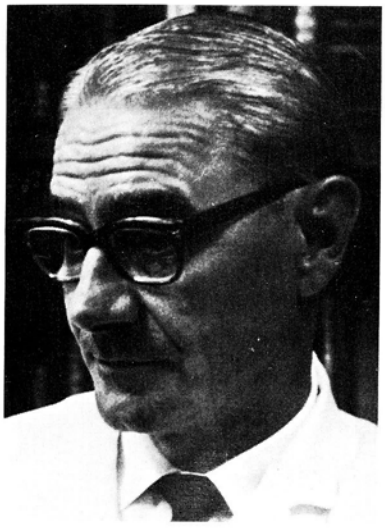
OUR GUEST SPEAKERS

HAROLD O. PETERSON, M.D.

Professor of Radiology, University of Minnesota, a widely known teacher of neuroradiology and a frequent lecturer on this subject. Dr. Peterson is a past President of the American Society of Neuroradiology and one of the best known figures of American radiology.

L. J. RUBINSTEIN, M.D.

Professor of Pathology (Neuropathology), Stanford University School of Medicine. Dr. Rubinstein, a man of considerable experience in the field of tumors of the nervous system, is co-author of a well known text on the subject and has contributed numerous articles to this sub-specialty.



LYLE A. FRENCH, M.D.

Professor and Chairman, Department of Neurosurgery, University of Minnesota Medical School. Dr. French is a former President of the Neurosurgical Society of North America and has abundantly contributed to various aspects of the neurological sciences.