cancer seminar

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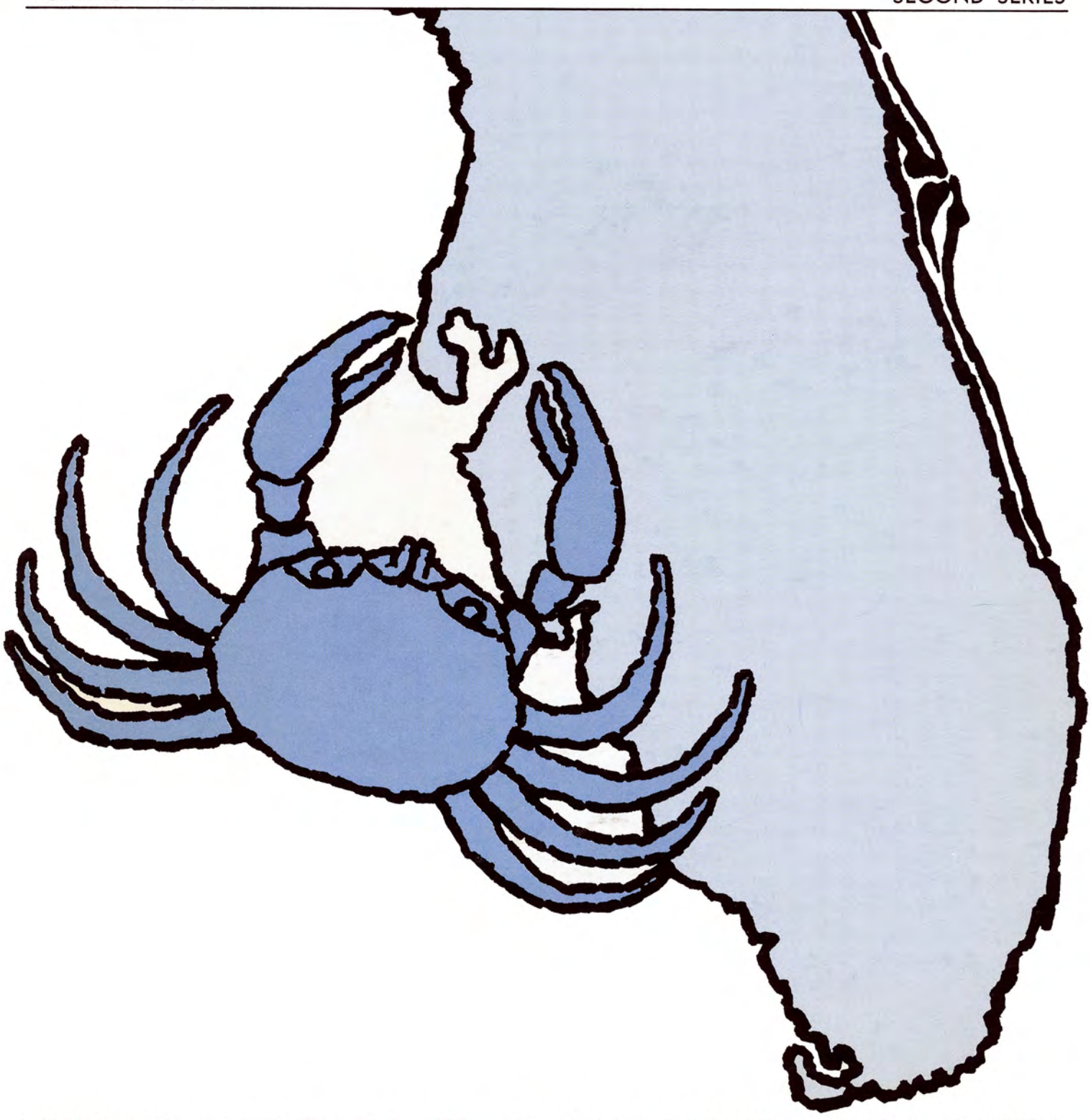

UNIVERSITY OF SOUTH FLORIDA • VETERANS HOSPITAL • TAMPA, FLORIDA

CANCER SEMINAR

SECOND SERIES, VOLUME ONE NOVEMBER, 1977 NUMBER TWO

Juan A. del Regato, Editor

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INTRACRANIAL TUMORS

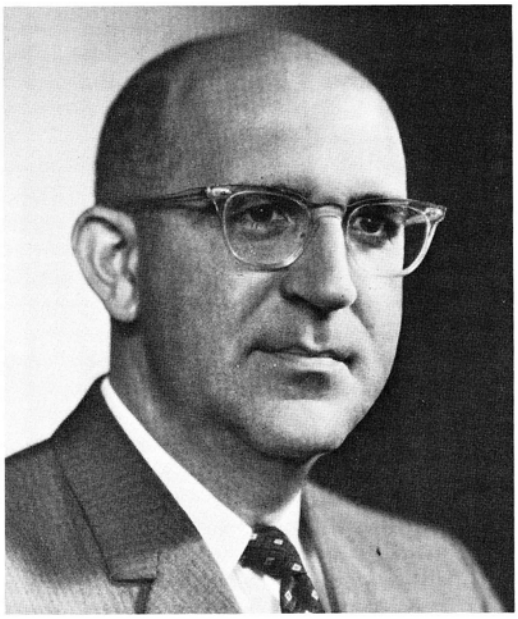
The variety of tumors that may arise from the brain and spinal cord or from the surrounding tissues of the cranial vault and spinal canal may cause protean clinical manifestations that are always a definite challenge to the clinician. The radiologic investigation of these tumors has undergone a remarkable transformation from pneumoencephalograms, ventriculograms, and angiograms to the more recent development of computerized tomography; the metamorphosis has quickened its pace, and the diagnostic momentum is of great interest.

The histopathologic diagnosis of these various tumors continues to require special histotechnical skills and the richness of experience that is not necessarily available everywhere. The surgical and radiotherapeutic measures applied have now undergone the mellowing influence of time and mature observation of results.

This CANCER SEMINAR, held in Tampa on February 14, 1976 under the auspices of the Department of Radiology of the **University of South Florida** and the **U.S. Veterans Hospital,** is now published thanks to a grant of the **Milheim Foundation for Cancer Research.** The reader will be regaled by the expert opinions of our distinguished guest speakers: **Juan Taveras, M.D.,** Professor of Radiology, Harvard Medical School, draws from an amazing wealth of experience in his radiodiagnostic interpretations. **Harry Zimmerman, M.D.,** Professor Emeritus of Neuropathology, Albert Einstein College of Medicine, is an international authority in the histopathologic diagnosis of these tumors. **Raymond Kjellberg, M.D.,** Professor of Neurosurgery, Harvard Medical School, added his experience in the surgical approach to the discussions. The stimulating dissent and additions of members of the audience round out the proceedings.

We are thankful to the contributions as well as to the participants for the excellence of this CANCER SEMINAR. Its publication is the result of our efforts, those of the sponsoring institutions and of the Milheim Foundation to contribute to the continued education of those interested in this exceptionally interesting group of neoplasms.

J. A. del Regato, M.D.
Tampa, Florida
November, 1977



JUAN A. TAVERAS, M.D.

Professor of Radiology, Harvard Medical School, Boston, Massachusetts. Dr. Taveras is a widely famous teacher of neurodiagnosis.

HARRY M. ZIMMERMAN, M.D.

Professor Emeritus of Neuropathology, Albert Einstein College of Medicine, New York, New York. Dr. Zimmerman is an international authority in the histopathology of tumors.

RAYMOND KJELLBERG, M.D.

Professor of Neurosurgery, Harvard Medical School, Boston, Massachusetts. Dr. Kjellberg is an enthusiastic researcher in the field of intracranial tumors.

1. Granuloma of the Frontal Lobe

Contributed by **E. V. Grayson, M.D.**, Hollywood, Florida
and
R. L. Hackett, M.D., Gainesville, Florida

The patient was a 40-year-old man in January 1973 when he complained of loss of equilibrium. For a few months, he had noticed a tendency to veer his car to the right instead of alignment while driving, and there was also somnolence and loss of memory; this was followed by fecal and urinary incontinence. On examination, there was marked ataxia and bilateral positive Babinski signs.

Dr. Taveras: The frontal tomogram demonstrates the presence of a slightly lobulated calcific area consisting of a shell of very dense calcification without much calcium within the area circumscribed by the calcific shell. The tomographic cut passed through the anterior clinoid process at least on the left side. On the right side, it seems to have passed through the base of the anterior clinoid process and the anterior portion of the planum sphenoidale. On the right side in the planum sphenoidale, there is apparent thickening of the bone that extends to a point just beyond the midline on the left side (Fig. 1).

The lateral angiogram shows a separation of the pericallosal artery and the upper margin of the Sylvian triangle, which suggests either ventricular dilatation or elevation of the corpus callosum that pushes the pericallosal artery upwards. I cannot see the exact location and shape of the calcific mass in lateral projection because it is probably covered over by the vessels in the anterior portion of the Sylvian triangle. The location of the mass that appears to be centered at the anterior clinoid process in the A-P tomogram would easily explain the presence of compression of the third ventricle and obstruction at the foramen of Monro leading to dilation of the lateral ventricles. There are no specific features in this angiogram that would help me determine the type of lesion we are dealing with. There are no abnormal vessels, and there is no evidence of displacement of the anterior cerebral vessels in a manner commonly seen in presellar or suprasellar lesions (Fig. 2).

Regarding the nature of the tumor mass, I would tend to favor a lesion that started at the level or above the anterior cerebral artery because there is no evidence of upward displacement of this artery. I would expect that a meningioma that crosses the midline would elevate the lower segments of the anterior cerebral artery, which is not the case here. However, the apparent thickening of the bone in the posterior portion of the planum sphenoidale on the side of the tumor is difficult to explain except on the basis of a meningioma. I wonder if this may not

Fig. 1—Tomogram through the anterior clinoids showing apparent thickening of the sphenoid.

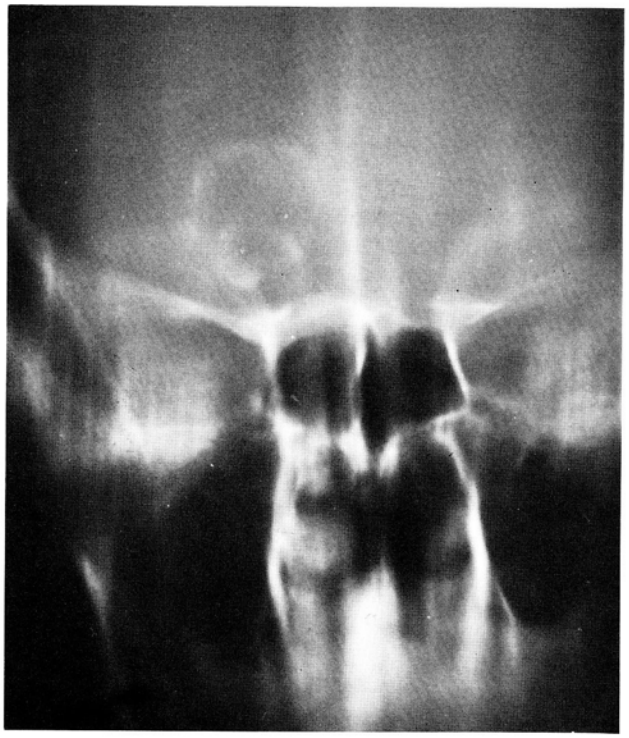
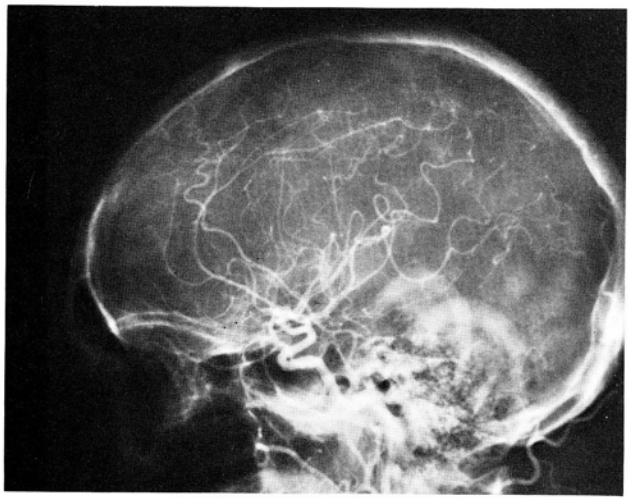


Fig. 2—Lateral angiogram showing separation of the pericallosal artery and the upper part of the Sylvian triangle. No abnormal vessels are seen.



be an anatomical variant. In general, lateral tomograms and other tomograms in the frontal plane taken anterior-posterior to the one shown may clarify this point. The other lesion would be a cranial pharyngioma. The sella turcica is not particularly enlarged as seen through the internal carotid siphon, but the configuration of the sella is not against a diagnosis of cranial pharyngioma. Cranial pharyngiomas often will be situated in the suprasellar region and do not elevate the anterior cerebral artery because they arise from the pituitary stalk. Another possibility is that of a teratoma. The configuration would suggest that there is a calcification in the wall of the tumor, which would be compatible with teratoma, and the nearly midline location also favors teratoma. I have seen a chronic abscess with a calcified rim around it associated with bony changes. This is a possibility, but it is an extremely rare one.

In summary we have here a lobulated calcified mass measuring about 2.5-3 cm in diameter on the right side of the presellar region just to the right of the midline. The possibilities include cranial pharyngioma, meningioma and teratoma. In spite of the bone changes that apparently are demonstrated in the frontal tomogram, I believe meningioma is unlikely because of the lack of upward displacement of the initial portions of the anterior cerebral artery.

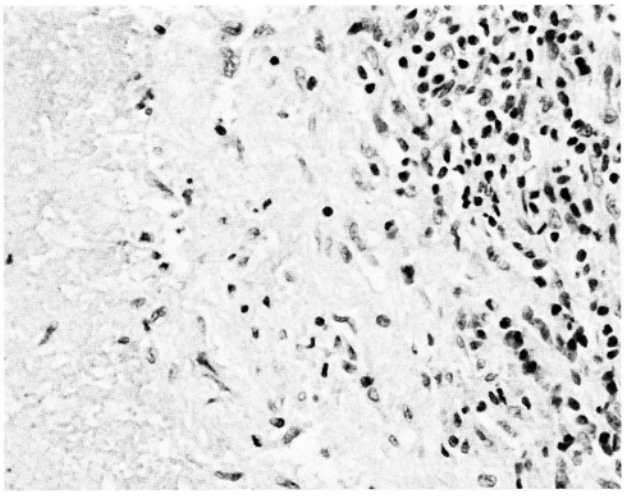
Dr. Taveras' Impression:

1) **TERATOMA** 2) **CRANIOPHARYNGIOMA**

Radiologic impressions submitted:

Craniopharyngioma	23
Glioma	22
Epidermoid	6
Frontal lobe tumor	6
Meningioma	18
Others	20

Fig. 3—Wall of chronic granuloma with coagulative necrosis and inflammatory reaction. H and E stain; x450.



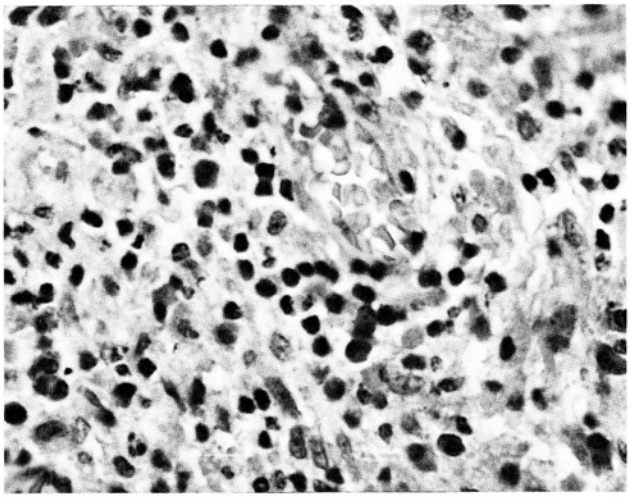


Fig. 4—Inflammatory cells in wall of encapsulated granuloma. H and E stain; x720.

Dr. Taveras: The majority favored craniopharyngioma. I think a diagnosis of glioma is perfectly justified, for it could be a glioma arising from the anterior portion of the frontal lobe. The only thing is that glioma and astrocytoma usually calcify in a different manner. Frontal lobe is only a localizing diagnosis; in general, we attempt to tell where the lesion is and later give a diagnosis. Localization of the lesion is not enough. We have to try to determine ahead what it might be in order to give the surgeon an idea of what the trouble is.

Dr. del Regato: Dr. R. Byhardt of Milwaukee and Dr. Greg Arterburn of Mayfield, Kentucky also suggested craniopharyngioma. Dr. R. Latchow of Minneapolis submitted epidermoid. Dr. Edward Vining of Miami, Florida offered a diagnosis of meningioma.

Operative findings: On February 21st, 1973, a craniotomy was done; several frozen sections were taken.

Dr. Zimmerman: It isn't often that I have to disagree with my friend Dr. Taveras in a diagnosis. On occasion he discouraged me from pursuing a career in neuropathology because he often makes the correct histological diagnosis from his roentgenograms, almost counting the number of tumor cells in mitotic division! Of what use then is the neuropathologist?

Yet, I have had to disagree with some neuroradiologic colleagues who have a tendency to diagnose lesions on the basis of statistical frequency. On that basis, Dr. Taveras is correct when he states that the most likely diagnosis in this case is either a craniopharyngioma or a meningioma. The pathologist, on the other hand, is obliged to deal with the tissue diagnosis in a given patient, and it is frequently the case that a most unexpected diagnosis is the correct one in a given instance. To the patient himself, of

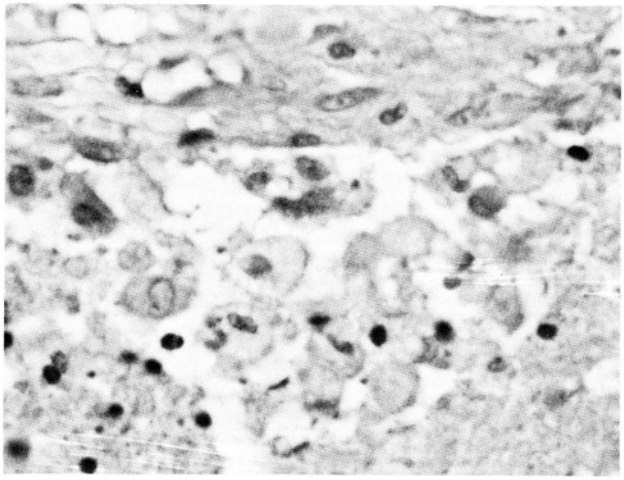


Fig. 5—Collection of large mononuclear phagocytes as part of the inflammatory process within the wall of the granuloma. H and E stain; x720.

course, it doesn't matter that 99 per cent of patients have something other than his rare lesion; to him, he is 100 per cent.

In the present case, we are dealing with a tumor, a space occupying lesion, perhaps even an expanding lesion, but not a neoplasm. There is a mass that histologically can be interpreted in only one way: namely, a chronic inflammatory lesion in the nature perhaps of an abscess or a granuloma. The first figure shows coagulative necrosis on the left, dense collagenous connective tissue (dura?) in the center, and an inflammatory cellular infiltration on the right. The inflammatory cells (Fig. 3) consist of polymorphonuclear leukocytes, lymphocytes and occasional plasma cells. The necrotic inflammatory lesion is encapsulated by connective tissue. There are collections of large mononuclear phagocytic cells that are free of foreign bodies, bacteria and parasites (Figs. 4 and 5).

The nature of the necrosis suggests a tuberculoma, but acid-fast stains are negative. There are also no multinucleated giant cells. More remotely, the coagulative necrosis and the presence of plasma cells suggest a syphiloma or gumma, but the cellular reaction is not specific enough for a definitive diagnosis.

Histologically, there is no room for consideration of a craniopharyngioma, meningioma, or any other neoplastic process. The possibility of histoplasmosis occurred to me, but again this could not be substantiated with special stains. Thus, the etiology of this chronic inflammatory lesion remains unresolved. No help is to be derived in this case from the clinical history, which is silent with regard to a bronchogenic abscess, chronic bronchiectasis, or pleural empyema from which intracranial dissemination could occur. The same may be said for subacute bacterial endocarditis. A history of trauma that could leave behind an inflammatory process is also absent, especially trauma involving the base of the skull.

Dr. Taveras demonstrated a thickening of the bone on one side in the region of the ethmosphenoid sinus. Could this be a manifestation of a chronic sinusitis? If so, it would point to an adjacent subdural abscess, as the lesion in this case.

Dr. Zimmerman's Diagnosis:

CHRONIC INFLAMMATORY PROCESS: GRANULOMA

Histopathologic diagnoses submitted:

Granuloma	34
Gumma	6
Blastomycosis	5
Others	7

Dr. Zimmerman: The pathologists apparently were not fooled; they almost unanimously came down to granuloma. I think it takes a lot of courage to make a specific diagnosis of gumma, even in the absence of any serology, in this case. I would be convinced that this is a gumma if I could demonstrate spirochetes in sections. The only other way is to have the neurosurgeon send to the laboratory a fresh piece of the tissue to be ground up and injected into the testicle of a rabbit; in due course, the rabbit would develop a gumma.

I think it is better yet to say that it is a chronic inflammatory granulomatous lesion, rather than gumma or even blastocycosis. I stained one of the sections for fungi, and I could not find any organisms or any fungi that I could identify.

Dr. del Regato: Dr. W. J. Kirsch of St. Petersburg, Florida made a diagnosis of gumma. Dr. Leo Lowbeer of Tulsa offered necrotizing granuloma, compatible with syphilitic gumma because of plasma cells and endarteritis. Drs. Magda and John Kepes of Kansas City, Kansas made a diagnosis of fibrocaseous granuloma, compatible with tuberculosis, provided other agents are ruled out by special stains. Dr. D. R. Dickson of Santa Barbara, California suggested an amebic granuloma.

Subsequent history: In August, 1975 the patient had a shunt for hydrocephalus. He had no headaches or seizures. There had been good post-operative improvement. He was last seen and reported doing well on January 9, 1976.

Dr. Kjellberg: My task was made substantially easier in discussing these cases by having the deliberations of Dr. Taveras and Dr. Zimmerman before I was obliged to do much at all; it makes the surgeon's task much easier, just as it does in the hospitals, to have that kind of information by which to make judgements.

In lesions of the parasellar region, the kind of tissue that one expects to find will often influence very much the route that the surgeon

takes in order to gain access to the tissue. If a lesion is of the sella or parasellar region, it is expected to be an adenoma, and the transsphenoidal route is heavily recommended because it has a much lower morbidity and mortality. The transsphenoidal route can also be used for certain craniopharyngiomas, but the requirement is that the sella be sufficiently enlarged so that the access to the intrasellar and suprasellar mass is adequate to really handle the bulk of the neoplasm. If it is neither an adenoma nor craniopharyngioma and if the diagnosis were in doubt, as here it obviously was, then that approach should not be taken. When meningioma is a significant consideration, it is inappropriate to consider the transsphenoidal route, and one is obliged to select the transfrontal route.

In any case, it is a very good idea to plan on using the operating microscope. This technical device has substantially changed the prospects of a patient's getting through a procedure and having a suitable clinical state postoperatively. The microscope is essential to the transsphenoidal route but equally applicable to the transfrontal route. We do not know whether or not a microscope was used. If on frozen sections the suspicion of a chronically infectious process were high, this lesion could have had reasonable prospects of total excision with a minimal deficit or injury to adjacent substance, had the operative microscope been used. I do feel that this is an important feature of the surgical operative management of a patient.

There are also some points that might be mentioned regarding the postoperative course; postoperatively, it probably would have been advisable that a very aggressive search be made to confirm the diagnosis. If the lesion were due to syphilis or tuberculosis, the patient's long-term prospects certainly are well served by seeking to confirm that diagnosis. Usually, in septic intracranial lesions of this order, there is some clinical hint elsewhere that such might be the case. An infection in this region could have been due to an extension from one of the sinus cavities, but that would usually be associated with thickening of mucosa of an adjacent sinus; that clue was missing, and nowhere in the history is there any suggestion that the patient had sepsis elsewhere in his body so that the lesion might have been a metastatic one.

Dr. J. Maxey Dell, Gainesville, Fla.: I would like to ask Dr. Taveras if this type of calcification usually occurs in meningioma.

Dr. Taveras: It is unusual for meningioma to calcify in this fashion, that is, only in the capsule of the tumor. Both of them have the so-called psammoma type calcification; they would produce relatively homogenous appearance on the radiograph, or they could have a conglomeration of calcium deposits in certain areas but distributed throughout the tumor. The capsule, however, sometimes can calcify, and that's another reason why I did not choose meningioma as my first diagnosis. Of course, I was wrong on both counts anyway; I only had one film, however.

Dr. J. Rush, St. Petersburg, Fla.; What were the events that led to the shunt?

Dr. Kjellberg: I would judge this to be the case: say hydrocephalus was found on the initial films; whatever the septic process was, it may well have obliterated the subaracnoid pathways. In any case, even if cause could not be established, if the hydrocephalus persisted and if it could be confidently determined by angiography or, more conveniently, by T-scan, then one would go ahead and shunt such a patient, irrespective of cause.

Dr. Prockop, Tampa, Fla.: Dr. Zimmerman, is there a category for non-specific granuloma, some of which are sarcoid? Is this at all suited to that possibility, so that we don't have to worry about infection in the man?

Dr. Zimmerman: I don't believe that a non-specific granuloma would have this appearance. I think, most likely, a bacteria rather than fungi has produced this lesion. The reason why in chronic abscesses of chronic granulomas even cultures sometimes fail to reveal the etiologic agent is because organisms tend to die off in chronic processes; we have had the experience of attempting to culture known cases of tuberculosis with intracranial tuberculomas without success.

Dr. H. Azar, Tampa, Fla.: This patient came from central Florida. I believe the possibility of amebic or malarial etiologies should perhaps be given more notice than it has. The portals of entry would be through the nose, sinus and perhaps others.

Dr. Zimmerman: I too was intrigued by that possibility, but I could not find ameba that I could identify. The best I could do was to show you these macrophages.

Dr. D. Howie, Tampa, Fla.: Were any serological tests done for ameba or syphilis?

Dr. del Regato: I am unable to tell you at this time. I am almost certain that it was done. Obviously, that would have immediately tipped the diagnosis if the serological test had been positive, but I have no report that it was.

Editor's Note: Patient's relative reported on Oct. 4, 1977 that the patient is doing much better and has not seen the need for returning to the hospital.

2. Metastatic Mesodermal Tumor of the Frontal Lobe

Contributed by **J. J. Kepes, M.D.** and **O. D. Smith, M.D.**, Kansas City, Kansas

The patient was a 78-year-old man in May 1975 when he became confused and lost his memory. On examination, he was unable to walk straight and kept falling to the right. Brain scan showed positive uptake in the frontal region.

Dr. Taveras: The frontal projection demonstrates the presence of moderate shift of the anterior cerebral artery, somewhat more pronounced on the distal or superior aspect. The angiographic Sylvian point is possibly slightly closer to the inner table of the skull than might be expected, which would indicate either the presence of central white matter swelling or ventricular dilatation. There are many vessels in the region of the lenticulostriate arteries arising from the middle cerebral artery (Fig. 1).

The lateral projection reveals little disruption of the arteries. However, there appears to be a slight separation of branches of the middle cerebral artery in the suprasylvian region anteriorly, and at least one, possibly two, of these branches show diffuse narrowing of the lumen as outlined by contrast. In addition, the pericallosal artery presents an area about 2 cm in length, which is narrower than the noted caliber of the artery either proximal or distal to this area of narrowing. I get the impression of the presence of diffuse small straight vessels in the general area overlying the abnormalities I am describing. In the lateral view, the appearance does not suggest a large mass effect in any given area but rather a diffuse process (Fig. 2).

I believe we are dealing here with a somewhat diffuse process, possibly multicentric. Because of the diffuseness of the changes, I would not consider metastatic disease. The most interesting finding here is the presence of focal narrowing of some vessels both in the middle cerebral and in the anterior cerebral territories. There are two neoplasms that I can think of that could produce this finding. One of them is glioblastoma multiforme, and the other one is reticulum cell sarcoma. Multicentric glioblastomas sometimes occur and could produce findings on the angiogram that would be identical to these. However, the presence of what appears to be many fine vessels would tend to favor the diagnosis of reticulum cell sarcoma.. Also, the location near the surface, both on the opercular region and in the midline, favors reticulum cell sarcoma-microglioma, which sometimes presents with findings suggestive of a diffuse meningeal process.

Dr. Taveras' Impression:

1) **RETICULUM CELL SARCOMA**
2) **GLIOBLASTOMA MILTIFORME**

Radiologic impressions submitted:

Glioma	38
Frontal tumor	10
Metastatic tumor	24
Arterial occlusion	8
Corpus callosum tumor	6
Sarcoma	6
Others	10

Fig. 1—Angiogram showing moderate shift of the anterior cerebral artery.

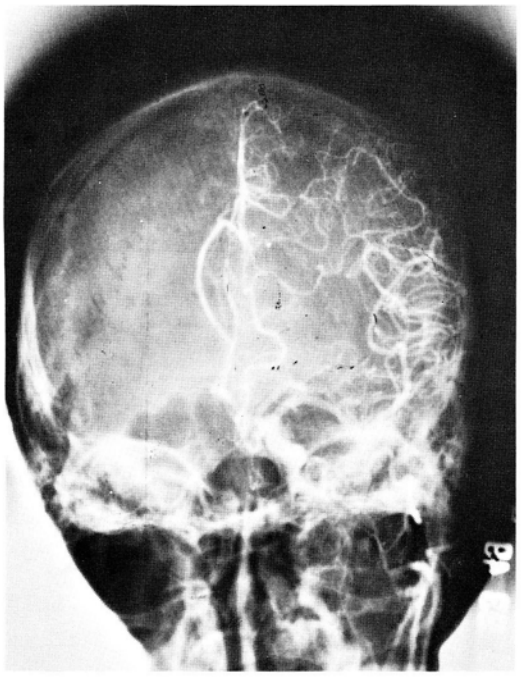
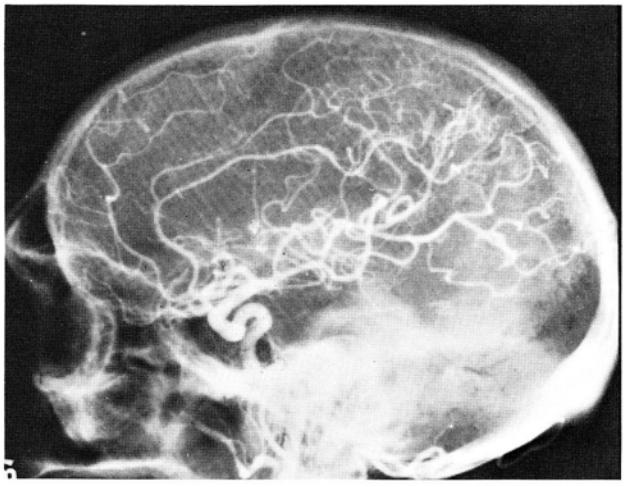


Fig. 2—Lateral projection shows little disruption of arteries.



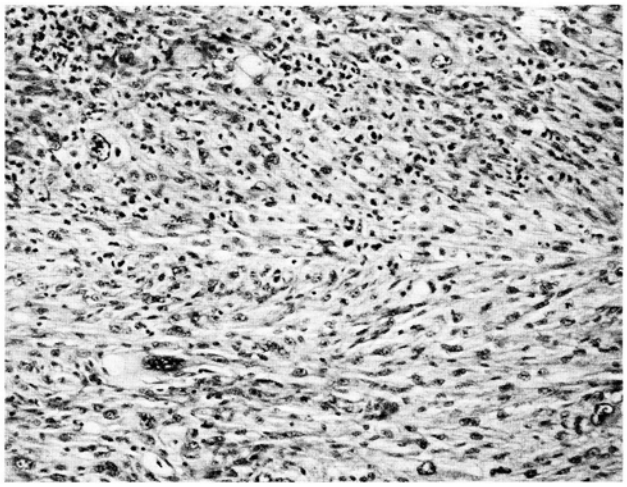
Dr. Taveras: Glioma I think is a perfectly good diagnosis. Frontal tumor is only a localizing diagnosis and does not really tell us anything; I like to go beyond if possible. Metastatic tumor is another obvious possibility; were it not for the computerized tomography that is now available, we would continue to have difficulty diagnosing these. Computerized tomography has been of great help in diagnosis of multiple metastatic tumors. I did not see any arteries occluded. Corpus callosum tumor is a perfectly good diagnosis on the basis of the narrowing of the vessels, but there is really nothing else to go along with that. While I feel that the tumor may well have infiltrated and gone all the way over the midline, I would not diagnose a corpus callosum tumor. Regarding sarcoma, I would have to know sarcoma from where.

Dr. del Regato: Dr. L. Gold of Minneapolis suggested sarcoma of the corpus callosum. Dr. J. L. Kestel of Waterloo, Iowa submitted glioma of the hypothalmus.

Operative findings: On May 9th, 1975 a right frontal craniotomy was carried out.

Dr. Zimmerman: This time we are dealing not only with a space occupying lesion in the location which Dr. Taveras indicated, but with a neoplasm. This consists of fairly uniform, elongated cells arranged in parallel sheets and containing processes that are pink-staining and fibrillary (Fig. 3). Occasional large tumor cells are also present with large nuclei and ground glass cytoplasm that is sometimes vacuolated. The vacuoles suggest the presence of a lipid-like substance. The fibrillary processes are of mesodermal origin, as demonstrated in preparations stained for reticulin (Fig. 4).

Fig. 3—Elongated tumor cells arranged in sheets. Some cells are large and vacuolated with ground glass cytoplasm, and all have fibrillary processes. H and E stain; x150.



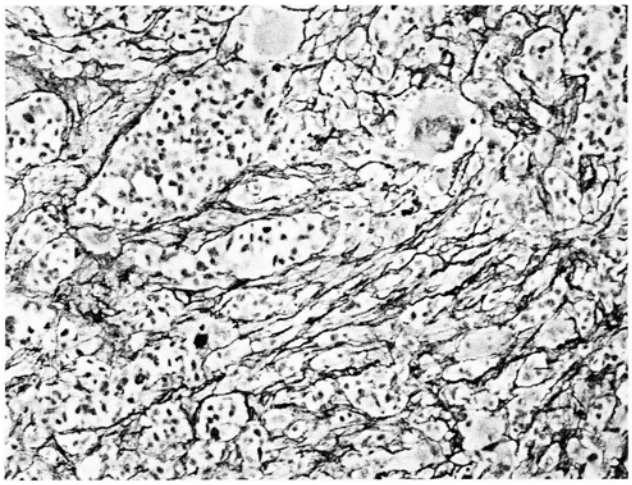


Fig. 4—Abundant fibrillary stroma of reticulin fibers laid down by tumor cells. Wilder stain; x180.

Some areas of the tumor have many bizarre shaped cells with huge nuclei and pale, foamy cytoplasm (Fig. 5). Some tumor cells are seen in longitudinal section and form parallel rows; others seem to have been cut transversely and thus appear round. The arrangement of tumor cells strongly suggests a mesodermal neoplasm. Cellular pleomorphism is conspicuous, as are cells in mitotic division, and these features indicate a malignant tumor.

Under high magnification, the granular nature of the cellular cytoplasm is conspicuous (Fig. 6). It suggests a lipid storage material. The latter is perhaps seen even better in the next illustration (Fig. 7) where the cells are sectioned transversely and hence appear to be round. The cytoplasmic contents strikingly suggest lipid storage.

Tumor cells of the kind forming this neoplasm are not uncommonly seen in extracranial new growths. They are not rare tumors in subcutaneous, retroperitoneal and mesenteric locations. They are malignant mesodermal tumors of the liposarcoma variety. Intracranially, tumors of this variety present an especially difficult diagnostic problem. They are unlike the sarcomas that sometimes one encounters in malignant gliomas (glioblastomas multiforme) that have a mesodermal component derived from the perivascular connective tissue. A primary intracranial liposarcoma of this variety would be unique in my experience. A metastatic liposarcoma in the brain must be considered, but the patient evidently has no evidence of an extracranial neoplasm. Could this, therefore, represent a xanthosarcoma described several years ago by Kepes, Kepes and Slowik?

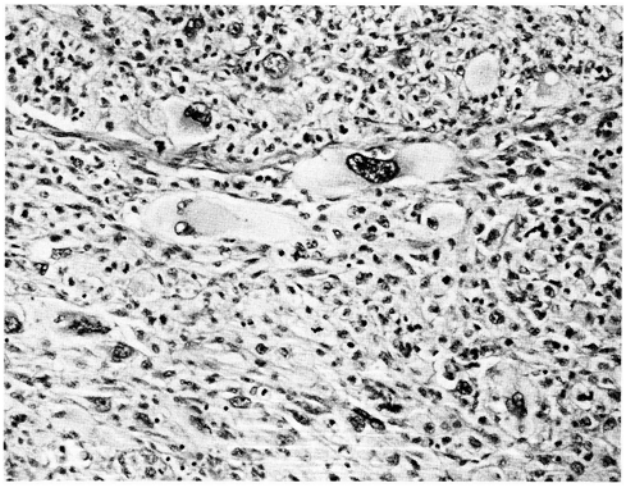


Fig. 5—Tumor cells sectioned transversely and longitudinally. Many are large and bizarre and contain foamy cytoplasm. H and E stain; x180.

Dr. Zimmerman's Diagnosis:

MALIGNANT METASTATIC MESODERMAL NEOPLASM (liposarcoma?)

Histopathologic diagnoses submitted:

Xanthosarcoma	10
Ganglioneuroblastoma	10
Metastatic tumor	10
Astrocytoma	8
Glioblastoma	7
Liposarcoma	5
Others	4

Dr. Zimmerman: I found no neuroblast and no glial cells in this case. If this is truly a liposarcoma, from where would it arise in the brain? There are a few places, like the corpus callosum and the hypothalamic region, from which a malignant liposarcoma could conceivably arise and invade the brain tissue. It is possible, but in some eight thousand brain tumors that I have studied, I've never seen that happen, so I was a little doubtful. Therefore, I thought that if it is a liposarcoma, it would have to be of extracranial origin.

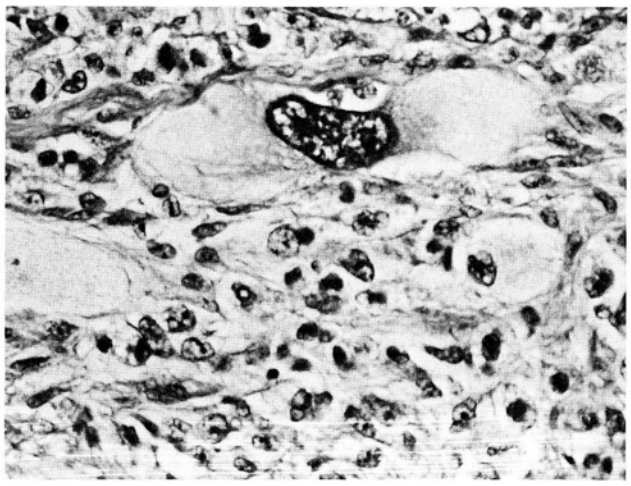
In recent years, Dr. John Kepes and his coworkers have practically appropriated the diagnosis for their own and have suggested that certain tumors resembling this may be what they call xanthoma or xanthosarcoma. I think one has to consider this very seriously. For this case, I don't quite like that category described by Dr. Kepes. His previous cases had other elements that are missing in this case. His previous cases were much younger people; that does not exclude the diagnosis, of course. However, the lack of lymphocytes and multinucleated tumor cells are reasonable reservations. One cannot cast aside this suggestion of Dr. Kepes; I think it has to be considered. I personally favor a diagnosis of mesodermal malignant neoplasm of liposarcomatous type, therefore probably metastatic.

Dr. del Regato: Dr. Henry Azar of Tampa made a diagnosis of malignant fibrous histiocytoma. Dr. Renu Jalota of Salt Lake City also questioned the possibility of metastasis from a liposarcoma. Drs. Magda and John Kepes of Kansas City, Kansas made a diagnosis of xanthosarcoma.

Dr. Leo Lowbeer of Tulsa, Oklahoma, one of the contributors to this and past Cancer Seminars, made a diagnosis of xanthosarcoma, which he designates as **"Kepes' tumor."** It is said to be confused with giant-cell glioblastoma or monstrocellular sarcoma; it occurs mostly in children and has an excellent prognosis, in spite of dreadful morphology.

A case that Drs. Kepes and Lowbeer considered similar was presented to a Cancer Seminar on Intracranial Tumors held in Colorado Springs in November 1962. Both Dr. Taveras and Dr. Zimmerman were the featured speakers of that Cancer Seminar. It was the case of an 11-year-old boy with a large cystic tumor of the temporal lobe. Dr. Taveras thought that it was a subdural hematoma, and Dr. Zimmerman diagnosed a meningiomatous hemangioblastoma. Under pressure by additional evidence presented at the Seminar, Dr. Zimmerman agreed to the diagnosis of glioblastoma multiforme, under which the case was published in Cancer Seminar of 1963. Following operation, the patient received thorough irradiation and was reported well. In 1973 Dr. Kepes republished the case in **Acta Neuropathologica** as a case of fibroxanthoma of the meninges. Dr. Lowbeer has now reported that the patient is living today, 15 years after surgery and irradiation.

Fig. 6—Bizarre tumor cells with ground glass cytoplasm. H and E stain; x450.



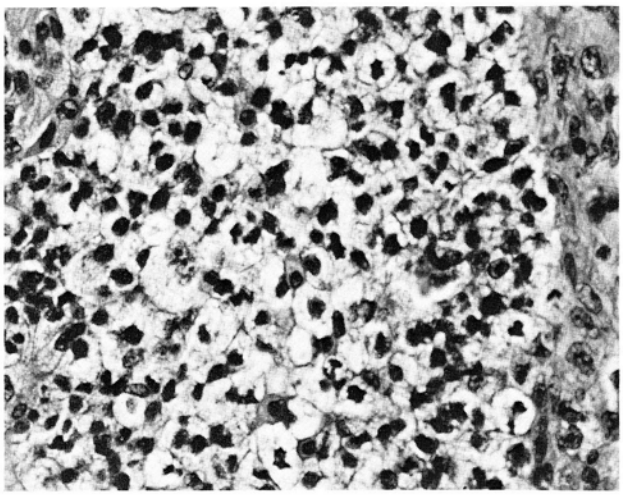


Fig. 7—Transversely sectioned tumor cells with pale, granular cytoplasm suggesting fat storage. H and E stain; x450.

Subsequent history: Upon discharge the patient appeared neurologically improved. He returned to his home. Two months later, he developed symptoms and signs of acute congestive heart failure without change in his neurological status. In August 1975 he expired. No autopsy was done.

Dr. Kjellberg: Among the things that come to mind whenever surgical procedures are done on masses of this dimension is that it is very valuable to prepare the patient with steroids in large doses, beginning several hours before the procedure. The brain handles the procedure much better, and the steroids can be tapered postoperatively. In this case, the radiographic diagnoses, and in fact, most of the histopathologic diagnoses, suggest lesions that are capable of surgical cure. The range of diagnoses certainly requires that the nature of the tumor be confirmed so that the operation has for its goal only getting some tissue. For the sake of carrying the patient reasonably well through his postoperative course, a certain amount of decompression of the tumor mass is probably also appropriate. In regard to the diagnosis considered, it would be my opinion that radiotherapy might very well be used. I think, however, other considerations are at play here in view of the age of this gentleman, who is 78. Probably the option elected was to permit the man to have his remaining years in the greatest degree of comfort without more medical intrusion. Otherwise, I think the diagnosis itself would have warranted radiotherapy in a patient with otherwise good prospects.

Dr. Henry Azar, Tampa, Fla.: For the sake of clarity, my diagnosis was malignant fibrosis histiocytoma; a much better term, xanthosarcoma, was suggested by Dr. Kepes. There is always the possibility of metastasis. This is where a radiologist can help tremendously.

Dr. John Kepes, Kansas City, Kans.: The article to which Dr. Zimmerman so kindly referred deals with xanthomatous tumors; it was written by Dr. Magda Kepes and I, and it includes variants that we thought looked frightful histologically but biologically may have a beneficial outcome. One of the cases we included was a fibroxanthoma in a young woman; she died within a year. We perhaps made the mistake of writing one paper instead of two, and these two entries are somewhat confused at times. I did not think that this would come under the category of a typical fibroxanthoma, the kind that would possibly behave in a benign fashion. I thought, as Dr. Zimmerman did, that this is an outright malignancy and that there can be no question about the outcome. The Cancer Seminar slides I received didn't have any giant cells in them. The slides that Dr. Zimmerman showed are the exact replica of a case we had of a lady who on autopsy had no primary tumor anywhere.

As Dr. Zimmerman pointed out, not only is there a lot of reticulin present, but there is also the presence of reticulin fibers surrounding individual cells. The entire circumference of one giant cell is invested by reticulin, and even in the sarcomatous forms, it is rather uncommon to have individual cells enveloped like this. This is also expressed in the reticulin stain where advancing areas of the tumor had the reticulin fibers; the surrounding brain doesn't have any.

Everybody wonders where these tumors are coming from; since we are away from the dura and away from the leptomeninges, that leaves us some questionable hamartomatous remnants, such as a lipoma or the blood vessels. Many of the sarcomas in the brain originate from the blood vessels.

Dr. Zimmerman very graciously did not argue strongly the possibility that this would be a glioma because whenever they see a giant cell malignancy, most people say it must be a glioblastoma. We did look through the electron microscope. There are lipid droplets in these large cells, and we didn't see any glial fibers. In spite of some primary liposarcoma possibly hiding somewhere in the body, it is more likely with carcinomas that there is metastatic carcinoma in the brain with the primary detected sometime later. Liposarcoma is not a shrinking violet; it usually shows up in the primary site, but it is quite possible.

Dr. A. Gonzalvo, Tampa, Fla.: The slides that we saw during this presentation are different from the original ones. I associate many of these changes in my slides with malignant histiocytoma or part of a xanthoma type of lesion. I couldn't find this in the tumor that was presented today.

Dr. Zimmerman: It is true that metastatic tumors to the brain are much more frequently epithelial in type, rather than mesodermal, but in any large series of metastatic tumors to the brain, a small number of mesodermal tumors, like liposarcoma, fibrosarcoma, all kinds of sarmomas, leiomyosarcomas, and rhabdomyosarcomas, are present. I want to emphasize that diagnoses are not made histologically on the basis of probability but on what you actually see. If one case in a thousand turns out to be a liposarcoma, that is it. In the absence of postmortem confirmation of a primary or a metastatic tumor, there isn't anything more than can be said in this case.

Dr. J. F. Dunkel, East Lansing, Mich.: Is there any biochemical or histochemical differentiation of a lipid in a tumor versus the garden variety body lipid?

Dr. Kepes: Cholesterol may be deposited in some cells.

Dr. L. Prockop, Tampa, Fla.: Does the fact that you know of the narrowing of and pressure on the blood vessels indicate that the tumor may have arisen from the blood vessel; is it suggested histopathologically?

Dr. Taveras: We see that in glioblastomas, which presumably did not arise from the blood vessel, but they do irritate the blood vessel in such a way that you get actual pseudosarcomatous changes involving the endothelium of the blood vessel itself. I think it is a tumor that was either wrapped around some of the larger vessels or was actually invading the walls of the vessels.

Dr. Zimmerman: I will have occasion to discuss this very point in another case where the tumor arose in the vessel wall. It is a different picture than this. I do not believe that this is a leiomyosarcoma, an endothelial sarcoma or a hemangioblastomatous type of lesion at all. I think I would agree with Dr. Kepes; it is a malignant mesodermal neoplasm. He tends to favor xanthoma, and I can't deny it. It is just a difference of opinion. I think it is a liposarcoma, rather than a xanthoma, but the distinction isn't that great between the two.

References:

Kepes, J. J., Kepes, M. and Slowik, F.: Fibrous xanthomas and xanthosarcomas of the meninges and the brain. Acta. Neuropathol. **23:** 187-199, 1973.

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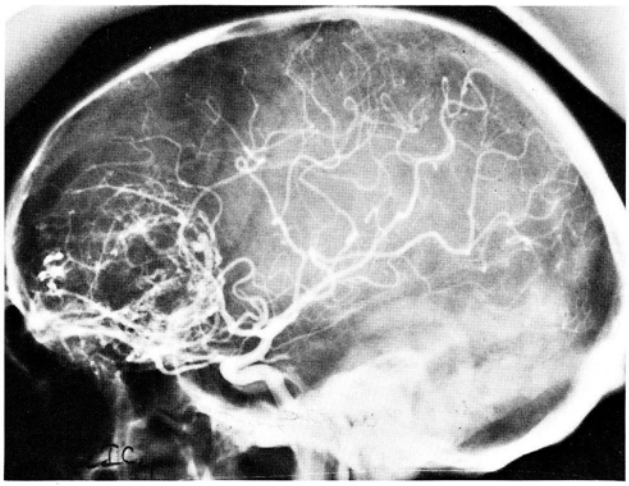
3. Meningioma of the Frontal Fossa

Conributed by **H. G. Jacobson, M.D.,** Bronx, New York

The patient was a 48-year-old man in June 1975 when he complained of headaches of 4 months duration, coinciding with poor vision and personality changes. On examination, he appeared confused and presented a left facial paresis, bilateral papilledema and minimal drift of the left upper extremity.

Dr. Taveras: The lateral angiogram shows the presence of a rounded mass (Fig. 1) in the inferior frontal and fronto-polar regions. Even during the arterial phase, there is a well-developed area of tumor circulation. The tumor is well circumscribed and shows what appears to be early filling of a number of veins. I get the impression that these veins are mostly in the periphery of the tumor. One branch of the anterior cerebral artery is displaced upward, and another branch appears to be displaced downward. Therefore, this is not a subfrontal tumor from the angiographic point of view or at least, it did not arise in the midline. It could have arisen somewhat lateral to the midline and grown against the falx cerebri. The ophthalmic artery is prominent, and as it bends up to pass over the optic nerve, it becomes apparently enlarged. The enlargement always suggests the possibility of blood supply of the tumor by the ophthalmic artery. Under these circumstances, the meningeal branches arising from the ophthalmic would be supplying the tumor, which becomes very likely a meningioma. On the other hand, the type of

Fig. 1—Lateral angiogram showing a rounded mass in the inferior frontal region.



circulation that is shown at this particular stage of the angiogram is not that of an ordinary meningioma, although it could be the type of circulation seen in an angioblastic meningioma. The rest of the angiogram might be revealing in that usually in the later stages of an angiogram in meningiomas, the tumor circulation becomes more homogeneous, and it tends to persist into the venous phase. This is contrary to glioblastomas where the tumor stain usually disappears by the time the full venous phase is reached. If the frontal film had been included, we might have observed in meningioma the presence of lateral displacement of branches of the anterior cerebral artery away from the falx, which is typical of meningiomas arising in this location.

The computerized tomograms (Figs. 2 and 3) show one taken before injection of contrast and one after the intravenous injection. They show a medially placed mass, which is close to the falx and which is large enough to bulge behind the edge of the falx towards the other side. It compresses the lateral ventricle backward and is accompanied by a fairly diffuse area of cerebral edema, particularly in the right hemisphere. The mass is about as dense as the brain. This is against the diagnosis of meningioma, which is usually denser than the brain, although it may be compatible with the diagnosis of angioblastic meningioma, which does not contain psammoma bodies. The CT scan taken after the intravenous injection shows a homogeneously, rather densely stained mass. There is no evidence of central necrosis, although the technique of the photography may be such that the center may be as dense as the periphery, even though that may not be the case. I am assuming that the entire tumor is homogeneous and that there are no areas of necrosis. This favors again a meningioma because glioblastomas are apt to have areas of necrosis within them.

In summary, I feel that the irregular tumor stain with early venous filling seen in the arterial phase of the angiogram apparently favors a malignant tumor, but the apparent supply by the ophthalmic artery favors meningioma. Angioblastic meningiomas can have early venous filling, and the location is favorable for meningioma coupled with the apparent ophthalmic supply.

Dr. Taveras' Impression:

1) **ANGIOBLASTIC MENINGIOMA**
2) **ASTROCYTOMA**

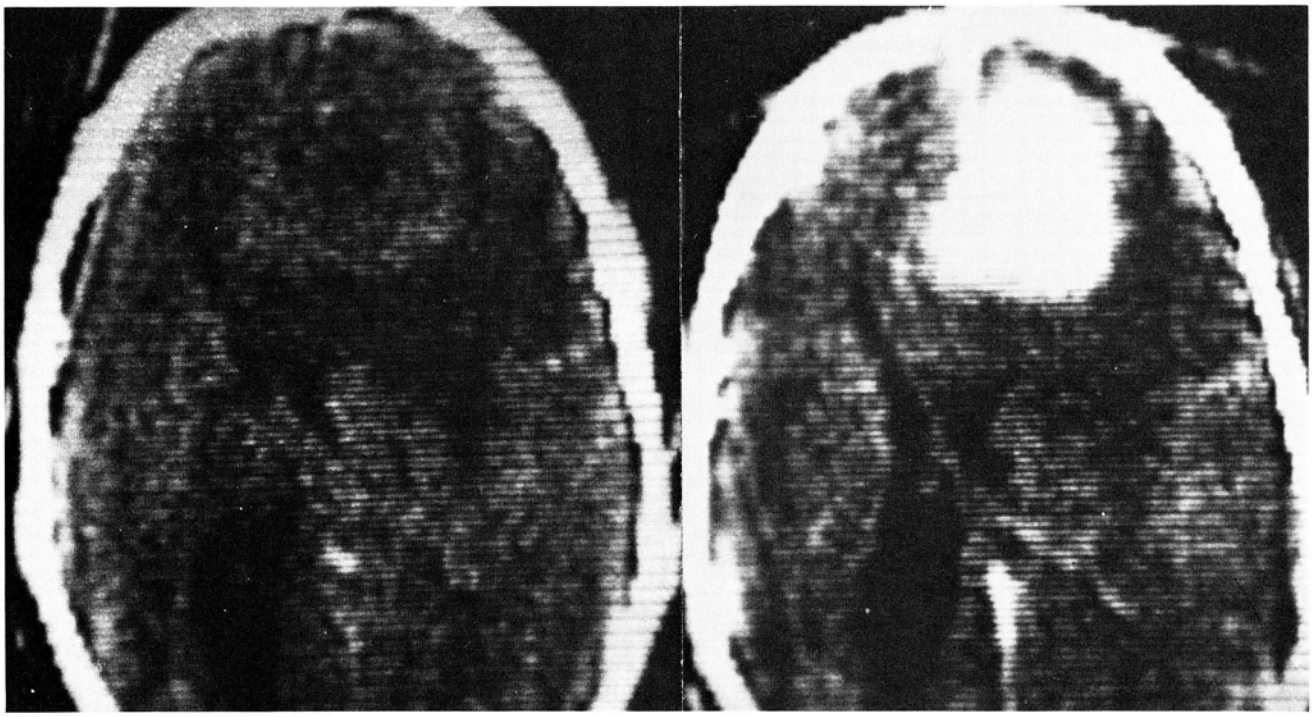
Radiologic impressions submitted:

Meningioma	42
Glioblastoma multiforme	23
Glioma	6
Frontal lobe tumor	5
Metastatic tumor	5
Others	12

Dr. Taveras: Glioblastoma multiforme is a perfectly good second choice diagnosis. The only thing is that after enhancement, the CT scan shows a homogeneous staining tumor without central necrosis; when glioblastomas get to this size, they would ordinarily show areas of necrosis. This is a homogeneous solid mass; meningioma, for that reason, would be a much better choice. However, glioblastoma is one possibility, and metastatic tumor is another.

Fig. 2—Computerized tomogram showing medial mass close to the falx.

Fig. 3—CT scan after injection of contrast material.



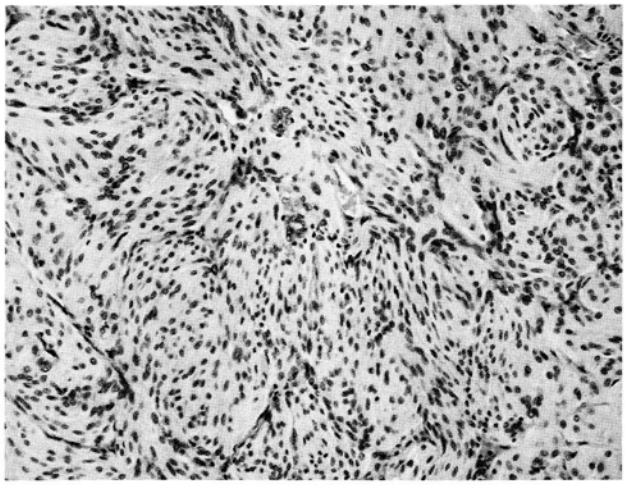


Fig. 4—Meningioma with meningocytic whorls. H and E stain; x180.

Dr. del Regato: Dr. S. Chandra Mouli of Chicago and Dr. Harold Peterson of Minneapolis offered an impression of meningioma. Dr. Edward Grayson of Hollywood, Fla. suggested meningioma or glioblastoma multiforme. Dr. Ritsuko Komaki of Milwaukee offered an impression of meningiosarcoma. Drs. E. Vining and Judith Post of Miami offered meningioma of the anterior falx.

Operative findings: On January 24th, 1975 the patient had a right frontal craniotomy. A very vascular mass was found 3.5 cm from the frontal lobe; piecemeal removal from the orbital groove was done. The removed pieces weighed a total of 6 gm.

Dr. Zimmerman: This was not a tumor **in** the frontal lobe, but rather in the frontal lobe region. It was attached to the falx—an extraparenchymal tumor that compressed the frontal lobe but did not invade it. There was no true infiltration of the brain substance.

Microscopically this tumor present no problem. A tumor that has the structure seen in figure 4 is a meningioma and can't be anything else really. There are distinctive meningeal whorls in which clusters of meningocytes are arranged in concentric layers reminiscent of the cross section of onion tips. The tumor cells are elongated with abundant pink staning cytoplasm (in hematoxylin-eosin preparations) but indistinct cell walls.

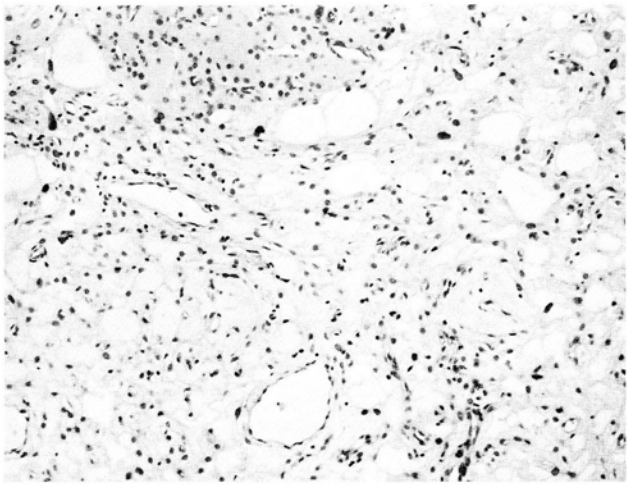
There are two features that are characteristic of meningioma, and at least one or the other must be present to warrant a diagnosis of this tumor. One is the characteristic lobulation or meningocytic whorl formation (Fig. 4), and the other is the psammoma body. Without either one or the other of these features, the diagnosis is hazardous.

Dr. Taveras stressed the vascular nature of this tumor and suggested the term angioblastic meningioma. To the neuropathologist, this term is somewhat bothersome because it was employed by Cushing and Eisenhardt in their splendid book on meningiomas to designate a tumor that has since been found to be an hemangiopericytoma and not a meningioma at all. To avoid any confusion that may arise from the use of the term angioblastic meningioma, it is perhaps preferable to designate vascularized meningiomas as simply meningiomas with a vascular component.

The blood vessels in the meningioma of the present case are numerous and have thin walls (Fig. 5). The question of an A-V malformation arises for a moment but is soon dispelled. Both arterioles and venules are present in considerable numbers, but both categories of vessels are well formed and constitute neither a vascular malformation nor a vascular tumor such as an hemangioma.

Special note should be taken of some meningocytes that are large and have hyperchromatic nuclei of bizarre shape. Such cells in a patient whose history suggests tumor invasion (erroneously in this case) may lead to a diagnosis of malignant meningioma or meningeal sarcoma. It is well to remember, therefore, that bizarre cells and even frequent mitoses in an otherwise well-differentiated meningioma are not indicative of malignancy. Actually, in my experience, malignant meningiomas are quite rare. In over 700 meningiomas in my collection, I have seen but 2 or 3 that justified the designation of malignancy. These were tumors that metastasized distally in liver or lung. Even local invasion of the calvarium with subsequent involvement of the tissues of the scalp are not indicative of malignancy. Rapid recurrence of an incompletely excised tumor may occur, even in the absence

Fig. 5—Meningioma with a vascular component. H and E stain; x150.



of bizarre cells and cells in mitotic division, to suggest biologic if not morphologic malignancy.

Dr. Zimmerman's Diagnosis: MENINGIOMA

Histopathologic diagnoses submitted:

Meningioma	48
Malignant meningioma	3
Meningotheliomatosis	3

Dr. Zimmerman: I've already commented upon malignant meningioma. It is well known that some meningiomas are multiple intracranially. There are beautiful charts in the book to which I referred by Cushing and Eisenhardt and in which they have outlined as many as six or eight meningiomas in different parts intracranially; they could be called meningotheliomatosis, if you will, but these are really meningiomas.

Dr. del Regato: Dr. Edward Lee of Tampa also made a diagnosis of meningioma. Dr. R. Jalota of Salt Lake City called it a meningotheliomatosis of very vascular type. Dr. Leo Lowbeer of Tulsa added that this is Cushing Type V, variant 2, with bizarre nuclei but benevolent behavior and that it is also called neuroepithelial type of Roussy.

Subsequent history: The headaches decreased, but the papilledema persisted, and the vision remained poor. On January 23rd, 1976 there had been no improvement of vision, had retained light perception only. He was otherwise normal.

Dr. Kjellberg: A few surgical points come to mind. Angiography is very important in the work up of a patient with meningioma because there is frequently some clue as to where the primary blood supply is; it is a useful tactic early in the procedure to take the arterial supply, coagulate it and interrupt it so that the remainder of the procedure can be done with relatively little blood loss and in a relatively cleaner operative field. Such large tumors do not require microsurgical technique. However, if one is seeking to get small vessels arising from the opthalmic artery across the floor of the frontal fossa, microsurgical techniques may indeed be a definite advantage. It is also an advantage if the posterior extent of the tumor is unclear or if one cannot tell if the tumor really is attached to the optic nerve or not. The optic nerves can be visualized with greater clarity, separating structures, and thus, the prospect of protecting the optic nerves from injury is substantially better.

The possibility exists that there was some communicating hydrocephalus in this case. A bloody procedure has a greater prospect of leaving the communicating hydrocephalus than a procedure that does not spill as much blood into the subarachnoid space: this would have been another potential asset of microsurgical technique. A postoperative CT scan might be of some value to see if there is any communicating hydrocephalus, and that would warrant the placement of a shunt.

Dr. Zimmerman: There is no evidence of communicating hydrocephalus now. The neurosurgeon felt that the trauma of the operative procedure accounted for some of the symptoms. He assured me at the time of operation that the optic nerve was not implicated in the tumor. It was close to it but not attached to the optic nerve.

Dr. Kjellberg: What was the interpretation of the persistent papilledema postoperatively?

Dr. Zimmerman: It was a very bloody procedure, and I think that there was a lot of blood remaining in the subarachnoid space.

Dr. Kjellberg: Do you know if the pressure was high for a while?

Dr. Zimmerman: Yes, it was.

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La Presle, J., Netsky, M. G., and Zimmerman, H. M.: The Pathology of meningiomas. A study of 121 cases. Am. J. Pathol. **28:** 757-791, 1952.

4. Papilloma of the Choroid Plexus

Contributed by **Renu Jalota, M.D.,** Salt Lake City, Utah

The patient was a 6-weeks-old baby boy in May 1975 when he was admitted for investigation of abnormal increase in the size of his head (Fig. 1).

Dr. Taveras: The lateral view shows an irregular tumor mass, which is evidently intraventricular in location associated with marked ventricular dilatation. The frontal projection shows that the mass arises chiefly from an area near the midline and is far away from the lateral ventricular surface. Therefore, the origin of the mass is either from the region of the septum pellucidum, or it arises from the floor of the lateral ventricles. From these films, there is no way of telling whether the mass protrudes into the lateral ventricle; that is, whether it arises in the midline and projects into both lateral ventricles. I am going to assume that the mass arises from one side (Figs. 2 and 3).

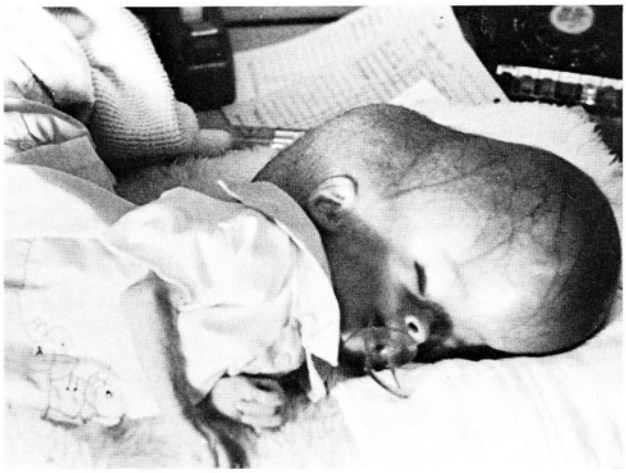


Fig. 1—Photograph of patient six weeks after birth.

In an infant of this age (6 weeks), there are two diagnostic possibilities that should be seriously considered. One is a choroid plexus papilloma, and the other is a teratoma arising from the midline structures. The ventricles are extremely large in this child, and it is noted that the lateral ventricular wall is far away from the surface of the tumor. This would indicate that the ventricle did not become enlarged because of the presence of the tumor such as one would expect to see in the case of a teratoma, but rather that there might be another cause. This could be obstruction of the aqueduct with aqueductal insufficiency or stenosis on a congenital basis or possibly on an acquired basis. It is known that fragments of an intraventricular teratoma or cholesteatoma could pass down through the foramen of Monro and lodge themselves in the aqueduct leading to hydrocephalus. Another possibility is that the tumor could be a choroid plexus papilloma. It is said that the tumor produces an increasing amount of cerebral spinal fluid beyond that which could be absorbed through the normal absorbtive mechanism. The other possibility is that hemorrhage within the cerebral spinal fluid leads to plugging of the arachnoidal granulations and the development of communicating hydrocephalus, such as that seen in subarachnoid hemorrhage from bleeding aneurysms or in post traumatic cases associated with subarachnoid hemorrhage.

In summary then, we have an infant with a tumor situated on the medial side and the floor of the lateral ventricle, irregular in shape with enlargement of the ventricle to an extent far beyond that necessary to contain the tumor.

Dr. Taveras' Impression:

1) **CHOROID PLEXUS PAPILLOMA**
2) **TERATOMA**

Radiologic impressions submitted:

Papilloma of the choroid	36
Ependymoma	16
Fronto-temporal tumor	6
Epidermoid	5
Benign lesion	15
Others	12

Dr. Taveras: At the age of six weeks, there aren't too many tumors. Ependymoma is a definite possibility, except for the age and for the fact that the tumor is too small for the size of the ventricle unless it were right in the foramen of Monro. Epidermoid tumor would fall into the category of a teratoma; the age is a little too young for epidermoid.

Dr. del Regato: Dr. Joel Tew of Chicago and Dr. Stephen Greenberg of Tampa also offered an impression of papilloma of the choroid plexus.

Dr. Zimmerman: The diagnosis in this case is easy and histologically obvious. There is no other primary tumor in the nervous system that has papillary projections lined by a layer of cuboidal or columnar cells (Fig. 4). These cells represent modified ependyma, which participates embryologically in the development of the choroid plexus. It has been shown long ago that the ventricular lining ependyma extends over the vascularized connective tissue projec-

Fig. 2—Irregular tumor evidently intraventricular.

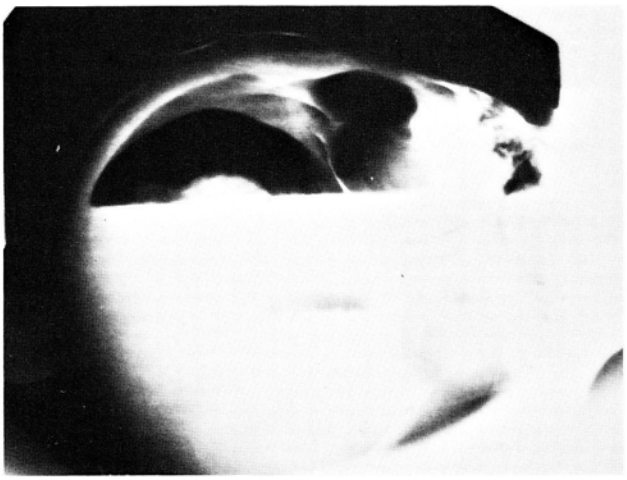
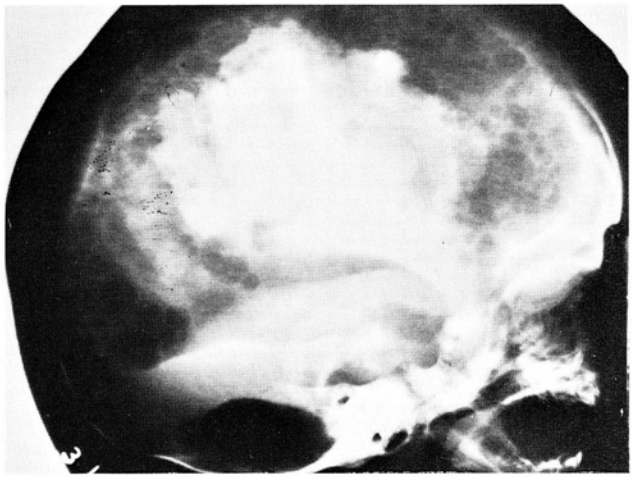


Fig. 3—Tumor seems to be primarily in the midline.



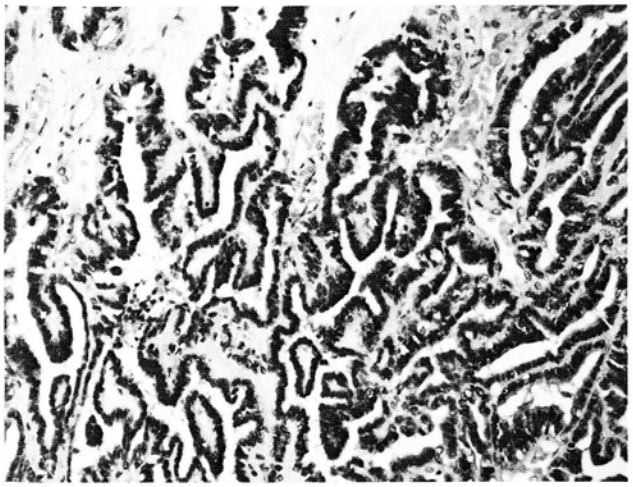


Fig. 4—Papilloma of choroid plexus. Note vascularized connective tissue projections covered by cuboidal and columnar ependymal cells. H and E stain; x180.

tions from the ventricular walls to form the choroid plexuses. Sometimes the lining cells of these papillomas contain cilia, as do embryonal ependymal cells.

I am not certain that I saw ciliated cells in this tumor, but I have seen them in other tumors of this variety. Fresh tissue fixed in glutaraldehyde and embedded in methylmethacrylate for electron microscopic study often reveals the cilia to advantage in the choroid plexus papillomas.

It is sometimes stated that the left lateral ventricle is somewhat more frequently involved by this tumor than the right and that girls have these papillomas more often than boys. Whether these differences will be borne out in larger series of cases still remains to be seen.

Papillomas of the choroid plexus are not confined to the lateral ventricles but occur also in the fourth ventricle. In any location, they have the same highly vascularized, papillomatous appearance. Their mere bulk serves to obstruct the foramen of Monro in the lateral ventricles or the outflow tract from the fourth ventricle. Obstruction to the ventricular fluid pathway as well as increased ventricular fluid secretion result in internal hydrocephalus and may sometimes be initiated by bleeding into the tumor.

On a few occasions, I have found fragments of these tumors growing in the subarachnoid space of the cauda equina region of the cord. These tissue fragments were evidently washed down from the cerebral ventricles and grew in their new spinal location as tissue cultures. These, of course, are not examples of distant metastases of malignant tumors, for they are all benign histologically and behaviorally. Their intraventricular location may, however, preclude their surgical removal and so contribute to a fetal outcome from unrelieved increased intracranial pressure.

In 1968 I compiled a table of brain tumors based on some 5,000 cases I had obtained either at biopsy or autopsy. Among these tumors were 19 examples of choroid plexus papillomas for an incidence of 0.4 of 1 per cent. This incidence compares to one of 2.3 per cent (52 cases) in the much smaller Cushing series. It should be noted, however, that my series contained many cases of metastatic disease to the brain, and Cushing's series contained but few such cases. The net effect was to dilute the incidence of papillomas in my series. The true incidence of papillomas of the choroid plexus among primary brain tumors is very probably represented in the Cushing series. Nevertheless, it is to be noted that Dastur reported an incidence of 0.3 of 1 per cent for this class of tumor in India and Zulch, 0.5 of 1 per cent in Germany.

Dr. Zimmerman's Diagnosis:

PAPILLOMA CHOROID PLEXUS

Histopathologic diagnoses submitted:

Choroid papilloma	54
Papillary ependymoma	9

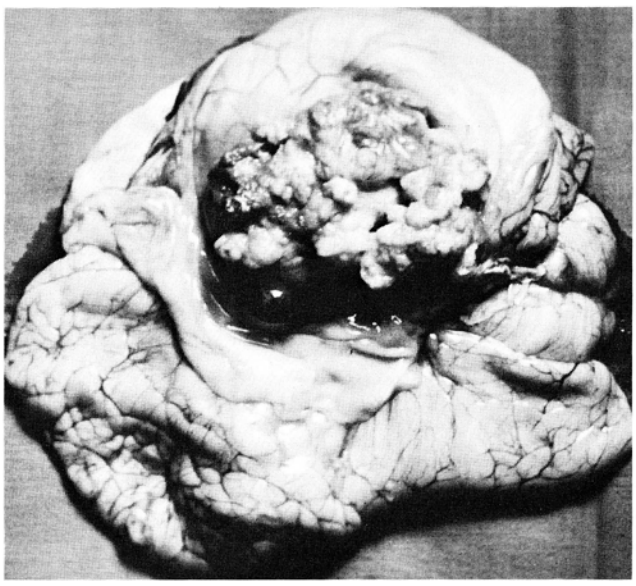
Dr. Zimmerman: I have already commented on the fact that it is splitting hairs to call this a papillary ependymoma rather than a choroid plexus papilloma because the cell covering of these papillomatous tumors is essentially the same.

Dr. del Regato: All experts agreed on a diagnosis of papilloma of the choroid plexus.

Subsequent history: The patient was considered inoperable and was only given supportive measures. On August 13th, 1975 he died. Autopsy revealed massive hydrocephalus with marked cerebral atrophy and erosion of the frontal bone. A cauliflower growth 8.5x6x6 cm was found in the right lateral ventricle with cystic as well as solid calcified areas (Fig. 5).

Dr. Kjellberg: I heartily agree with the management of this case, which is namely no surgery. There sometimes is a social factor that

Fig. 5—Cauliflower growth in the right lateral ventricle.



becomes important: if the parents of a patient with hydrocephalus get information that a shunt operation might be a good thing to do, the pressure is on the clinician to do "everything that is possible," which often becomes very hard. In these current medical/legal times, the position of a surgeon is a bit uncertain when he refuses therapy that somebody else proposes.

Dr. Taveras: One of the things we worry about in an infant with hydrocephalus is missing one of these tumors. You can easily see that if enough gas had not been injected, the fluid level would have been above the level of the tumor. In fact, the tumor only showed up about 6 or 7 mm above the fluid level. If there had been 10 or 15 cc less gas, you would not have seen it; that is one of the things that bothers us constantly. Of course, the more air you replace, the greater the morbidity, so you don't want to replace too much cerebrospinal fluid. You have the possibility of subdural hematomas as complications. However, with computerized tomography we can rule out the possible presence of a solid tumor contained within the fluid space; contrast enhancement probably will be used routinely in the future treatment of infants with hydrocephalus.

Dr. Renu Jalota, Salt Lake City, Utah: This was a large case of hydrocephalus, and our neurosurgeons decided not to operate; the parents agreed. We had a similar case where the parents insisted on operation; they put him through a tremendously long procedure and cancer removal, and the patient died anyway. In this case, we advised the parents, and they agreed.

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5. Microscopic Ganglioglioma of the Frontal Lobe

Contributed by **J. D. Cox, M.D.** and **V. Haughton, M.D.,** Milwaukee, Wisconsin

The patient was a 35-year-old woman in June 1975. A violinist, the patient saw unusual bright colors, and she saw notes leaping out of the score; she also heard voices but no specific words. On examination there were no localizing neurologic signs. The EEG suggested a frontal focus.

Dr. Taveras: The first CT scan was made without contrast enhancement and presents a roughly rounded area of diminished absorption that reaches the surface of the brain. It is producing deformity of the right frontal horn and slight midline shift of the septum pellucidum and the lateral ventricles. At this stage, it would be impossible to tell whether the mass is a neoplasm or some other lesion, such as an abscess, infarct, or a demyelinating process. Also this could be a small nodule of tumor that is either outside of the level of this cut or is also composed of tissue with diminished absorption and surrounded by an area of cerebral edema. The contours of the area of diminished absorption are too sharply defined, and I tend to believe that this whole area is the tumor itself surrounded by a thin rim of cerebral edema (Fig. 1).

The second picture appears to have been taken after contrast enhancement because I believe I can see the shadow of the straight sinus and of the vein of Galen, which is considerably more dense than is usually the case when they contain only blood. It is noted that the level of the cut is slightly lower than the one in the previous cut, and it shows what appears to be very minimal enhancement of some of the tissues in the periphery of the area of diminished density. However, the enhancement is only slight and, in fact, even somewhat less than the remainder of the brain itself. At this level, there appears to be an area of diminished absorption in the right hemisphere in the parietal region or temperoparietal area that is very ill-defined and could represent an artifact. If the head is tilted slightly, the level of the cut could be closer to the atrium and posterior portion of the temporal horn on the right side than on the left, and this could tend to produce a partial volume artifact (Fig. 2).

The lesions that could produce the type of abnormality described on CT are a metastatic squamous cell carcinoma, an astrocytoma, a cerebral infarct, an area of demyelination, a cerebral abscess, or a granuloma. The lesion is too sharply circumscribed to fit what we might expect to see in a demyelinating process. Abscesses usually show enhancement in their capsule, which is not present here. The granulomas that I have seen have tended to enhance more than is noted in this example. This leaves us with two lesions, namely, a primary or a sec-

ondary neoplasm. Metastatic squamous cell lesions could easily produce changes like these, but with contrast enhancement I would expect to see a nodule or a capsule around a necrotic center somewhere in the lesion. Therefore, I would tend to favor a primary neoplasm starting in the frontal or fronto-temporal region on the right side. The diminished absorption in the right parietal region could be hemispheric edema, or it could actually be part of a widely infiltrative process, such as is seen in high grade gliomas or in glioblastomas.

Dr. Taveras' Impression:

1) **HIGH GRADE ASTROCYTOMA OR GLIOBLASTOMA**
2) **METASTATIC SQUAMOUS-CELL CARCINOMA**

Radiologic impressions submitted:

Astrocytoma	25
Glioma	21
Epidermoid	7
Frontal tumor	7
Benign lesion	7
Porencephalic cyst	16
Others	10

Dr. Taveras: Astrocytoma and glioma are good diagnoses. I should have mentioned epidermoid, but because of the area of the brain, the parietal region, I was not very impressed with that possibility. Frontal tumor is only a location. Benign lesion is a perfectly good possibility, but I don't know whether abscess or infarct versus neoplasm was meant. Porencephalic cyst should be considered, but we don't see any changes in the ventricles that would go along with that. It could be one of those porencephalic cysts with a very narrow connection and otherwise normal ventricular system; these should have a very sharp outline on CT scanning, as sharp as the outline of the ventricle.

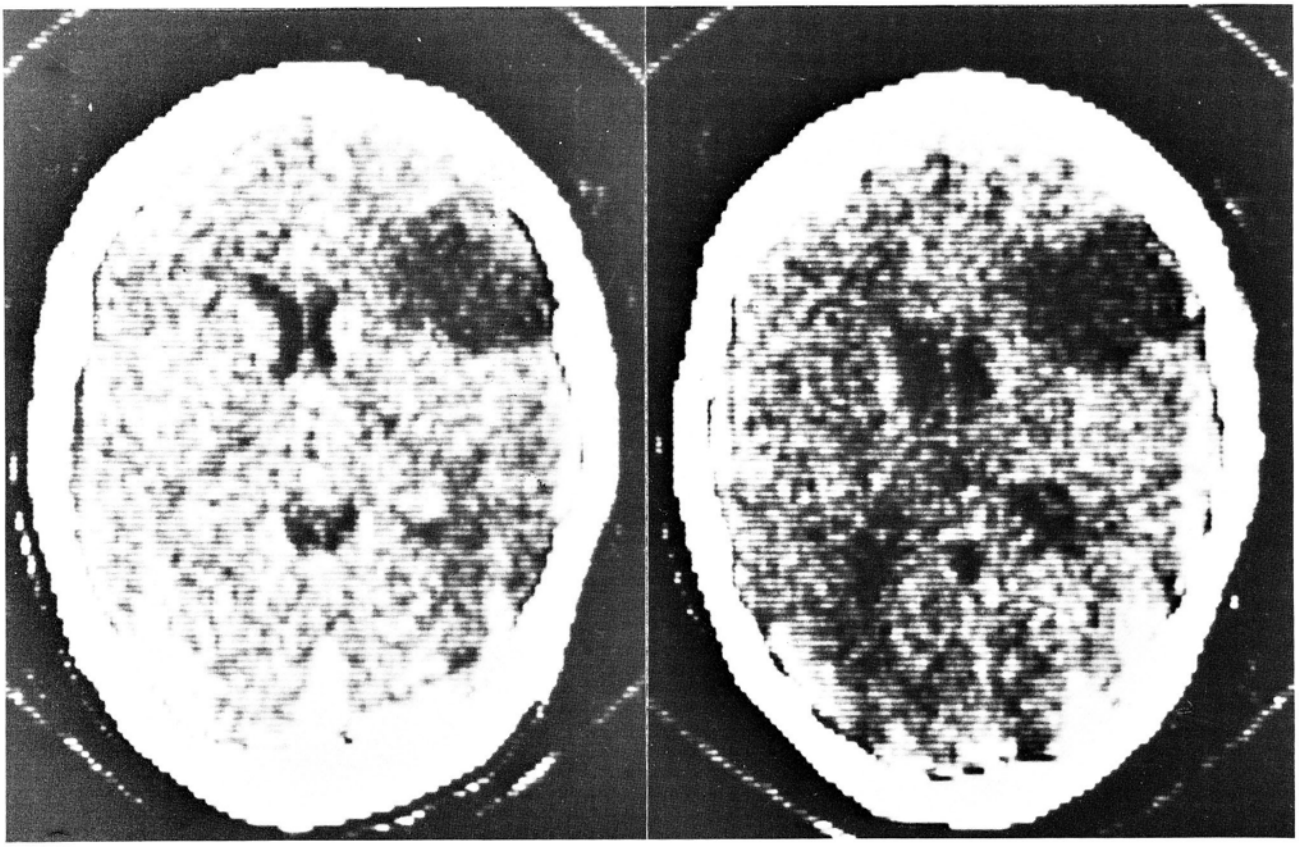
Dr. del Regato: Dr. Lawrence Gold of Minneapolis suggested epidermoid. Dr. Harold O. Peterson of Minneapolis commented that although there was no notation as to enhancement of one of the CT's, one of them has some dense areas within it, more than the other. He concluded that this could be an astrocytoma or glioblastoma.

Operative findings: On June 5, 1975 a right frontal craniotomy was carried out, and a subtotal removal of the tumor was done.

Dr. Zimmerman: Dr. Taveras' performance in calling attention to a possible second lesion in this case is one of the reasons why he is one of my favorite neuroradiologists. There is only slight clinical evidence of multiple lesions in this case, and I did not think there is any suggestive

Fig. 1—Computerized tomogram without enhancement, showing area of rounded absorption near the brain surface.

Fig. 2—CT scan after contrast enhancement with area of diminished absorption in the right parietal region.



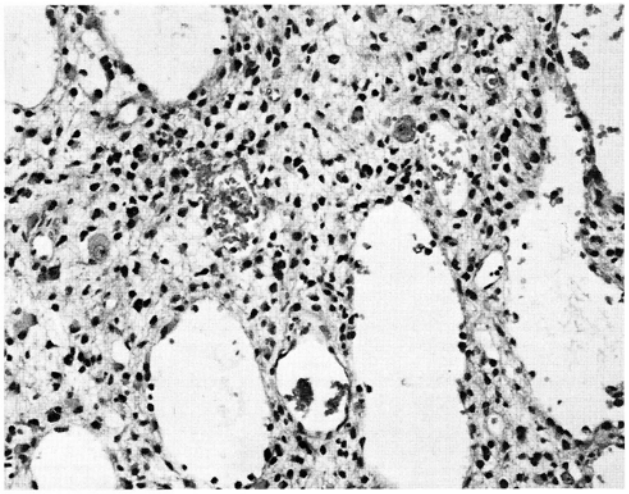


Fig. 3—Microcystic ganglioglioma. The majority of the cells are small fibrillary astrocytes, but a few protoplasmic astrocytes are also present as well as two neurons. H and E stain; x180.

roentgenologic evidence of this. Apparently there is.

We were told this patient had visual and auditory hallucination, in addition to a lesion that was removed from the major site indicated by Dr. Taveras. Could these hallucinations indicate lesions in the occipital and temporal lobes, in addition to a lesion in the frontoparietal area? Now that Dr. Taveras has called attention to the fact that there is a possible lesion, perhaps an artifact, at a second site, it is intriguing to speculate what this may be. Pathologically, the slide we have been given for study represents a lesion that may well be multicentric.

In the slide of the tissue you received in this case, there is a spongioform appearance of a zone that represents cerebral cortex (Fig. 3). The normal lamination is disrupted, and the whole cortex has a completely disorganized appearance. Here and there one finds a ganglion cell and an occasional protoplasmic astrocyte of large size (Fig. 4). Most of the cells, however, are small and stellate in shape and give rise to fibrillary processes that form a loose meshwork in which are present many small cystic spaces. The bulk of this lesion is therefore a microcystic astrocytoma. The disorganization of the cortex and the presence of abnormal neurons, coupled with a microcystic fibrillary astrocytoma, call to mind the kind of lesion one sees in tuberous sclerosis. This condition is, of course, frequently multicentric. This is the reason I was intrigued with the suggestion offered by Dr. Taveras that there may be roentgenographic evidence of several lesions in this case.

The histologic picture is one of a mixed tumor in which ganglion cells and astrocytic glia are both present. This makes the neoplasm a ganglioglioma. A tumor of this variety was recently described in the temporal lobe by Rubinstein and Herman.

Dr. Zimmerman's Diagnosis:

MICROCYSTIC GANGLIOGLIOMA

Histopathologic diagnoses submitted:

Astrocytoma	34
Hemangioma	9
Others	6

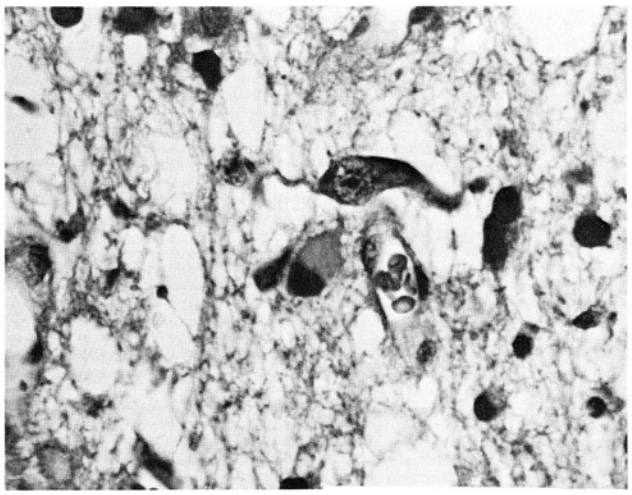
Dr. Zimmerman: I do not see any reason for a diagnosis of hemangioma here. Only a few called attention to the possibility of ganglion cells being involved; I think one or two indicated that it is probably just an instance of ganglion cells in the cortex where an astrocytoma developed and the ganglion cells, where entrapped by the proliferating glial cells, did not by themselves constitute part of the tumor. My impression is that this is one of the few instances in which the ganglion cells also represent tumor, if not a proliferating neoplasm in the tumor, due to abnormal position in the cortex.

Dr. del Regato: Drs. Magda and John Kepes of Kansas City offered a diagnosis of protoplasmic astrocytoma, grade II; they suggested that the neurons present were probably "trapped" from the infiltrated territory. Dr. Leo Lowbeer of Tulsa diagnosed a hemangioma, cavernous and papillary.

Subsequent history: From June 19th to August 6th, 1975, radiotherapy was administered with a 25 MEV betatron; a total of 6,300 rads was received at the cranial midplane. On January 31st, 1976 the patient was in good health (Fig. 5).

Dr. Taveras: The follow-up CT shows an area of diminished absorption in the same area where the tumor was located previously. I am unable to see any other abnormality on these films; I can't say one does not exist, but I'm not sure either that one does, for there was motion artifact. I can only say that the normal area is in

Fig. 4—Ganglioglioma with a spongioform background in which lie one ganglion cell and an adjacent protoplasmic astrocyte. H and E stain; x720.



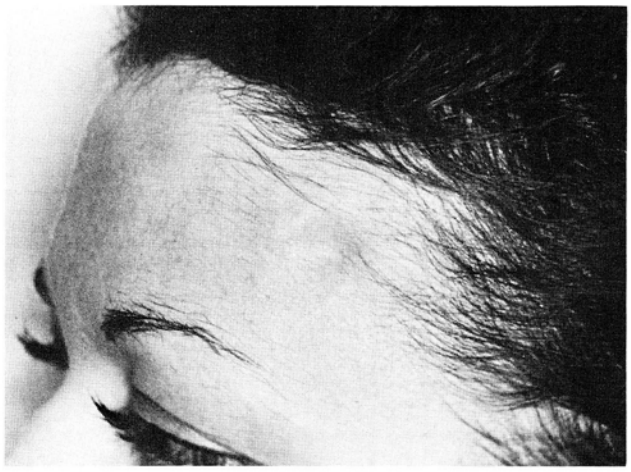


Fig. 5—Appearance of patient following irradiation with regrowth of hair.

the same location and that the ventricles are not displaced; there is still a little compression on the right frontal tip, which indicates some residual swelling in the tissues (Figs. 6 and 7).

Dr. Kjellberg: There is a big difference if one is trying to resect an intrinsic tumor of the brain on the right side or the left side. The right sided lesion allows a fairly generous tumor resection with the principle consideration being not to carry the resection so far posteriorly as to interfere with corticospinal function and not to carry it so deep as to interfere or injure basal ganglia structure.

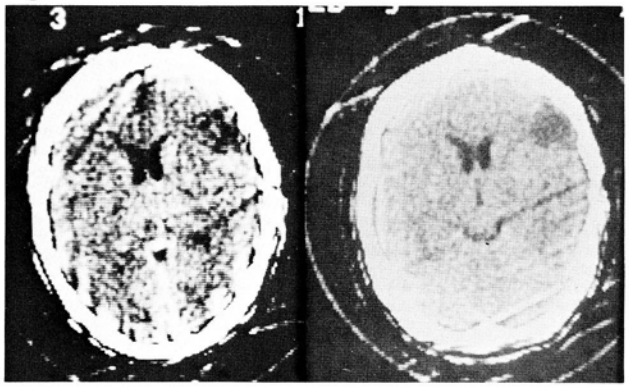
In Kernohan's classification, a grade II astrocytoma has about twice as good a prognosis as a grade III or IV, and a grade I astrocytoma has a 5 or 10 times better prognosis than a grade II. The distinction between grade I and II in Kernohan's classification has always been particularly helpful to me in appraising the prognosis. It also influences therapeutic decisions. The radiotherapy department in our hospital will not normally irradiate post-operatively a grade I astrocytoma; rather, it will wait and withhold the full effect of radiotherapy for the time when it progresses to a higher grade lesion because the radiotherapy is more effective in grades II or IV, and particularly grades III and IV. We have irradiated tissue cultures with protons; I can't extend this observation to x-rays, but I don't think there is any difference. The radiosensitivity of a grade I lesion is almost exactly the same as normal brain, so you're not really getting anything with irradiation unless you go to doses that are liable to injure the brain, which you are not going to do, of course. If you wait and save the shotgun until you run a grade III or IV lesion, the prospect of radiotherapy in full doses having a good effect is greater.

Dr. Zimmerman: Paul Bucy has categorically said that there is no benign grade I astrocytoma above the tentorium; all his patients have died with tumor. He said they are all malignant but in a different degree of malignancy. This is in contrast to subtentorial astrocytomas that he has cured, and I have also seen a good many patients cured. As a grader, I take on the appearance of a prophet, which I am not. One tiny segment of tissue from a large tumor mass is all that the average neuropathologist gets; on the basis of that slide section, which is 6 or 8 microns in thickness, he counts a few mitoses and assumes that the rest of the tumor shows the same thing. Then he makes a diagnosis of grade I malignancy. In this case, I would grade it I and ½. I don't honestly believe I can tell grade I from grade II in this case. I doubt very much if any neuropathologist is that much better that he can tell a grade I from a grade II. I can tell a grade I from a grade IV, but the trouble with a grade IV is that the more malignant it is, such as the gliblastoma multiforme, the less responsive it is to irradiation. All neurosurgeons and all radiotherapists know that the results with glioblastoma multiforme, even with heavy irradiation, leave much to be desired. The best results I have seen have been with the more benign forms of astrocytoma.

At a symposium at the New York Academy of Medicine, the former chief of neurosurgery of the College of Physicians and Surgeons and I agreed that the best results following irradiation were with grade I astrocytoma, whether they were cerebellar or supratentorial. I think that is probably true; from all the hundreds of cases of astrocytoma that I have seen, the more malignant ones have survived the shorter period of time and have tended to be less well affected than the more benign ones. This has led me to loathe the grading of these tumors. I do it because I am forced to by neurosurgeons, but I am not very happy about it; in many instances, I am partly guessing.

Dr. Kjellberg: I think it is perfectly true that the thinking about this type management differs from place to place. I certainly agree that the

Figs. 6 & 7—Follow-up CT scans.



outlook of low grade astrocytomas is much better with or without irradiation than high grade astrocytomas. According to the most recent figures, the life expectancy following surgery alone for glioblastoma is four months, and for high grade III or IV astrocytoma, radiotherapy doubles that life expectancy. When you're dealing with highly malignant disease, I think this level of palliation is warranted, or at least not easily withheld.

Dr. Zimmerman: In practice, don't you irradiate all incompletely removed gliomas?

Dr. Kjellberg: It is our policy not to irradiate grade I. A few years ago, Dr. Taveras and I considered the value of withholding therapy from grade IV's, that perhaps the irradiation done at a later time might prove more valuable than that done immediately post-operatively. We did not come to any strong conclusion, but as a result, I have not irradiated glioblastoma post-operatively. I started lining the cavity with gold foil and then took annual films to see what the cavity was doing. I now think the gold foil is no longer the best way to do it. I think CT scanning is much better than gold foil.

About two years ago, we had a patient with glioblastoma under consideration who was totally asymptomatic post-operatively. He had no neurological deficit whatsoever, and we opted not to provide radiotherapy. He's now over two years post-operative and has no neurological deficit. We're waiting for him to develop enough change to warrant the introduction of radiotherapy in order to maximize the extension of his life.

Dr. Zimmerman: Your observation is at variance with Bouchard's and Kramer's experiences with effects of irradiation for a grade IV astrocytoma, the glioblastoma multiforme. Is that right? You have not had the good results in survival length that they have reported. Is that right?

Dr. Kjellberg: I am making no argument for not delivering radiotherapy; it is a question of when it is delivered, not whether or not it is delivered.

Dr. del Regato: Also, how it is delivered.

Dr. Kjellberg: 4500 rads, four and a half weeks.

Dr. del Regato: Actually, that is no standard, and it is not enough qualification. It is true that the more differentiated tumors appear to be less **radiosensitive** in the sense of their promptness to respond, but they may be no less **radiocurable** and in fact, more so in view of their greater confinement.

The normal nervous tissue is rather radioresistant. However, the entire brain can be necrotized, depending on how brutally it is irradiated; it is a matter of the amount given and the time in which it is given. The destruction, the necrosis that may follow the melting of the tumor, and the creation of a defect are all complicating factors for which radiotherapy should not necessarily be blamed. Sometimes the operative sucking out of the tumor from the brain is to be blamed just as much for the necrosis that follows.

This patient's picture shows that it is possible to irradiate the patient and to even have a regrowth of the hair; in the same manner, it is possible to gently irradiate children and cure them from medulloblastomas of the cerebellum that are not curable by surgery.

Dr. Kjellberg: There may be reasons for believing that the interval before delivery of full course radiotherapy may be a useful tactic.

Dr. Taveras: I wonder about the wisdom of not irradiating a high grade tumor. I wrote a paper once on the treatment of 425 glioblastomas, and the prognosis was very bad. It would appear, as Dr. Kjellberg indicated, that the survival is at least doubled when radiation therapy is added to whatever the surgeons accomplished on the operating table in terms of tumor removal. However, in my estimation, to withhold radiation therapy following surgery in a tumor that is a high grade astrocytoma would probably not be the best course to follow, although an occasional one may turn out very well.

Out of the 425 cases, we had only one patient who lived for seven years; the others lived an average of under 18 months. We had a small number who lived two years, three years, and three and a half years. It is a very malignant tumor if it is called glioblastoma, which is what we are discussing now. In the low grade that the pathologist might call grade I, I would certainly agree with Dr. Kjellberg that radiation therapy should be withheld.

Dr. Kjellberg: I have read Dr. Taveras' publication with considerable care. One of the things that has interested me is that a few months after the therapy, the survival began to fall off. It is absolutely a straight line down to two years with 5 to 10% of the patients surviving. Then there is a sharp change in the course of that curve, and it levels out to the ten year interval. Looking at a graph like that, it comes to mind that this represents two populations, two standard distribution curves added to each other.

Bucy feels that these cases having long life expectancies in excess of two years are perhaps biologically a slightly different tumor. He makes the case that most of these are mixed glioblastomas and that the distinction might be important because it very much altered the prospect of life expectancy, resulting in the multi-year survivals of glioblastomas.

Dr. Zimmerman: I think that when there is a portion of a glioblastoma that is astrocytoma grade I and another portion of the same tumor that is a grade IV glioblastoma multiforme, the glioblastoma soon takes over, outgrows and outstrips by growth rate. It has been my practice to always make a diagnosis based on the most malignant cell available because I believe that determines the ultimate prognosis.

I am somewhat loathe to comment on the irradiation of fairly benign astrocytomas other than in the region where a surgical extirpation is not feasible, such as involvement of the speech center. Some years ago I conducted a symposium in Philadelphia on life expectancy of patients with various gliomas. On presentation of Louis Eisenhardt from the Cushing series, I discovered that if a patient had an astrocytoma and had Cushing remove it, he might have lived for 30 or 35 years after removal of a benign astrocytoma, or longer than the life expectancy for this age group of patients.

Dr. James Cox, Milwaukee, Wisc.: I do not think that we deal as well with a bulky tumor as with microscopic disease; therefore, it is very difficult to make a case for waiting until a gross tumor has developed instead of dealing with the microscopic residual, which would be in place immediately following the operative procedure.

This lady, unfortunately, is left-handed instead of right-handed, and the lesion in the right frontal lobe was in the dominant hemisphere. It was the understanding prior to the operative procedure that if the tumor extended posteriorly in the vicinity of the motor strip, no attempt to remove this area would be undertaken, that this would be left to radiation therapy. This was indeed the case. She recovered very well and returned to playing the viola with the Milwaukee Symphony three months later. She performed the Schubert String Quintet a week ago and is doing very well at present.

The interpretation of the most recent CAT scans projected was that this was a stable situation between November 3 and February 9, that this represents a residual defect at the site of the tumor, and that there is no evidence of progression. We initially thought this represented a temporal lobe focus of some sort; reviewing the history very carefully, we had the impression immediately post-operatively that this was a visual hyperacuity, not visual and auditory hallucinations, and that this was a disturbance of her perception while performing. Therefore, we did not irradiate the area posteriorly; we irradiated a more limited portion of the brain. She is without evidence of disease at present.

The slide of this case was originally seen by Dr. George P. Sayre at the Mayo Clinic, and we were given the impression of a grade III. We don't like to play with numbers either, but we felt that it was sufficiently ominous to oblige us to irradiate. If somebody had told me that this was a very minor grade I, I might have been inclined to hold off.

Dr. del Regato: Perhaps it is just as well no one did! Also, the patient was treated in a total of 50 days, or more than seven weeks. The time in which any amount of radiations is delivered has as much importance as the dose.

Dr. Joseph Rush, St. Petersburg, Fla.: Dr. Kjellberg, have you had any experience with BCNU post-operatively but without irradiation?

Dr. Kjellberg: I don't handle this part of it. There is a recent report that BCNU will extend life; if surgery, radiation and BCNU are used, the added increment to life is about three weeks. I think the increment of irradiation is so important that withholding irradiation post-operatively is really unwarranted, but I think BCNU is a distinct advantage.

Dr. Mason Trupp, Tampa, Fla.: How many rads did this patient receive?

Dr. del Regato: The patient received a total of 6,300 rads in a total of 50 days from June 9 until August 6. The time in which it is delivered we believe is an important consideration.

Dr. Kjellberg: I couldn't agree more about the importance of time. When we use proton radiation, we deliver doses between 5,000 and 15,000 rads in less than an hour, so we have to be acutely aware of the interval effect. I would add one other factor that I think is important: the size of the volume irradiated in relation to the response of the tissue. In neurological circles, left-handedness is not the opposite of right-handedness; that is, in a left-handed person, not all of his speech mechanisms are in his right hemisphere. In general, only about half of the patients who are left-handed will become aphasic with right hemisphere carotid injection of barbiturates. An equally large number of left-handed patients become aphasic with left-handed injections, and the degree of the aphasia is different; the fixation of speech function in the right hemisphere in left-handed patients is just less firm than it is in right-handed patients. It is a complicated subject.

Editor's Note: Dr. Cox reported on Oct. 4, 1977 that his patient is doing perfectly well and is performing actively. She is normal at this time.

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6. Hemorrhagic Infarct of the Temporo-Parietal Region

Contributed by **H. M. Zimmerman, M.D.**, New York, New York

The patient was a 66-year-old woman in July 1975 when she complained of frontal headaches, mental confusion and urinary incontinence of 2½ years duration. On examination she was aphasic, disoriented and showed symptoms of right hemiparkinsonism, mildly increased tendon reflexes and slight left hemiparesis.

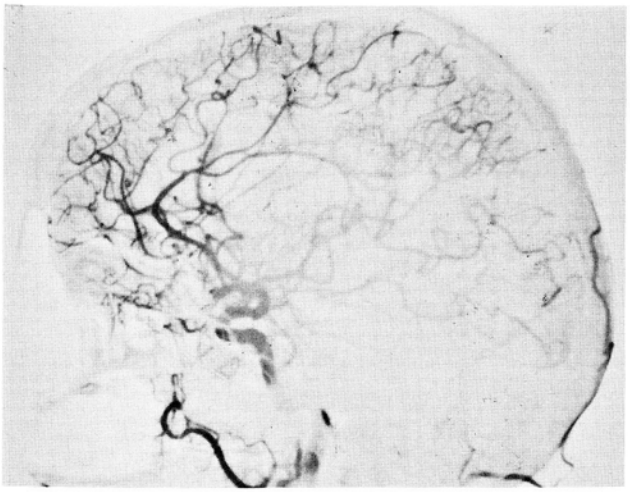
Dr. Taveras: The lateral view of a carotid angiogram made during the arterial phase after injection of contrast in the common carotid artery shows that there is an area of relative avascularity low in the frontal parietotemporal region. One vessel is arched posteriorly, located in the mid-posterior frontal region and presents an area of focal narrowing measuring about 1 cm in length. There are no other narrowed vessels that I can see. No abnormal vascularity or tumor stain can be appreciated at this stage (Fig. 1).

There are two slices from a computerized tomogram, one passing through the anterior horns and the other one slightly above and outlining part of the body of the right ventricle. The lower cut shows an area of increased absorption posteriorly in the posterior frontal region and anterior to that, in the frontal lobe, there is an area of non-homogeneous low absorption. The higher cut shows that the area of increased absorption is much larger, and it is surrounded by a halo of diminished absorption that could be produced by edema around a mass or hemorrhage that appears to be homogeneous at this level. The lower cut shows solid dense tissue posteriorly, but anteriorly there is an area of irregular diminished absorption that could represent partly necrotic tumor or could represent a partial volume effect with brain edema cut at the same time as tumor. As far as I can see, both cuts were taken without intravenous contrast enhancement, or perhaps both were taken after contrast enhancement. If so, the interpretation of the findings may be entirely different (Figs. 2 and 3).

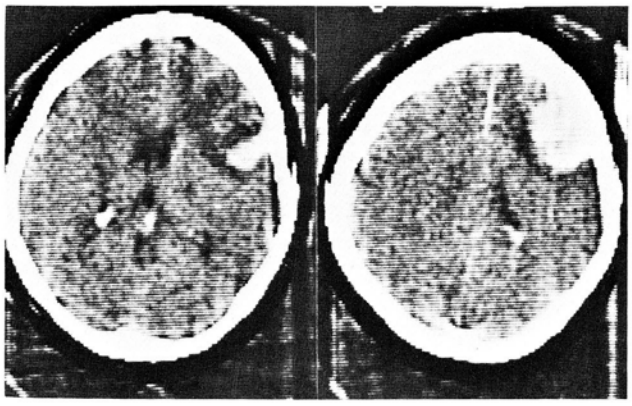
This is obviously a superficially placed mass. If it is a tumor, it must have started superficially and is growing towards the brain. The symptoms that the patient presents suggest that there is involvement of the brain tissue. These include aphasia and right hemiparkinsonism. Yet, the tumor mass is situated fairly far anteriorly where one would ordinarily not expect compression of the thalamus and basal ganglia.

The high density of the mass favors a meningioma and suggests a bloody mass. Gliomas don't usually present such a high density unless there has been a hemorrhage within the tumor, which is uncommon. Metastatic adenocarcinomas can have this degree of density, but this diagnosis cannot be justified unless more than one lesion is seen. The focal narrowing of one of the branches of the middle cerebral artery suggests encasement by tumor or intrinsic vascular disease. In fact, there may be an occluded artery that cannot be evaluated without a complete serialogram. In addition to glioblastoma and reticulum cell sarcoma previously mentioned as possible causes of arterial wall invasion, meningioma should be listed. It is true that meningiomas produce arterial encasement usually around the base of the skull, mainly in the para and suprasellar region. In the case under discussion, I would have to suspect the possible

Fig. 1—Right carotid angiogram subtraction showing area of relative avascularity in the parieto-temporal region.



Figs. 2 & 3—Computerized tomograms showing area of increased non-homogeneous absorption in the posterior frontal region.



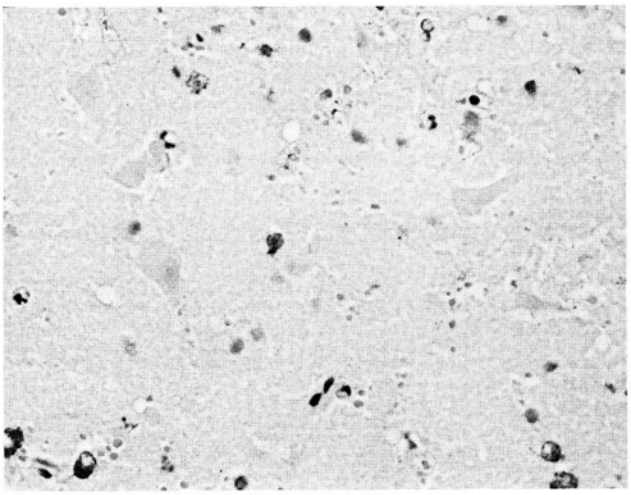


Fig. 4—Cerebral cortical infarct revealing ghost-like, necrobiotic ganglion cells, karyorrhectic nuclei and extravasated erythrocytes. H and E stain; x450.

presence of invasion of the brain, and if meningioma were the cause, I would tend to call it a malignant meningioma or meningeal sarcoma.

Hemorrhagic infarction is another possibility; a frank cerebral hemorrhage is a definite possibility, particularly because of the well developed radiolucent zone around the dense area, but the location away from the basal ganglia region is a bit unusual.

Dr. Taveras' Impression:

1) **HEMORRHAGE OR HEMORRHAGE INFARCT**
2) **MENINGEAL SARCOMA**

Radiologic impressions submitted:

Meningioma	36
Glioma	26
Choroid papilloma	3
Benigh vascular lesion	6
Metastatic tumor	5
Others	15

Dr. Taveras: Meningioma is alright except for some features in the angiogram that I thought did not go along with meningioma. The changes should be more localized, and I get the impression of an obstructed vessel. Glioma would be another possibility, but it is calcified; it contains enough calcium in a difussed manner to be seen by CT scanning but not necessarily by a plain radiograph of the skull. Computerized tomography is able to show us minimal amounts of calcium within the brain, within the tumor or within the organs that we cannot see at all by the best possible radiographic method, including very careful tomography. That is a much more sensitive method. With CT scanning you can also see edema of the brain that is just a little increase in the amount of water in the tissue as compared to the surrounding normal brain, and, of course, you can never see that on a plain film examination of the skull, by angiography or by any other method. However, this does not look like the kind of calcification that I would expect any glioma to have. Meningioma, yes, because of psammous distribution diffusely throughout the mass. I see no reason for choroid plexus papilloma. A vascular occlusion would not be benign; if a benign vascular neoplasm is meant, I would question it because this is not taken with contrast enhancement. Metastatic tumor is a definite possibility, as I have already indicated.

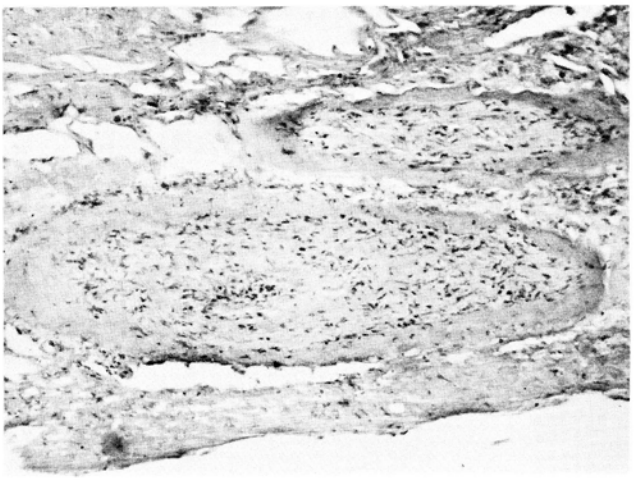
Dr. del Regato: Dr. Harold Peterson of Minneapolis saw no abnormality in the angiogram; he commented that the fronto-temporal lesion enhanced on the CT scan and concluded that this could be a meningioma or astrocytoma. Dr. James Cox of Milwaukee suggested a cystic astrocytoma.

Operative findings: On July 16th, 1975 an exploratory craniotomy was done. The brain was swollen and hemorrhagic. An aspiration brought 7 cc of blood. A biopsy was done, and a diagnosis of probable infarct was rendered.

Dr. Zimmerman: Prior to the time when our hospital became affluent enough to purchase an EMI scanner, we depended very heavily upon technitium scans in localizing space occupying lesions intracranially. In consequence, six patients in my opinion were operated upon unnecessarily in the past three years in our institution. This was because in each instance, the technitium scan revealed localized uptake that seemed to confirm the presence of a tumor as seen angiographically. The present case is in addition to the six just mentioned and had an EMI scan.

You will recall that Dr. Taveras pointed out the fact, overlooked by our radiologist, that there is probable evidence of vascular occlusion in the cerebral angiogram. In a moment you will see how right he was. The reason I said that our sudden affluence that resulted in the purchase of an EMI scanner was beneficial to our patients was because the acquisition of this instrument

Fig. 5—Thrombosed leptomeningeal arterioles adjacent to cerebral infarct. H and E stain; x150.



put a stop to these unnecessary craniotomies. I no longer see biopsies of massive cerebral infarcts that I once saw in our pre-EMI days. The occasional case that I still see is a referral for histologic diagnosis from an outlying hospital.

At operation in this case, the brain was found to be diffusely swollen and suggested the swelling seen in an underlying, subcortical neoplasm. The exposed gyri were flattened and widened. As Dr. del Regato already told you, the insertion of a needle subcortically yielded seven cc of dark, discolored blood. There was probably more blood left behind that was not aspirated. A piece of cortical tissue was excised at operation for microscopic examination. The neurosurgeon felt that the lesion was a brain tumor of the glioblastoma variety.

Microscopic examination of the biopsy specimen disclosed a complete obliteration of the cortical lamination. There were no viable ganglion cells, but traces of them remained as pale, pyramidal bodies with faintly stained nuclei (Fig. 4). Occasional minute fresh hemorrhages were noted as evidence of the surgical removal of the specimen, but larger extravasations of red blood cells that were partially laked were also present. In addition, the tissue had collections of old, canary yellow blood pigment. Many of the injured neurons were eosinophilic in hematoxylin-eosin preparations. There was practically no survival of the normal glial matrix and no evidence of a proliferative glial response. Karyorrhexis was present in abundance, and a feeble phagocytic reaction on the part of microglia was also noted. Darkly staining granular material, probably calcium salts, was present in small amounts diffusely spread throughout the cortex. On the margin of the lesion, just beneath the pia, there was a fibroblastic and astrocytic proliferative reaction as evidence of a beginning healing process.

I want to call your attention to several thick walled blood vessels in the leptomeninges adjacent to the cortical infarct (Fig. 5). These are completely occluded by organizing thrombi in which fibroblasts and leukocytes, as well as phagocytosed old blood pigment, are all present. Undoubtedly these thrombosed vessels were responsible for the cerebral infarction.

Dr. Zimmerman's Diagnosis:

CEREBRAL HEMORRHAGIC INFARCT

Histopathologic diagnoses submitted:

Hematoma	16
Necrotic tissue	10
Infarct	18
Others	7

Dr. Zimmerman: There was indeed a hematoma, but it was not of traumatic origin or of any origin other than infarction; it is a hemorrhagic infarction. Necrotic tissue is quite correct.

The vast majority of pathologists recognized that this was an expanding space occupying lesion but not a neoplasm. Two years ago, I was in Japan and read a paper on expanding nonneoplastic intracranial lesions that had been published without my knowledge or consent in a new neurological journal published in Tokyo. The article is in English and shows four or five cases of cerebral infarction, all operated upon by different neurosurgeons with the mistaken view that a glioma or another brain tumor was present. This article, if you are interested, was published in 1974 in **Neurological Medicine,** a Japanese journal.

Dr. del Regato: Dr. R. Hackett of Gainesville, Florida diagnosed a hematoma in the necrotic cortex. Dr. Arnold Effron of Milwaukee also diagnosed infarct.

Subsequent history: The patient recovered from surgery and was discharged in August 1975 with residual mild hemiparesis. On September 26, 1975 she was readmitted with progressive lethargy and urinary tract infection that responded to medical treatment. She was last seen in January 1976; her condition has deteriorated slowly.

Dr. Kjellberg: I have written a list of cited phenomena that I was not quite clear about. She had a right hemiparkinsonism and aphasia, but in the follow-up, it is not clear whether or not she had residual aphasic disturbance. I do not know if she is right- or left-handed, but the history would suggest that she has a left hemisphere lesion of some sort. The scans did not show any such lesion. She is only 66 years old, and she is not reported to be hypertensive. There might be some value in pursuing an additional diagnosis in the left hemisphere of this woman because she still has prospects.

Dr. J. Maxey Dell, Gainesville, Fla.: Do you need are arteriogram when you have a scan with the dense area around it?

Dr. Taveras: One of the easiest diagnoses to make by CT scanning is a brain hemorrhage; it is really an excellent tool. God knows all the difficulties we used to have in diagnosing brain hemorrhage by angiography or any other method. In the angiogram, all we see is a mass effect, and we may or may not see the reason for the hematoma. I would say that we do not need the angiogram to make the diagnosis. In this particular case, I would have done the angiogram because the CT scan only tells us that this is a hemorrhage. The location is not the usual basal ganglia, the location of hemorrhages that we see in hypertensives. This is peripheral and under the inner table of the skull; consequently, we have to think that it is an aneurysm that is bleeding and that we need to do an angiogram to diagnose the aneurysm. A hemorrhage on the surface of the brain can be seen in patients who are receiving anticoagulants; in that case, we would not do an angiogram.

7. Glioblastoma Multiforme of the Frontal Lobe

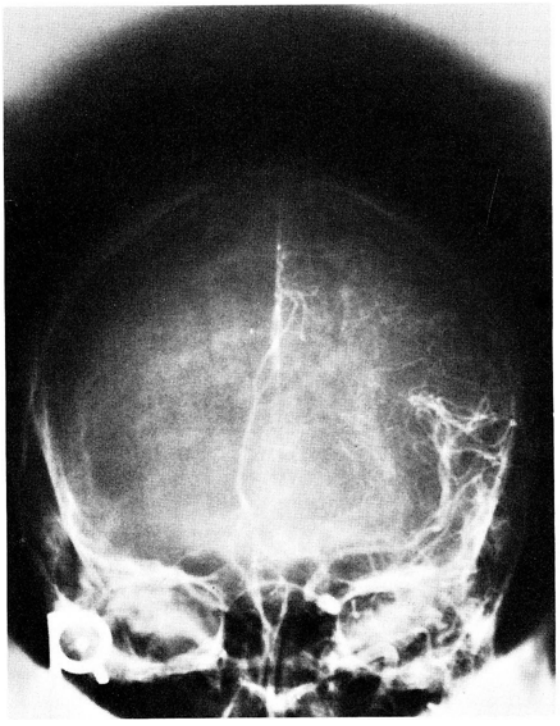
Contributed by **H. A. Azar, M.D.**, Tampa, Florida
and
E. V. Grayson, M.D., Hollywood, Florida

The patient was a 51-year-old man in May, 1975 when he complained of loss of memory, behavioral changes and "inadequate personality." For two years, he had had intermittent difficulties with the movements of his right upper and lower extremity. On examination, there were blurred discs and negative Babinski reflexes.

Dr. Taveras: In the frontal projection, there is a marked degree of midline shift of the anterior cerebral artery. The shift is more pronounced proximally than distally, indicating a lower position to the mass. The displacement is typical of a low frontal tumor. There is some lateral displacement of the middle cerebral branches over the insula, which usually indicates the presence of edema of the posterior portion of the frontal lobe (Fig. 1).

In the lateral projection, there is a relatively avascular area in the anterior third of the brain that is evidently associated with the presence of the mass. There is crowding of the branches of the middle cerebral artery and the Sylvian triangle due to swelling in the frontal region and posterior displacement of the branches of the middle cerebral artery (Fig. 2).

Fig. 1—Marked midline shift of the anterior cerebral artery.



The findings are those of a frontal neoplasm with considerable edema of the brain. There are no specific features that would help me in diagnosing this lesion. The location of it is definitely intracerebral. An intracerebral lesion producing edema that is a neoplasm would most likely be an infiltrative glioma, possibly of intermediate grade because of the length of the history, which is over two years. On the basis of these findings and with this clinical history, there is no reason for suspecting other types of pathologic processes such as abscess, cerebral infarction, demyelinating disease.

Dr. Taveras' Impression:

FRONTAL INTRA AXIAL MALIGNANT TUMOR

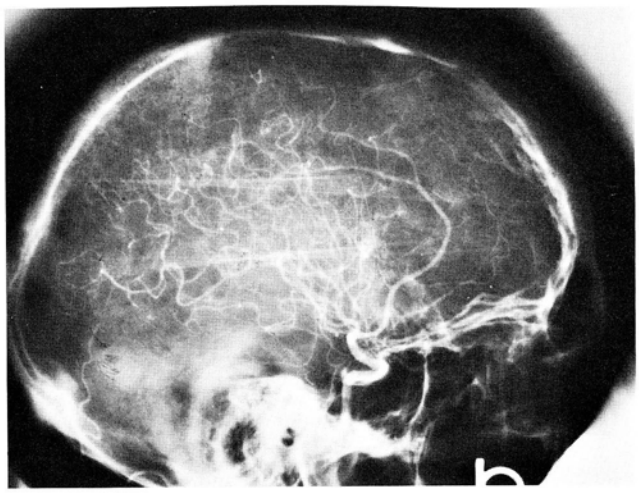
Radiologic impressions submitted:

Glioblastoma	22
Tumor (frontal, temporal, parietal)	30
Frontal lobe abscess	6
Thalmic glioma	14
Others	6

Dr. Taveras: This is definitely a frontal location, as I see it, and an abscess is not an impossible diagnosis due to the presence of edema of the brain in the frontal lobe. I would not place this in the thalamic region because, as I said, it is all in the frontal location, pushing the Sylvian triangle backward.

Dr. del Regato: Dr. Greg Arterburn of Tampa made a diagnosis of frontal glioma. Dr. Richard Latchow of Minneapolis suggested a fungal abscess.

Fig. 2—Relative avascularity of the anterior part of the brain associated with a mass.



Operative findings: On May 21st, 1975 a left fronto-temporal craniotomy was done with decompression and partial removal of the tumor, which was friable and hemorrhagic.

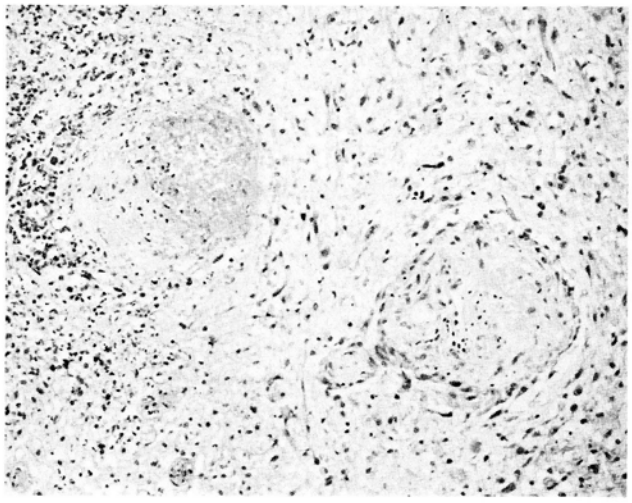
Dr. Zimmerman: In the microscopic preparations of this case, there is a neoplasm that is composed of pleomorphic cells of varied size and shape and staining quality. Some of the cells are fairly large and have multipolar processes (Fig. 3). These cells are obviously of astrocytic origin. There are foci of necrosis in this tumor and occasional petechial hemorrhages. The latter may be of traumatic (at operation) origin. Some cells are quite large, actually of giant size, but multinucleated tumor giant cells are infrequent. One such cell is illustrated in the right lower corner of figure

Many vessels in the tumor are thrombosed (Fig. 4). In some, the thrombi are well organized, whereas in others they are still quite fresh. These occluded vessels account for the fairly extensive necrosis in parts of the neoplasm. The necrotic foci have some of the appearance of infarction. There are, in addition, extensive endothelial vascular proliferative changes, and a few vessels are surrounded by cuffs of lymphocytes.

We have, then, a tumor with some hemorrhage and necrosis, with cellular pleomorphism in an essentially astrocytic glioma, and with vascular occlusions. However, there is no pseudopalisading of spongioblasts around central necrotic foci and only few multinucleated tumor giant cells. An additional feature is the perivascular lymphocytic collections. Most of the criteria for a diagnosis of a malignant astrocytoma (Grade III or possibly even Grade IV) are therefore present. It should be borne in mind that not every glioblastoma multiforme has all the histologic features of the classical tumor of this kind.

Around a few vessels in this tumor there was present a fibrillary stroma, which emanated from elongated tumor cells that resembled fibroblasts (Fig. 5). Some of you evidently were impressed with this feature sufficiently to suggest a malignant mesodermal neoplasm as the diagnosis. Indeed, mixed tumors of the glioblastoma multiforme and sarcoma varieties occurring together are not so very infrequent. These considerations prompted me to prepare reticulin stains of this neoplasm that were negative.

Fig. 4—Thrombosed blood vessels are present in this neoplasm. H and E stain; x150.



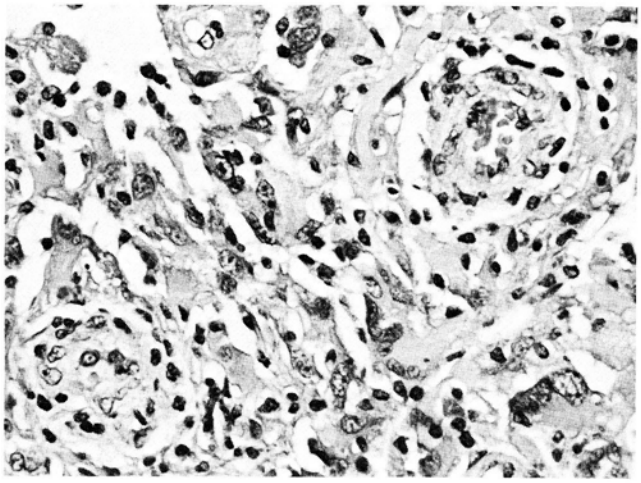


Fig. 3—Large protoplasmic astrocytes form the bulk of the tumor cells in this glioblastoma multiforme. A multinucleated tumor giant cell is seen in the right lower corner, and a vessel with endothelial proliferation is in the right upper corner. H and E stain; x450.

Dr. Zimmerman's Diagnosis:

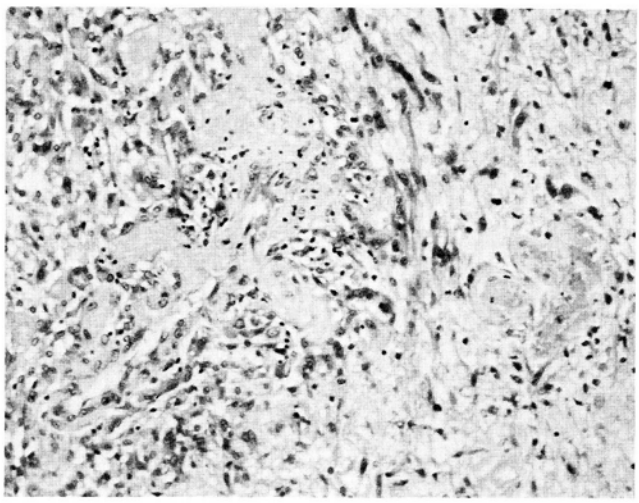
GLIOBLASTOMA MULTIFORME

Histopathologic diagnoses submitted:

Glioblastoma multiforme	28
Gemistocytic astrocytoma	15
Others	6

Dr. Zimmerman: Half of the pathologists have called it a glioblastoma multiforme. Technically,

Fig. 5—Elongated tumor cells resembling fibroblasts and evidently forming a fibrillary stroma lie adjacent to blood vessels. Wilder preparations of this portion of the neoplasm for reticulin fibers were negative. H and E stain; x180.



astrocytoma is correct because glioblastoma multiforme is a malignant form of astrocytoma. In order to avoid an error by thinking that this may be a benign astrocytoma, and in view of our lengthy discussion of radiotherapy for different types of gliomas, it is better to designate what kind of astrocytoma. I think it is a malignant astrocytoma grade III or IV.

Dr. del Regato: Dr. D. R. Dickson of Santa Barbara and Dr. W. J. Kirsch of St. Petersburg also made a diagnosis of glioblastoma multiforme. Dr. L. Lowbeer of Tulsa suggested that this was a gemistocytic astrocytoma converting to glioblastoma multiforme. Drs. Magda and John Kepes of Kansas City offered a diagnosis of fibrosarcoma.

Subsequent history: The patient received radiotherapy post-operatively, a total dose of 5500 rads measured at the midline of the brain in 44 days. His memory became extremely poor, and he became withdrawn, lost interest in surroundings and in his personal appearance. He was last seen on February 2nd, 1976 at which time he was considered to be irresponsive and subject to affective schizophrenia.

Dr. Kjellberg: In a case like this, biopsy is certainly imperative to establish a diagnosis that is unequivocal. There might be philosophical differences that can be raised about where to go from there. Once one is satisfied that it is a glioblastoma and in looking at the films, the chance that there is glioblastoma in the second hemisphere appears substantial. I do not think that much neurological deficit can be accounted for by unilateral glioblastoma. I have not encountered a patient with this much neurological deficit and diffuse glioblastoma, as suggested by the angiograph, who was actually restored to relatively normal neurological and mental function by radiation therapy.

Once this diagnosis was confirmed, unless the family absolutely demanded all modalities of therapy, my own course would be to do nothing further.

Editor's Note: This patient was hospitalized in September 1975 and expired on July 9th, 1976. No autopsy was done.

8. Epidermoid Tumor of the Temporal Fossa

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

The patient was a 51-year-old woman in September 1975 when she complained of syncopal episodes of 5 years duration recently associated with vertigo, lightheadedness and weakness. On examination, there were no neurological abnormalities except for nystagmus in left lateral gaze; the fundi were normal, and sensory was normal.

Dr. Taveras: The submitted pictures include a frontal and a lateral view of a left common carotid angiogram made during the arterial phase. They demonstrate the presence of a large inferior temporal mass that appears to be extracerebral in that there is marked elevation of the middle cerebral artery in its normally horizontal portion and elevation of its branches beyond its trifurcation, leaving a relatively avascular space in the anterior temporal region. There is, as expected, gross distortion of the Sylvian triangle, which is elevated and arched around the mass. Although the mass is large and apparently quite close to the vessels, there is no evidence of narrowing of the supraclinoid internal carotid artery or the middle cerebral artery and its branches. That is, there is no evidence of encasement of vessels (Figs. 1 and 2).

Two slices of computerized tomograms passing through the area of the tumor and through the frontal horns are shown. One was taken without, and the other after intravenous hypaque enhancement. There is an oval radiolucent mass lesion in the left anterior temporal and mid temporal regions, and there is no evidence of enhancement of either the radiolucent area or the surrounding space around the tumor mass. There is a shell of increased density along the lateral and posterolateral aspects of the mass that did not change after contrast enhancement (Figs. 3 and 4).

We are evidently dealing here with a slowly growing mass situated in the temporal fossa that is most likely extra-axial and is not producing encasement of the arteries. Among the possibilities we should consider are teratoma or epidermoid tumor with calcification in its capsule. Another possibility is a temporal or subtemporal arachnoid cyst. Meningioma is another definite possibility from the angiographic point of view but is not a good possibility from the point of

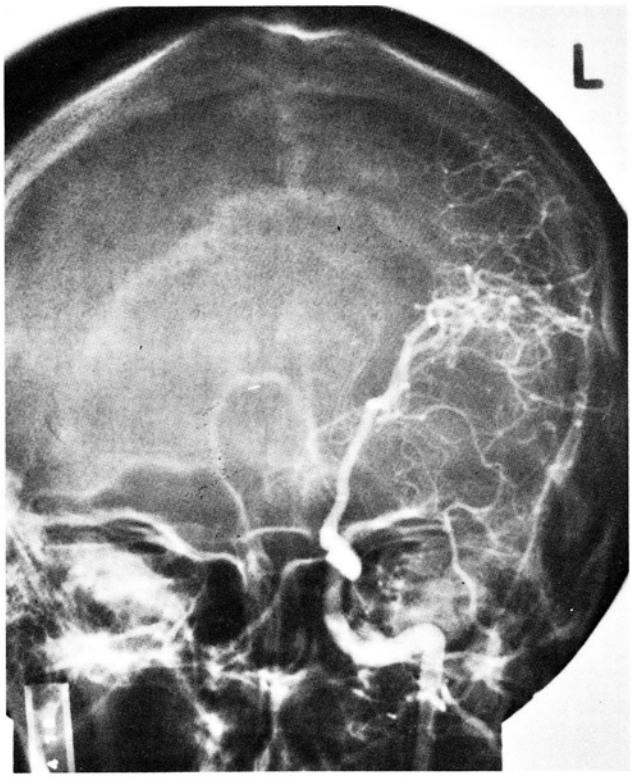


Fig. 1—Carotid angiogram showing inferior temporal mass.

view of the computerized tomography examination because it is a radiolucent mass that does not enhance. This would be rather unusual for meningioma. The other possibility is that we are dealing here with a tumor arising primarily from the inferior aspect of the temporal lobe, and in that case, it would be an intracerebral tumor, possibly of gliomatous origin and with cystic degeneration. I consider this possibility as much less likely.

In summary, we are dealing here with an inferior anterior temporal fossa tumor, most likely extracerebral in location and probably imbedded in the temporal lobe. Cholesteatomas do not usually calcify, but they can show calcium deposits in the capsule. The parasellar anterior temporal fossa is a good location for these tumors.

Dr. Taveras' Impression:

1) **EPIDERMOID CYST**
2) **MENINGIOMA**

Radiologic Impressions Submitted:

Glioma (cystic, temporal)	51
Epidermoid	5
Meningioma	8
Hamartoma	6
Abscess	6
Others	14

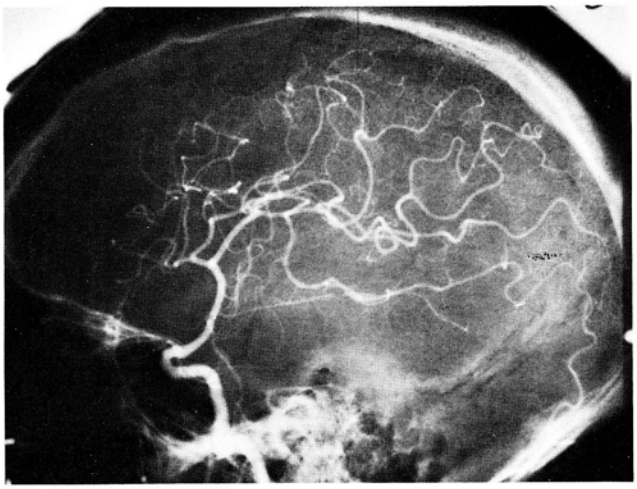
Dr. Taveras: I have discussed these possibilities. I do not think that cystic glioma is a bad diagnosis. The problem is that if we assume that the angiogram indicates an extracerebral location, we are already ruling out glioma solely on that basis. It could be a cystic astrocytoma except that it would probably calcify with a nodule in one location, rather than having a shell of calcium as you see here; that would be a satisfactory diagnosis had we not had the angiogram. The angiogram says it is extra-axial; therefore, it must not be a glioma. I would not diagnose abscess unless it is a very old abscess that has remained cystic with a little shell of calcium.

Dr. del Regato: Dr. Ying Lee of Orlando, Florida and Dr. Edward Grayson of Hollywood, Florida also made diagnoses of epidermoid. Dr. John L. Kestel of Waterloo, Iowa suggested temporal glioma.

Operative Findings: On September 18th, 1975 a craniotomy revealed the presence of a large 10x8x6 cm mass under a layer of normal brain. The mass was easily separated from the brain, but there was a zone of thick gliosis. On cut section, there were large areas containing caseous material, and there were other areas of necrosis.

Dr. Zimmerman: In making the diagnosis histologically of the tumor in this case, most of you must have felt like the anthropologist who, on the basis of a molar tooth which is before him, suggests the contours of the dinosaur from which it came. What we see in the microscopic preparation is a flimsy bit of material without a single viable cell (Fig. 5). Yet it is enough to warrant a diagnosis. It consists of interlacing strands of keratinized material that intracranially can be derived only from epidermoid epithelium. A careful search of the section failed to yield evidence of squamous epithelium of dermal appendages such as sweat glands, sebaceous glands or hair follicles. For one with even a minimal ex-

Fig. 2—Gross distortion of Sylvian triangle by anterior temporal mass.



perience with epidermoids, the keratinized strands of this case are diagnostic.

Many years ago Cruveilhier described this class of tumors within the cranial cavity. They occupy a favored position in the subarachnoid space beneath the frontal lobes in the region of the optic chiasm, or posteriorly beneath one of the occipital lobes, or in relationship to the eighth cranial nerve and the porus acousticus of the temporal bone. However, this frequently cystic tumor may occur anywhere intracranially and, indeed, even between the inner and outer tables of the skull. These tumors have a milky white, pearly appearance externally.

The wall of the epidermoid tumors consists of a connective tissue stroma lined internally by squamous epithelium. The latter tends to cast off exhausted epithelial cells and keratin, in variable proportions, into the lumen of the cyst. Cholesterol crystals may also appear in the contents of epidermoid cysts. A mixture of these constituents may have a "caseous" appearance, as was noted in the case under present discussion.

Dr. Zimmerman's Diagnosis:

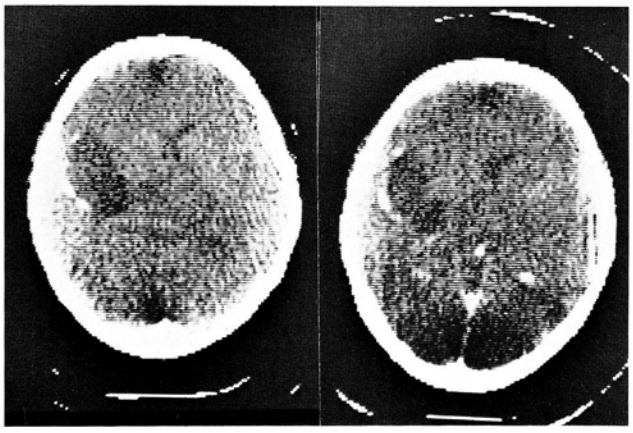
EPIDERMOID TUMOR ("pearly tumor")

Histopathologic Diagnoses Submitted:

Epidermoid tumor	28
Cyst	13
Necrotic neoplasm	3
Craniopharyngioma	3
Debris	10
Others	15

Dr. Zimmerman: I guess the thirteen who said cyst were not willing to diagnose anything that did not have a single cell on the section. Necrotic neoplasm is not a correct diagnosis because the necrotic tissue is the desquamative keratinized epithelium that we were seeing. I do not believe that I could go as far as a diagnosis of craniopharyngioma. Some cells have to be seen in a craniopharyngioma in order to make a diagnosis of it. Debris is correct, but it is no diagnosis, even though that is what is seen on the slide.

Figs. 3 & 4—Computerized tomograms showing lesion of anterior and mid-temporal region.



Dr. del Regato: Dr. R. Hackett of Gainesville also made a diagnosis of epidermoid. Dr. Renu Jalota of Salt Lake City recognized fibrous debris, which she attributed to a berry aneurysm or some cystic lesion.

Subsequent History: The patient was last seen on October 15th, 1975. She had been put on dilantin and had stopped having spells; she is doing well.

Dr. Kjellberg: I think what this case illustrates is that a radiographic diagnosis is often a very fine art. Dr. Taveras and five other radiologists came up with this on the basis of very shrewd observation. This is a very nice case, and it speaks for itself.

Dr. Kepes, Kansas City, Kansas: I would like to ask about your experience with chemical meningitis through the cyst rupture.

Dr. Kjellberg: These things almost always have to come out piece meal, although I suppose there might be some examples of tiny ones that might come out intact. Coming out piece meal, they tend to distribute some of their material; my recollection is that almost all of them have some chemical meningitis that is sometimes suppressed to a certain degree with corticosteroids. It is often rather tedious, and it goes on week after week. About ten years ago, we looked at the spinal fluid of patients and established that there was debris that was doubly refractile.

Editor's Note: This patient was examined in June 1977 at which time she was reported without symptoms and in good health.

Fig. 5—Strands of interlacing keratinized material forming the contents of an epidermoid cystic tumor. H and E stain; x450.

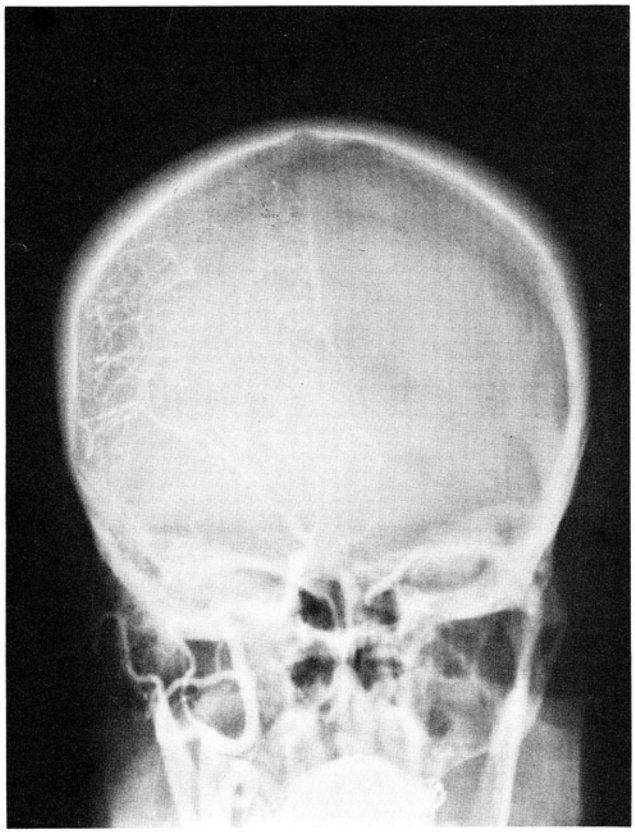
9. Metastatic Uterine Tumor in the Brain (?)

Contributed by **S. Stefani, M.D., F. Rubino, M.D., E. Ross, M.D.** and **E. Palacios, M.D.**, Hines, Illinois

The patient was a 60-year-old woman in April 1975 when she suffered sudden left hemiparesis; she gave a history of hypertension and diabetes. She was 6 years post-meopausal but had some vaginal bleeding in the previous three months. On examination she had left hemiparesis and left hemianopsia. The EEG suggested an abnormality of the right temporo-parietal area. The isotope scan showed increased uptake in the right temporal area.

Dr. Taveras: The frontal film of the angiogram shows elevation of the horizontal portion of the middle cerebral artery before and after its trifurcation. Some branches of the middle cerebral artery appear to come downward towards the base of the skull. The anterior cerebral artery is elevated in its initial portion because the bifurcation of the internal carotid artery is also somewhat elevated and probably slightly displaced medially. The anterior cerebral artery in its horizontal portion is slightly elevated and displaced towards the opposite side. The anterior choroidal is displaced medially. I get the impression that some of the vessels at the base of the brain are thinner than they should be, possibly because they are surrounded by tumor (Figs. 1 and 2).

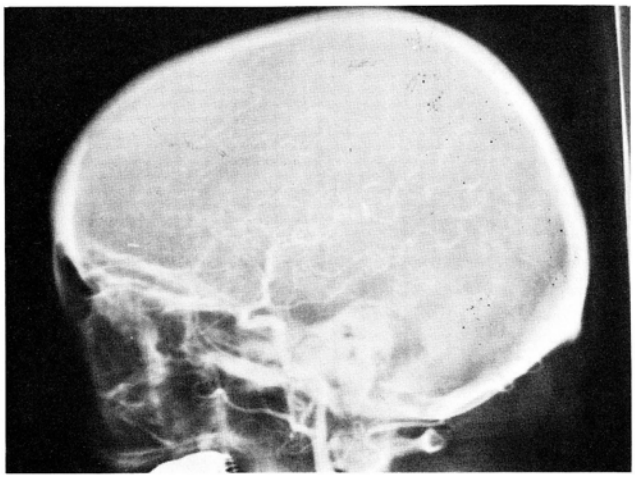
Fig. 1—Angiogram showing elevation of the frontal portion of the middle cerebral artery.



The radionuclide scan shows increased uptake, and the single slice of the CT scan shows the presence of a mass that reaches the midline and is compressing and deforming the right lateral ventricle to a considerable extent. There is an area, oval in shape, that is slightly denser than the surrounding brain and is poorly circumscribed. Films made after contrast enhancement are not included (Figs. 3 and 4).

The appearance suggests a highly invasive type of tumor that is in the temporal lobe region as well as deeply placed in the deep frontal and basal ganglia region. Regarding the probable histology of the tumor, I would tend to look along the infiltrative lesions, primarily in the brain. The history of vaginal bleeding was of recent origin. The only lesion that I can think of that might be related would be a metastatic tumor originating in the uterus or in the cervix that could be either an adenocarcinoma or a squamous cell carcinoma. The fact that this appears to a single lesion invading both the temporal lobe and the deep portions of the frontal lobe and basal ganglia region is against the diagnosis of metastatic disease. If the tumor were extra-axial in location, such as a metastatic tumor to the meninges, it could straddle both lobes and elevate the structures as shown. This would be an unusual type of metastatic tumor. The sudden onset of hemiplegia always raises the question of hemorrhage within a tumor, but while this presented a problem in the past, since the advent of computerized tomography, it is easy to detect hemorrhage clot formation because of the high density of clotted blood. Therefore, the

Fig. 2—Thin vessels at the base of the brain.



sudden onset of hemiplegia will have to be attributed either to occlusion of a vessel, secondary to tumor invasion, or to hippocampal herniation with compression of the brain stem. I tend to favor an infiltrative primary brain tumor as the most likely possibility; it could be either a glioma or possibly a malignant tumor of meningeal origin.

Dr. Taveras' Impression:

1) **INFILTRATING GLIOMA**
2) **METASTATIC TUMOR**

Radiologic Impressions Submitted:

Meningioma	21
Hematoma	12
Metastatic tumor	21
Glioma	16
Others	10

Dr. Taveras: Meningioma is a definite possibility. I thought it was intracerebral, rather than extracerebral, and for that reason, I would not consider meningioma seriously. Hematoma is definitely out of the question because, as shown in the CT scan, there is no increased density of this lesion, not to the extent that you see with blood. Metastatic tumor has already been mentioned.

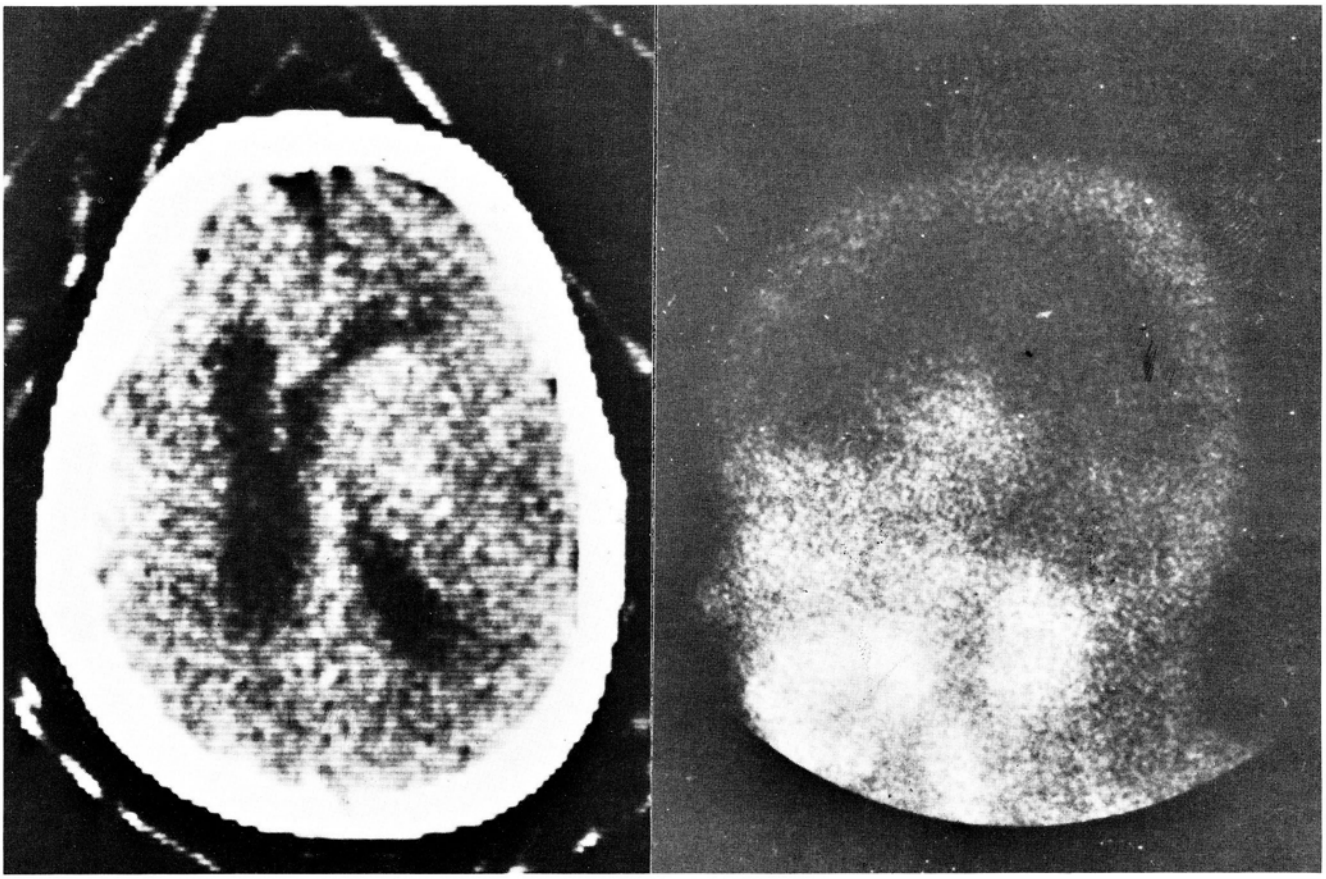
Dr. del Regato: Dr. S. Chandra Mouli of Chicago and Drs. R. Byhardt and Frank Wilson of Milwaukee diagnosed a temporal metastasis from a carcinoma of the endometrium. Dr. Harold O. Peterson of Minneapolis commented that this appears as a large avascular mass in the right temporal area, extending to the basal nuclei, indenting the ventricles and causing a contralateral shift; he favored a large hematoma, possibly on the basis of a pre-existing tumor. Dr. Cesar Triallanes of Milwaukee offered an impression of thalamic tumor.

Dr. Zimmerman: The nature of the tumor in this case is well shown in figure 5 where elongated cells with bipolar processes are present. The cells are arranged in sheets of parallel rows with the cells in longitudinal planes alternating with sheets of cells that have been sectioned transversely. The effect of this arrangement is to simulate the pattern in herring-bone material. Such patterns are often seen in the so-called polar spongioblastomas but also in fibromas and leiomyomas. From this hematoxylin-eosin stained preparation, it is difficult to conclude with which of these tumors we are confronted, whether glial or mesodermal.

At higher magnification, it becomes apparent that many cells are in mitotic division. Now it can be seen that the cells are more elongated than previously suspected and that they have distinct bipolar processes (Fig. 6). I now begin to doubt that these are glial cells. There are no

Fig. 3—Computerized tomogram showing and deforming the right temporal ventricle.

Fig. 4—Radionuclide scan showing increased uptake.



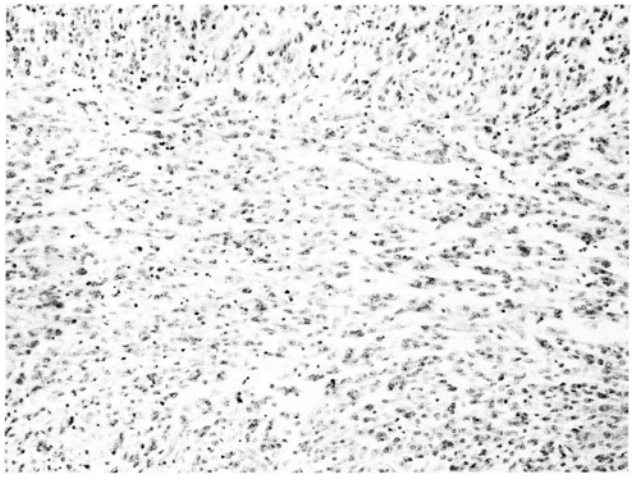


Fig. 5—Spindle-shaped tumor cells arranged in sheets. Some cells are cut transversely and some longitudinally. H and E stain; x150.

multipolar processes as in astrocytes. The fibrillary stroma laid down by these tumor cells, though scant, is definite. At this point it is obvious that the tumor is malignant, that its cellular constituents are elongated and bipolar in shape and that they form a definite fibrillary stroma.

We then see zones in this tumor that are somewhat suggestive of large pools of blood within very thin walled vessels. The appearance of the intervascular tumor cells now begins to suggest the possibility that they are of mesodermal rather than glial origin, perhaps even of endothelial origin. The thought occurred to me, why not a leiomyosarcoma? I then recalled, as did Dr. Taveras, that the patient was postmenopausal but recently had some vaginal bleeding. I too then considered the possibility of a metastatic tumor, non-epithelial and non-glial, possibly related to the adnexa, uterus, or cervix.

Further study of the tumor in the brain of this patient revealed small zones of necrosis but no pseudopalisading of tumor cells that one sees in malignant astrocytic neoplasms. At this point, I had blank slides of the tumor stained with phosphotungstic acid-hematoxylin, and there were revealed neither striations as in a rhabdomyosarcoma nor blue-staining cellular processes as in a glioma of astrocytic origin.

At about this time, I met Dr. Emanuel Ross, one of the contributors of this case, at a scientific meeting, and he asked if I had seen his case and what I thought of it. I told him that it was very probably a metastatic neoplasm of uterine origin, and my interpretation of his response was that he thought so too. He then sent me a set of slides of the uterus of this case as well as additional slides of the brain tumor. The latter revealed nothing more than we have already seen, but in the uterus there was a definite well-differentiated endometrial carcinoma with a component of elongated polar cells that are either sarcoma or leiomyosarcoma. On blank sides of the brain tumor supplied by Dr. del Regato, I had reticulin stains made, and these were all negative. Only the perivascular regions within the tumor disclosed reticulin fibers.

Now that we have excluded a glioma and a fibrosarcoma, we have to consider the possibility of an undifferentiated uterine carcinoma. Endometrial carcinomas do occasionally become so undifferentiated as to resemble a sarcoma, but the uterine tumor in situ in this case was quite well-differentiated. The possibility must also be considered that the cerebral neoplasm represents a metastatic leiomyosarcoma of uterine origin.

Dr. Zimmerman's Diagnosis:

METASTATIC UTERINE TUMOR (Leiomyosarcoma or undifferentiated endometrial carcinoma)

Histopathologic Diagnoses Submitted:

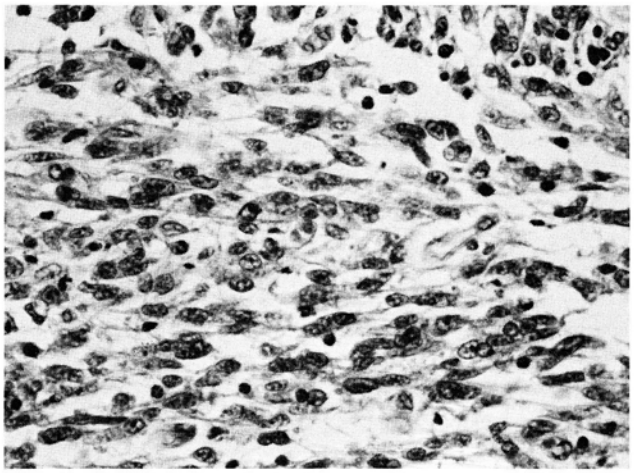
Astrocytoma	22
Glioma	11
Hemangiopericytoma	3
Metastatic uterine tumor	6
Others	7

Dr. Zimmerman: I have already indicated why some might consider this a glial tumor, except that these are polar processes. This is definitely not a hemangiopericytoma; that has a totally different histological appearance. Six pathologists agreed with me on a metastatic uterine tumor. I think probably this is the correct diagnosis in this case.

Dr. del Regato: Dr. Henry Azar of Tampa, Dr. W. J. Kirsch of St. Petersburg and Dr. D. R. Dickson of Santa Barbara, California made a diagnosis of astrocytoma. Dr. Leo Lowbeer called it protoplasmic astrocytoma, and Drs. Magda and John Kepes called it piloid astrocytoma.

Subsequent History: The patient was considered inoperable, and radiotherapy was planned, but on June 9th, 1975 she expired. The autopsy revealed a very extensive tumor involving three

Fig. 6—Spindle-shaped tumor cells with polar processes that form a scant fibrillary stroma. H and E stain; x450.



lobes, the medulla and the hippocampus. There was severe pulmonary congestion with hemorrhages associated with thrombosis. There was a well-differentiated adenocarcinoma of the endometrium without infiltration of the myometrium or metastatic manifestations within the pelvis.

Dr. Kjellberg: I think the key to the case was the uterine bleeding, but when you read the protocol of this session, you do not know whether this is coming as a curve ball or a straight one.

Dr. Zimmerman: I would like to comment on a remark that Dr. Taveras made in regard to metastatic tumors being multiple. Some years ago, I was prompted to examine 1400 consecutive metastatic brain tumors. Nearly one-third of them at autopsy had single nodules in the brain. The concept that you must always find multiple nodules just does not hold for one-third of the cases and probably for a considerably larger proportion in non-fatal cases. This is why I have always supported our neurosurgeons who want to go into metastatic disease and remove a nodule. There is a chance in some of them that it is a single nodule that can be removed.

Dr. Taveras: That is precisely the problem: we are able to diagnose or suspect a metastatic tumor if we see more than one. If you do not see more than one, we really have no right to call it metastatic unless there are some very important features that tell us this is the case. This case shows that there is a multi-centric location, as I indicated in the examination of the angiogram, and, on that basis, many favored metastatic tumor. The reason why I did not was because I thought they were in contiguity, that the frontal and temporal lobe involvement was continuous; therefore, it was an invasion right across the sylvian fissure, which is not that common. I do agree that this is one of our main problems in trying to evaluate a single mass. If this is single, we have no right to say that it is metastatic.

Dr. W. J. Kirsch, St. Petersburg, Fla.: Dr. Zimmerman, what was the largest single metastatic nodule you discovered in the study?

Dr. Zimmerman: They were sometimes 5 cm in diameter. They can be very large, or sometimes the metastatic multiple ones are very small, so there are all sorts of variations.

Dr. Kjellberg: How often did you encounter solitary metastasis from the lung?

Dr. Zimmerman: The statistic holds true for the lung carcinomas as well. There is another very interesting fact about pulmonary carcinomas that metastasize very frequently to the brain: most of them (99%) are parenchymal metastases within the brain tissue itself, and in one-third of the cases, they are single metastatic foci. In contrast, about 85% of the cases of mammary carcinoma involved the dura or leptomeninges and not the parenchyma. We can tell at a glance and with a high degree of assurance that if the nodule is deep in the brain tissue, it is probably bronchogenic carcinoma. If the mass involves the dura or leptomeninges, it is most likely a mammary carcinoma, ruling out some of the other things like liposarcomas and a few rarer entities.

Dr. A. A. Gonzalvo, Tampa, Fla.: Glial tumors may also present multiple foci. Dr. Zimmerman had the advantage of seeing the uterine section, and he saw that the cells resembled the ones in the brain. Probably, the best diagnosis is carcinosarcoma of which the sarcomatous components have metastasized. I found it hard to believe that a well-differentiated adenocarcinoma of the endometrium that had not invaded the parametrium could metastasize exclusively to the brain. There is no reticulin here, and you indicated that glial cells would not produce reticulin. Therefore, I presume that this would not be a glial tumor in this case.

Dr. Zimmerman: I did not use the reticulin stain to rule out glia. Having come to the conclusion that this is not a glial tumor, I wanted to also rule out reticulum-cell sarcoma or a leiomyosarcoma. This is what I meant to imply.

I agree that frequently, but not nearly as frequently as in metastatic disease, gliomas are multiple. I have a few cases in which an ependymoma was seen in the region of the lateral ventricle, or an astrocytoma in the occipital lobe on one side, and a glioblastoma in the frontal lobe on the opposite side of the same patient. Such things can happen, but it does not happen as often as the metastatic disease, which in two-thirds of the cases is multiple.

Dr. Henry Azar, Tampa, Fla.: In view of the findings at this autopsy, Dr. Zimmerman, would you reconsider the possibility of an astrocytoma?

Dr. Zimmerman: Now you force me to put down my trump card. I was sent unstained slides that I used for reticulin stains, but I also used phosphotungstic acid hemotoxylin stain preparations. These are not glial fibers. I tried to get photographs of them that I could project as lantern slides, but they came back with some artifacts. Therefore, you will have to take my word for it that there are no glial fibers of an astrocytic nature in the phosphotungstic acid hemotoxylin sections. I did not have wet tissue to a Cajal stain, so I cannot answer you.

Dr. Gonzalvo, Tampa, Fla.: The uterine slide looked like the one in the brain anyway; it was a well-differentiated adenocarcinoma.

Dr. Zimmerman: I think it is a mixed tumor, which often happens in an endometrial carcinoma.

Dr. del Regato: Dr. Azar, I want to assure you that Dr. Zimmerman is quite capable of changing his mind. In another Cancer Seminar 15 years ago, Dr. Leo Lowbeer presented some additional evidence to him, and Dr. Zimmerman was quite willing to accept Dr. Lowbeer's suggestion.

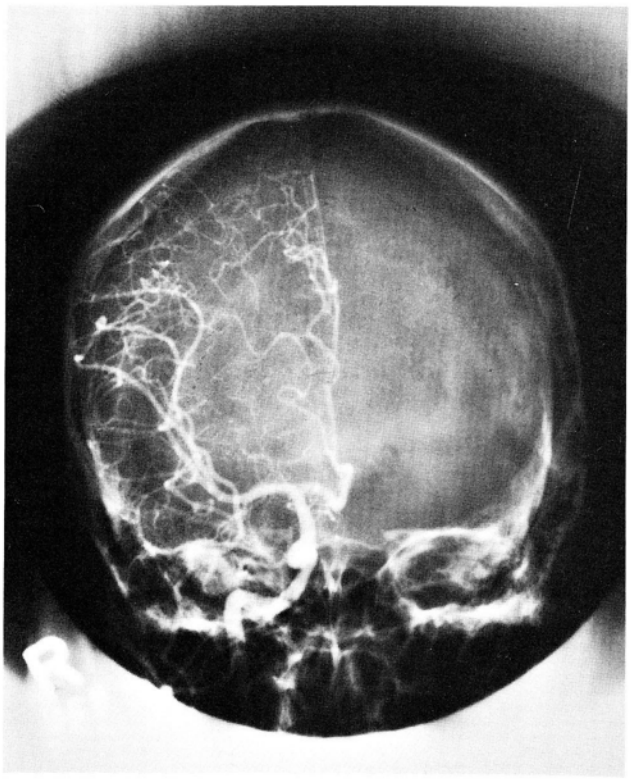
10. Giant-Cell Temporal Glioblastoma Multiforme

Contributed by **G. H. Wilson, M.D.**, Los Angeles, California

The patient was a 22-year-old woman in June 1975 when she was examined because of repeated episodes of sudden bilateral retro-orbital pain, which lasted four days and were accompanied by nausea. Four years previously, she had been thrown from a horse and found unconscious. Physical examination uncovered no important signs. The EEG showed intermittent right temporal sharp waves.

Dr. Taveras: The CT scans were apparently taken without contrast enhancement. There is a large irregular tumor that is all radiolucent with no evidence of dense portions. Unfortunately, we do not have one with contrast enhancement. If it would not enhance, I think meningioma would be rather unlikely. A tumor that contains fat could easily be as radiolucent as this. Of course, as you can see, the radiolucency of the mass is the same as that of cerebral spinal fluid, so it is a very transparent type of tumor. I suppose that glioma is still the best possibility. Whether or not it turns out to be a very malignant one that might kill the patient rapidly is something that will have to be determined.

Fig. 1—Angiogram showing right to left shift of the anterior cerebral artery.



Dr. Taveras' Impression:

INTRACEREBRAL TUMOR:
(1) EPENDYOMA
(2) ASTROCYTOMA

Radiologic Impressions Submitted:

Glioma, astrocytoma	38
Subdural hematoma	18
Porencephalic cyst	11
Temporal tumor	8
Others	9

Dr. Taveras: I see no reason for diagnosing subdural hematoma. As I indicated, that would have elevated all of the vessels, not just the middle cerebral, whereas the branches that supply the temporal horn are streaming down towards the lobe. I suppose the reason for a diagnosis of porencephalic cyst is that the CT scan showed enlargement of the temporal horn. That would be a possibility, but there is a mid-line shift; a porencephalic cyst can elevate the temporal vessels, but ordinarily, the middle cerebral vessels that pass over the temporal lobe would not produce a midline shift. I would say that porencephalic cyst should be most unlikely.

Dr. del Regato: Dr. Lawrence Gold of Minneapolis submitted an impression of right temporal glioma. Dr. John Kestel of Waterloo, Iowa and Dr. Stephen Greenberg of Tampa considered a temporal hematoma. Dr. James Strohmenger of Panama City, Florida offered a diagnosis of temporal glioma.

Operative Findings: On June 12th, 1975 a craniotomy was done with removal of the right anterior temporal tip.

Dr. Zimmerman: Having removed tumor like a porencephalic cyst that left such a big hole in the brain, it defies my understanding why we are asked to make a diagnosis on a bit of tissue that is about 4 mm in greatest diameter. When I requested an unstained slide of this case from Dr. del Regato, I was informed that additional slides were not available because there was no more tissue.

We are thus forced to attempt a diagnosis of a tumor from a fragment of tissue that represents a very small part of the total neoplasm. That is a hazardous procedure. What we see in the available section are considerable numbers of multinucleated tumor cells in a pink-staining stroma (Fig. 5). Is this stroma of glial or mesodermal origin? That is the question. There is no resolution of the problem because no additional slides are available for special staining.

Now, when I first looked at this slide I thought that it may well represent a "Kepes" tumor, but on further study I have become unconvinced of

this diagnosis. The tumor cells have fairly deeply pink-staining cytoplasm without vacuolization. There is no ground-glass appearance of the cytoplasm. Multinucleated tumor giant cells are numerous. Some of the blood vessels are surrounded by collections of small round cells indistinguishable from lymphocytes (Fig. 6). I cannot identify distinct macrophages or histiocytes. In view of the limitations created by the paucity of material for study, perhaps a definitive diagnosis is not justified, but I believe an intelligent guess is that the tumor is a glioblastoma multiforme. I would, however, be willing to change my mind if Dr. Kepes comes up with more and better sections of this neoplasm that shows a xanthoma.

It is of some interest that two of the patients described by Dr. Kepes and his collaborators had histories of trauma. Their patients were also relatively young people. A traumatic episode was present in the patient under discussion, and she was 22 years of age. Are these facts simply coincidental? After all these considerations and purely on morphological grounds, I favor the diagnosis of glioblastoma multiforme. The involvement of the leptomeninges in this case is not helpful because a glioma may grow out from the brain into the pia-arachnoid, and conversely, a xanthoma may extend from the meninges into the brain.

Dr. Zimmerman's Diagnosis:

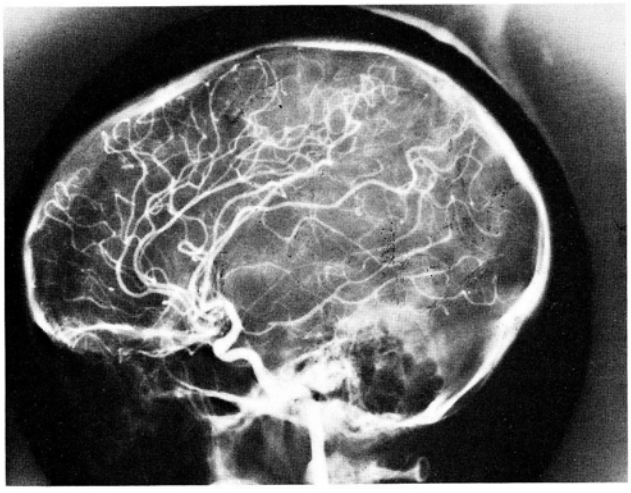
GIANT-CELL GLIOBLASTOMA MULTIFORME

Histopathologic Diagnoses Submitted:

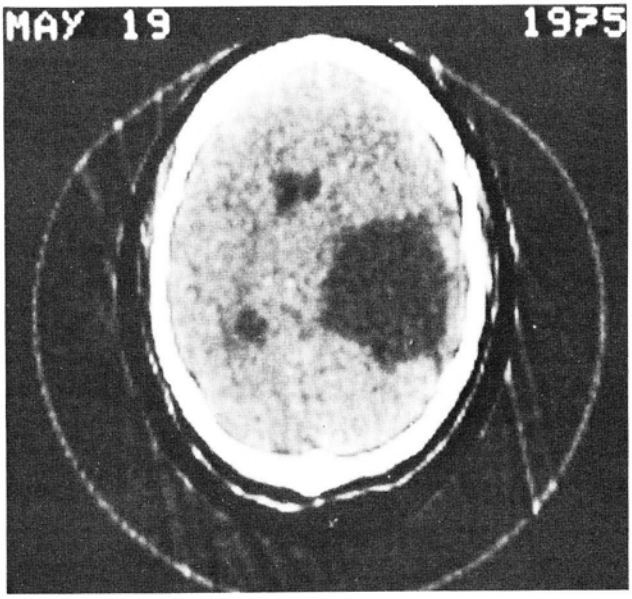
Giant-cell astrocytoma	13
Angioblastic meningioma	6
Sarcoma (embryonal, stromal)	15
Metastatic melanoma	3
Others	15

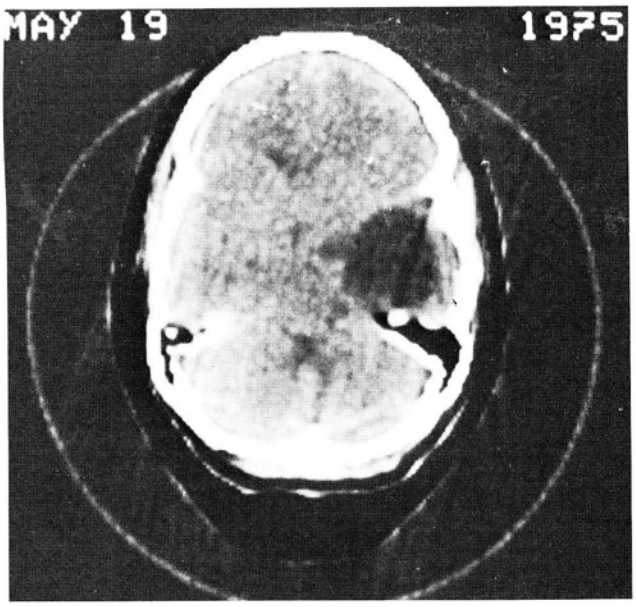
Dr. Zimmerman: By giant cell astrocytoma, I suppose it is meant a grade III or IV astrocytoma, which is in the category of glioblastoma multiforme. What I call a giant-cell glioblastoma, the romantic neuropathologists call giganto-cellular glioblastoma, and the more romantic ones call it a monstrocellular glioblastoma. I do not think this is a sarcoma, and I am quite sure that it is not a metastatic melanoma. I do not see the type of cell that I would call a melanoma. Angioblastic meningioma has possibilities; some of these newly formed blood vessels that are in the leptomeninges may conceivably fool us. I am not sure it is a meningioma. I do not believe that the cells are meningocytes, but in the meninges, angioblastic cells do develop that may resemble this tumor. Frankly, I would have to stretch a point or two, and on the basis of what I see, I cannot go any further than I have gone. In all probability, it is a giganto-cellular or monstrocellular glioblastoma, but I may be willing to

Fig. 2—Elevation of the Sylvian triangle.



Figs. 3 & 4—Large radiolucent tumor of the right temporal region.





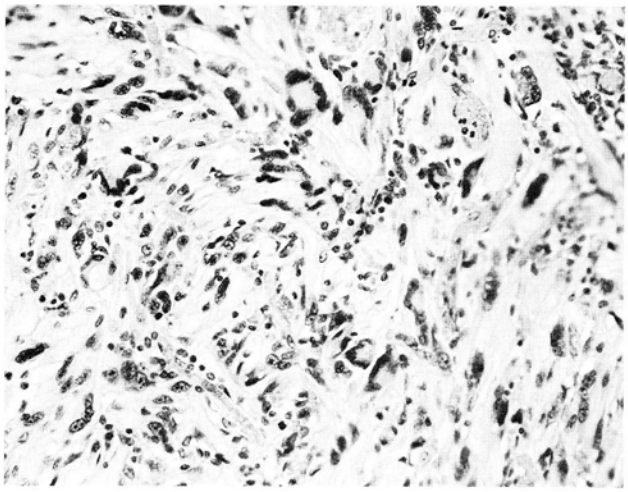


Fig. 5—Glioblastoma multiforme with many multinucleated tumor giant cells. H and E stain; x250.

concede to Dr. Kepes if he shows evidence that I would be willing to accept.

Dr. del Regato: Dr. Renu Jalota of Salt Lake City offered a diagnosis of giant-cell astrocytoma. Dr. W. J. Kirsch of St. Petersburg offered angioblastic meningioma. Dr. Henry Azar of Tampa preferred a sarcoma of meningeal or brain stromal origin.

Subsequent History: Radiotherapy was given postoperatively; a total dose of 5950 rads was received in 45 days at the mid-cranial plane.

On October 23rd, 1975, the patient was reported doing well. Her hair had not grown back; her weight was 115 pounds. She had not menstruated for the last two months, but pregnancy tests were negative. On February 5th, 1976 she was doing very well and getting A's in college. Her hair was coming back (Figs. 7 and 8).

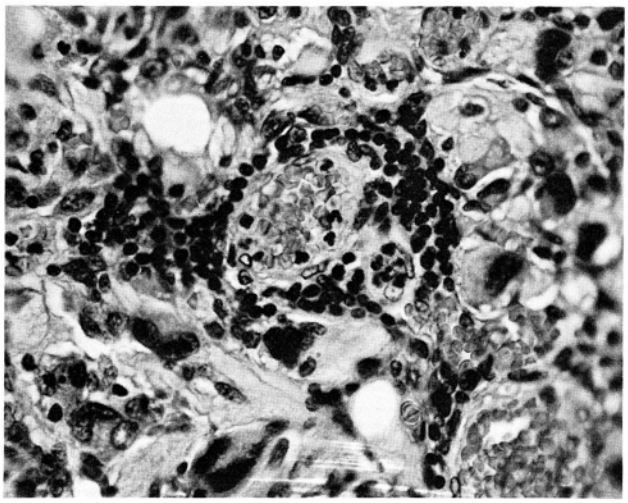
Dr. Kjellberg: The therapy was very standard and appropriate, I think. It is interesting to try to put this together into a unified whole. The patient's examination was inaugurated because of repeated episodes of sudden bilateral retro-orbital pain. I find it very difficult to relate that symptom to the history of her having been thrown from a horse four years previously and having been unconscious as a result. I find it equally difficult to relate this symptom to the pathology of the case. The EEG showed right temporal shock waves; that is evidently the whole clue in this history. That led to more substantial examinations, CT scans and ultimately to the diagnosis and therapy.

Sometimes frontal lobe tumors are associated with loss of inhibitions, but I am not familiar with that in the temporal lobe.

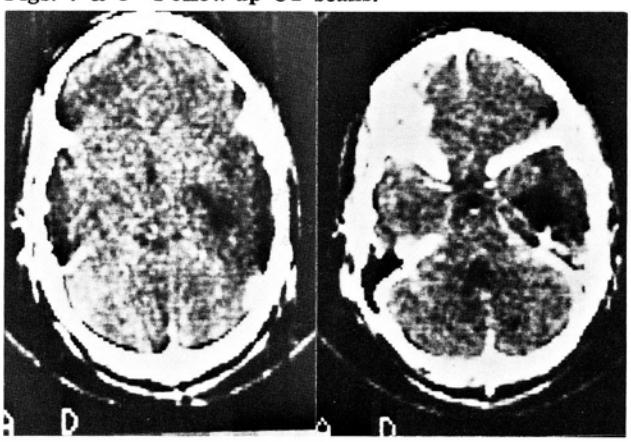
Dr. J. J. Kepes, Kansas City, Kans.: I think this is a case that was sent to me last summer from Los Angeles. I received a little more tissue than Dr. Zimmerman, and I was able to do some special stains. In an atypical fibroxanthoma, the prognosis is so much better. As Dr. Zimmerman mentioned earlier, all the supratentorial gliomas are dead. It is just a matter of degree; they may live a few years, but in the long run, they do very poorly. In the fibroxanthomas that we described, one was a 13-year-old boy who now has a 20-year symptom-free survival. The patient we saw in Colorado Springs in 1962 was a boy who at that time had a 2-year and now has a 16-year history of symptom-free survival.

There is no demarcation between brain and meninges here as far as the tumor is concerned. As Dr. Zimmerman pointed out, it is perhaps something coming out of the brain that involves the meninges or is going the other way. There was a certain foamy appearance to a number of these cells; we had frozen sections, and they were very heavily loaded with lipid. All these clear cells were severely filled with lipid, and the ones with processes do resemble astrocytes to some extent. However, I think that these multinucleated cells would fall into the category of atypical histiocytes. Something quite impressive to me is that although astrocytomas are found in very close relationship to blood vessels, we do not usually see them engulfing the blood vessels as if to eat them, almost like a foreign body giant-cell surrounding a blood vessel.

Fig. 6—Glioblastoma multiforme with multinucleated giant cells and perivascular lymphocytic cuff. H and E stain; x450.



Figs. 7 & 8—Follow-up CT scans.



I think the reticulin stain is impressive in this case. One has to emphasize that whenever glioma grows into the meninges, it may elicit marked reaction by the meninges; this is particularly true of medulloblastomas, but it is also true for other gliomas. Still, the cells would not be individually surrounded by reticulin as they are without exception in this case.

I was very lucky to receive a piece of fresh tissue. For the first time, I was able to do electromicroscopy on one of these tumors, and I was delighted about one finding. Individually, these cells are surrounded by basement membranes. I did not see any glial fibers in any of these cells.

Dr. Zimmerman: This is a lot more impressive than case number 13 from the Cancer Seminar of 1962. Taking into account the age of the patient and the fact that there are these cells that I did not see, this looks more possible. Evidently, you received most of the material, whereas the rest of us were cheated in a sense because we only saw a tiny fragment of tissue fixed longer in formaldehyde.

If you make a diagnosis of xanthoma (a Kepes tumor), you have to realize that not all of them follow a benign course. Malignant xanthosarcomas may be a possibility, so do not base your diagnosis on the assumption that it is going to be a benign lesion. Some years ago when Dr. Martin Netsky was in my laboratory, he reported three cases of glioblastoma multiforme. One patient had been diagnosed by Percibal Bailey of the University of Chicago. Following subtotal removal of the tumor and irradiation, the patient was reoperated at Montefiore, where we confirmed the diagnosis of glioblastoma multiforme. Irradiation was given again, and the patient lived for six more years; ultimately, he died of glioblastoma multiforme but survived a total of 14½ years, having had three craniectomies and three series of x-ray treatments. Even a patient with glioblastoma may live longer than the seven month average that a patient survives following surgery. In the same paper, Dr. Netsky reported a patient with a glioblastoma multiforme who survived eight years with two craniectomies and irradiation; another patient survived seven years.

Dr. Kepes: Dr. Zimmerman is absolutely right that the diagnosis of xanthoma does not mean a definition of a benign lesion. We made the mistake of lumping these cases together in an article on fibroxanthomas, xanthomas of the brain and meninges; these cases actually contained both benign and malignant lesions.

Dr. J. F. Dunkel, East Lansing, Mich.: I hoped Dr. Zimmerman might raise the question of the so-called viral transformation idea that is apparently developing. This is where the glial cells, particularly the oliglial, show highly metamorphic changes, and the ganglionic cells show pleomorphism. I understand that those cases can drag on, but I also understand that the idea is only three or four years old; presumably, that is the extent, judging by the duration of five of the cases that have been described.

Dr. Zimmerman: There is no good evidence that human gliomas, including the glioblastoma multiforme and the giant-cell type of tumor, have a viral etiology in man. Dr. Fusahiro Ikuta, who was formerly associated with me and is now in Japan, has been able to take a human adenovirus type 12 from the lung of a 14-year-old child who had bronchopneumonia and implant this virus particle into the brains of hamsters and mice, producing glioblastoma multiforme. All evidence that gliomas may possibly be related to changes in the DNA and RNA components by viral interaction it based on experimental animals in the lower series. At the present time, it is a debatable question. That is all I can tell you about it.

In the past as well as now, we are looking at multi-electromicrographs of human tumors. However, I have never been able to demonstrate something that even remotely resembles a viral particle. The only success we have had is in cases of human leukemia with cerebral involvement.

References:

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11. Leiomyosarcoma (of Vessel Wall Origin?) in Temporal Lobe

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

The patient was a 58-year-old woman in December 1973 when she developed speech difficulties and nausea. On examination she substituted words in her sentences; there were questionable blurred discs, and the muscular strength of the left arm was diminished. Reflexes were normal. The EEG suggested an abnormality of the left hemisphere.

Dr. Taveras: The A-P projection in the venous phase shows marked displacement of the internal cerebral vein to the opposite side with elevation of the thalamostriate vein. It appears that the basal vein is also displaced towards the midline, although this is difficult to ascertain on these films. There is a vague increase in density in the interior portion and in the mid-convexity

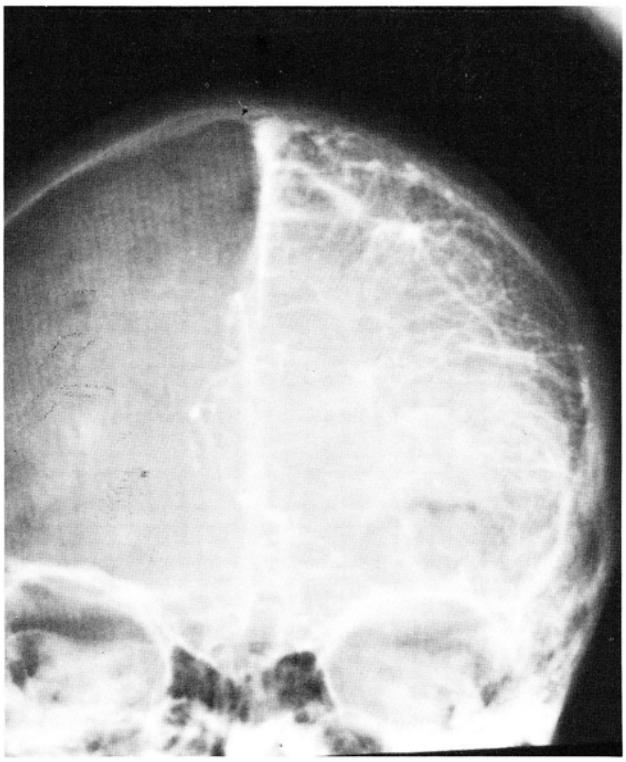


Fig. 1—Venous phase shows marked displacement of the internal cerebral vein to opposite side.

regions with what appears to be concave deformities of the veins that are visualized in this region. The concavity is downward, which would suggest that there is a mass in the temporal region, possibly extending deeply. The lateral projection, also in the venous phase, shows rounded elevation of the internal cerebral vein. The subependymal branches of the internal cerebral vein are somewhat more prominent than usual. The basal vein is depressed in its midportion, and this may be associated with an uncal or hippocampal herniation (Figs. 1 and 2).

Regarding the nature of the lesion, I am unable to determine exactly where the mass is located because the arterial phase was not included. The sharp displacement of the internal cerebral vein and its branches would indicate that the mass may well be partly deep in location, and the curving of the veins as seen in the frontal projection would suggest that it is also superficial in location. Therefore, a posterior temporal mass with deep extension would be a definite possibility. The local could primarily be in the thalamus, however. Against this location is the fact that the basal vein appears to be displaced medially, rather than laterally, as one might expect in a thalamic tumor.

Regarding the nature of the lesion, no real suggestions can be made on this rather limited amount of information.

My opinion is that this is probably a temporal tumor with deep extension. There are no diagnostic clues that would tend to suggest a specific histological diagnosis.

Dr. Taveras' Impression:

INTRACEREBRAL TEMPORAL TUMOR:
1) RETICULUM CELL SARCOMA
2) GLIOMA

Radiologic Impression Submitted:

Glioma (deep, main stern, intraventricular)	42
Thalamic tumor	12
Meningioma	8
Lowbeer's shenanigans!	1
Others	23

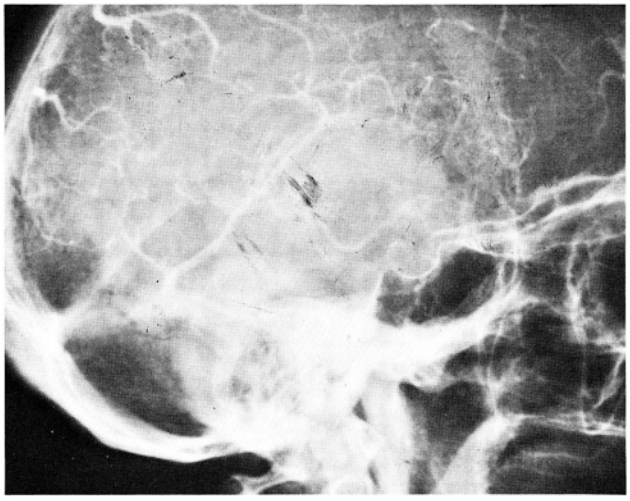
Dr. Taveras: Glioma is perfectly all right. It could be thalamic; I thought it was in the temporal lobe, invading deeply. I have no reason for calling it meningioma.

Dr. del Regato: Dr. Alfred L. Yao of Milwaukee also made a diagnosis of glioma. Dr. Judith Post of Miami, Florida offered glioma with ventricular invasion. Dr. Harold O. Peterson of Minneapolis pointed at negative shadows above the left orbit that could be due to a previous air study or simply artifact. He saw a large mass in the region of the basal nuclei in the middle; he attributed the long ependymal veins to stretching since the mass is pushing into the side of the lateral ventricle. He had no clues as to histology.

Operative Findings: On December 26, 1973 a craniotomy was done. A mass 8x12 cm was found in the left temporal region compressing the temporal lobe inferiorly; the tumor was adherent to the dura in the region of of the sphenoidal wing. The tumor was removed with a blood loss of 800 cc (Figs. 3 and 4).

In March 1974, the patient became confused, fell, broke her hip and was hospitalized. She complained of headaches, had speech difficulties and weakness of the right arm. An isotope scan suggested a left parietal recurrence. A second craniotomy was done; there was a 6 cm recurrent mass with marked vascularity and extensive necrosis. The tumor could not be removed in toto.

Fig. 2—Rounded elevation of the internal cerebral vein.



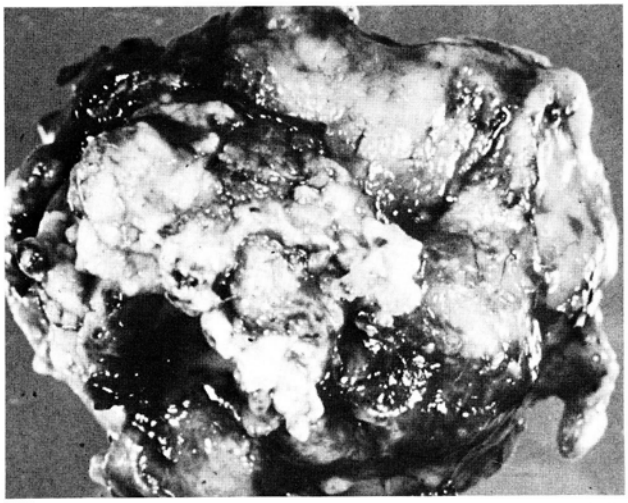


Fig. 3—Gross specimen of tumor removed from left temporal region.

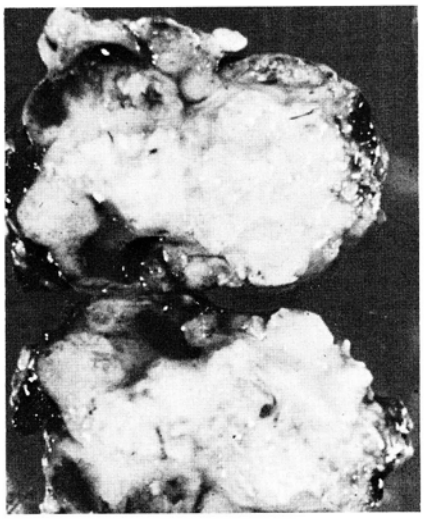


Fig. 4—Cut section of tumor.

Dr. Zimmerman: There are two tissue sections on the one slide that we were given in this case. I presume that they represent biopsy specimens from each of the two operative procedures. One consists of a tumor attached to or in the dura, and the other is of a tumor in brain tissue. In my opinion, they are totally different tumors but in the same patient.

In commenting on the gross slide, we can recognize this as a tumor, a mass, but it could be almost any kind of a tumor. More likely, from its appearance, it is a primary intracranial neoplasm, rather than a metastatic one. This is because there is not enough necrosis to suggest a metastatic neoplasm. From the macroscopic appearance, it could be a glioma, and I say this knowing that this is not so. Any intracranial tumor could look like this photograph. The tumor is lobulated and slightly hemorrhagic, with a little necrosis but no extensive liquifaction. Both a glioblastoma and a sarcoma may have this appearance. It could also be a meningioma. In the next photograph of the gross specimen, it appears that the tumor is attached to the dura.

Now we come to a photomicrograph of what I take to be the specimen removed at the first operation when a tumor attached to dura was encountered. For all the world, this tumor has the appearance of a fibroma (Fig. 5). On closer examination, one finds an occasional cell in mitotic division to tempt one into a diagnosis of sarcoma. The tumor is circumscribed but not encapsulated and seems to lie within the brain tissue (Fig. 6), in addition to being attached to dura. It has a fibromyomatous appearance, and with a little imagination, one can see suggestive palisading of tumor cell nuclei as in a neurilemoma. Within the brain, the neurilemal cells that correspond to the Schwann cells are, of course, the oligodendrocytes, and the tumors these cells produce are oligodendrogliomas. The

Fig. 5—Malignant mesodermal tumor in part resembling a fibrosarcoma and in part suggesting an origin in blood vessel walls. H and E stain; x180.

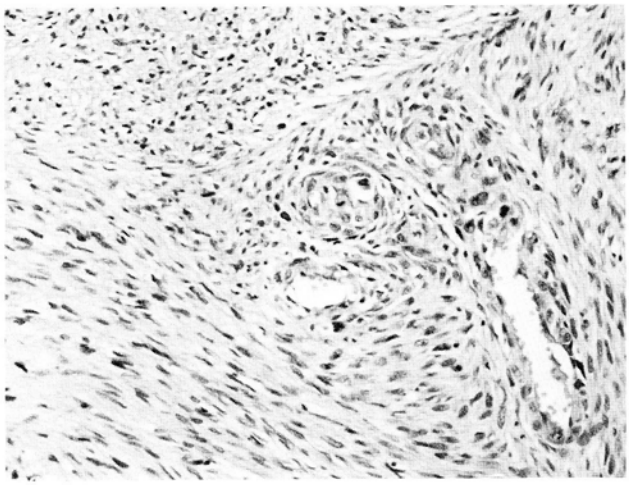
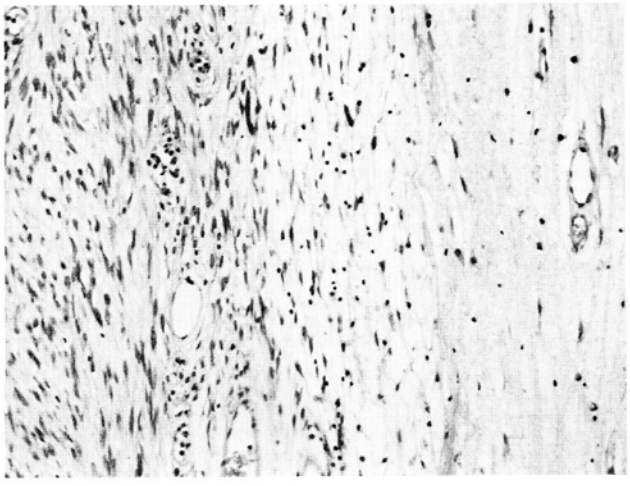


Fig. 6—Tumor in brain parenchyma. At left, tumor; in center, loose reticular connective tissue separating tumor from brain, seen at right of photomicrograph. H and E stain; x180.



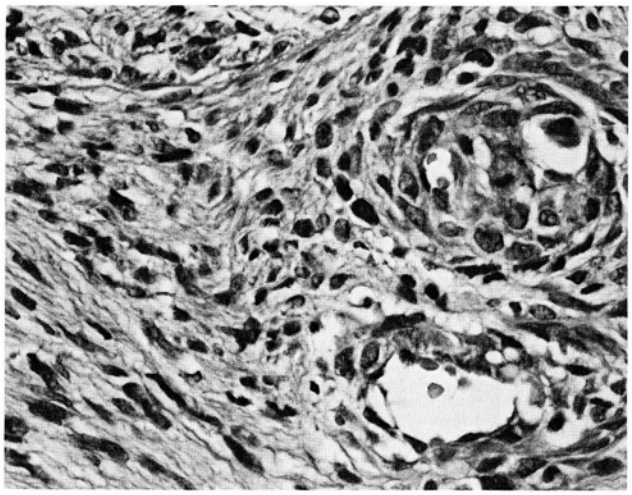


Fig. 7—Plump, roundish tumor cells in vessel walls, hinting at origin from smooth muscle. H and E stain; x450.

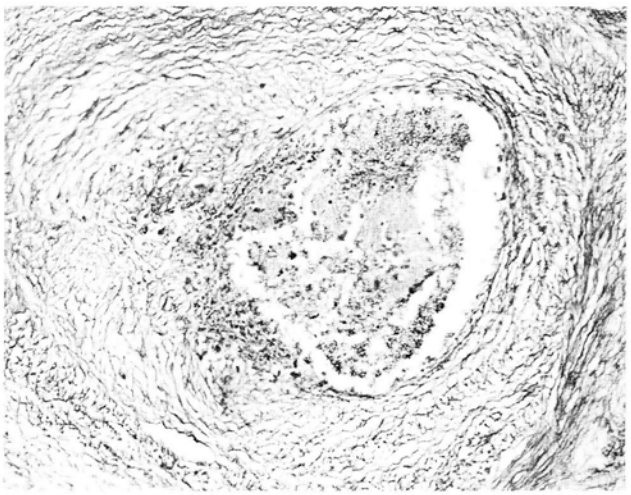


Fig. 8—Extensive reticulin formation in and around vessel wall in midst of tumor. Darkly stained tumor cells are seen among reticulin fibers on left side of vessel wall. Wilder silver impregnation; x150.

tumor in our present patient is not histologically an oligodendroglioma.

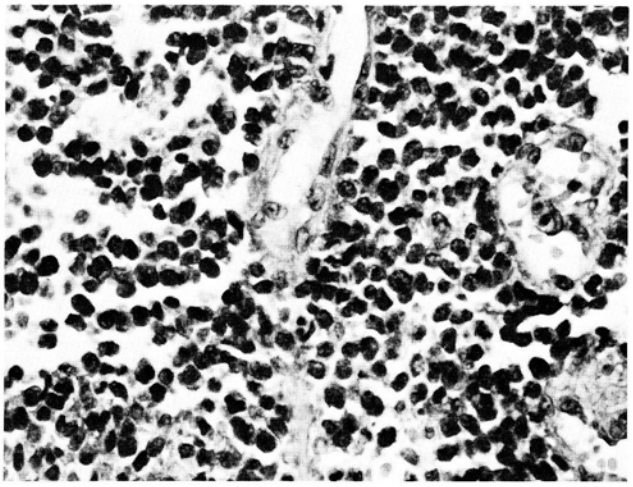
Under higher magnification the tumor cells appear to be elongated and have fibrillary processes that produce a loose connective tissue stroma. The tumor is separated and distinct from the nervous parenchyma, which it does not infiltrate as would a glioma. There seems to be a sharp demarcation between the brain tissue and the tumor itself (Fig. 6). By the way, none of the neoplastic cells resembles meningocytes; neither are there any meningocytic whorls nor psammoma bodies. This, in my opinion, would exclude the diagnosis of a conventional meningioma.

If the dura, rather than the brain, were the original site of the tumor, this neoplasm would need to be classified as a dural sarcoma, not as a malignant meningioma nor as a meningiomatous sarcoma.

A close look at the tumor cells reveals that many are related to blood vessel walls (Fig. 7). Indeed, some parts of the tumor contain large numbers of interlacing blood vessels that resemble those seen in granulation tissue. The walls of many vessels contain tumor cells that are apparently not of endothelial origin but suggest rather a derivation from the myocytes of the vessel wall. Smooth muscle cell tumors can, of course, arise in blood vessel walls either in the dura or in the brain itself. In either case, the tumor, if malignant, would be a leiomyosarcoma. Recticulin stains of such tumor-bearing blood vessels disclose an abundance of reticulin fibers in the vessel walls (Fig. 8). Among these fibers lie the tumor cells singly and in clusters. The impression of the intramural origin of this neoplasm is supported in microscopic preparations stained by the Masson trichrome and by the van Gieson-elastic tissue methods. The tumor then, is a malignant invasive and evidently recurring mesodermal neoplasm, possibly arising in the blood vessels of the dura or brain: a leiomyosarcoma.

Now for the tumor tissue removed at the second operation. The neoplastic cells have not the slightest resemblance to those in the first biopsy (Fig. 9). They resemble ordinary lymphocytes except that they are larger and are frequently in mitotic division. An inflammatory reaction comes to mind, but the invasiveness of the cells and the evidence of active proliferation bespeak a malignant lymphoma. This tumor is probably a lymphosarcoma, but reticulum cells are also present. Now, is this lymphoma related to the radiation therapy the patient received for the first tumor? I know that I raise this question at the displeasure of our host, Dr. del Regato. I must do so anyway, knowing also that only about

Fig. 9—Tumor cells of malignant lymphoma present in second biopsy. H and E stain; x450.



three months elapsed between the end of irradiation and the time of the second operation for presumable recurrence. This is a bit short for an irradiation-induced lymphoma. We shall have occasion to discuss some problems associated with malignant lymphomas in relation to another case that will come later in this seminar. As much as I cherish the diagnosis of "Lowbeer's shenanigans" suggested for this neoplasm by one of our conferees, I must reject it.

Dr. Zimmerman's Diagnosis:

1) **LEIOMYOSARCOMA** arriving in vessel walls
2) **MALIGNANT LYMPHOMA**

Histopathologic Diagnoses Submitted:

Meningioma	27
Fibrosarcoma	9
Schwannoma	5
Others	10

Dr. Zimmerman: Meningioma is a histological diagnosis of a meningocytic tumor, which this is not. Of course, it is attached to the dura, but this does not make it a meningioma. It can be a sarcoma arising in the dura leptomeninges, but not a meningioma. I already have said I cannot deny fibrosarcoma. I do not think it is a Schwannoma lying within the brain. Malignant tumors of cranial nerve origin are extremely rare. Acoustic neuronomas are rarely malignant; I have seen one or two in the optic nerve, and I have seen one in the 6th cranial nerve. It would have to be the cerebral equivalent of a Schwannoma, making it an oligodendroglioma, which this tumor definitely is not.

Dr. del Regato: Drs. R. Hackett of Gainesville and D. R. Dickson of Santa Barbara diagnosed a glioblastoma and a fibrosarcoma in the two sections provided. Dr. Henry Azar of Tampa saw a fibrous meningioma and microgliomatosis. Dr. Leo Lowbeer maintains that this was a case of fibrosarcomatous meningioma from the start.

Subsequent History: From April 22nd to May 14th, 1974, the patient received radiotherapy through two moderate size lateral fields. A total dose of 5436 rads was received at the mid-brain plane in 54 days (Dr. Dave Lhevine). She improved and did well until July 1974 when she developed nausea and vomiting. It was decided that no further radiotherapy was indicated. On May 1st, 1975 she expired.

Dr. Kjellberg: This case does not have much clinical attraction. There is one small item of clinical interest pointed out, that the left arm had diminished strength. The EEG abnormality was in the left hemisphere. It is possible to get an ipsilateral weakness when the brain stem is shifted due to the fact that the mid-brain presses against the tentorial edge on the other side, produring an ipsilateral hemiparesis.

Dr. A. Gonzalvo, Tampa, Fla.: Dr. Zimmerman, do you think there was radiation effect in one of these slides?

Dr. Zimmerman: No, I really do not, and I am not keen on the idea of the radiation effects, as you will see in a minute.

Dr. James Cox, Milwaukee, Wisc.: Would you refresh us on the history?

Dr. del Regato: Three months after the initial operation, the patient had an obvious recurrence and then was irradiated.

Dr. Cox, Milwaukee, Wisc.: At that time, was there a scalp tumor as well? Did the scalp lesion occur, or was it the cause of irradiation?

Dr. Zimmerman: Dr. Lowbeer talked to me on the telephone about this. Three months after the irradiation that followed the tumor removal, a mass appeared in the scalp and was biopsied. That is what you are seeing.

Dr. del Regato: As I understood it, the patient was operated, and three months later she had a recurrence. I talked to the radiotherapist in Tulsa; he gave me part of the information that I have. When the patient recurred, Dr. Lowbeer was given the initial biopsy, and he made his diagnosis; he maintained afterwards that it was the same thing. This had not been suspected by others, and this is the point that is being raised. It is a little confusing.

Dr. H. Azar, Tampa, Fla.: I wish this case had never been submitted; my understanding was that the recurrence was in the same area.

Dr. Zimmerman: I can straighten out this part of it for you. The original biopsy of the intracranial tumor was misdiagnosed as a benign mengiomatous fibroma or something of the sort, but when the slides were subsequently reviewed, they realized that it was malignant.

Dr. del Regato: However, it was malignant before it was irradiated.

Dr. Zimmerman: That is right. Dr. Lowbeer now realizes that the first biopsy was a malignant tumor, and as he told me, it looks exactly the same as the second biopsy. Three months after they made the diagnosis of malignant tumor and after irradiation had been applied, they noticed a mass in the scalp, and that is a malignant lymphoma.

References:

Zimmerman, H. M.: Malignant lymphomas in the nervous system. Acta. Neuropathl. Suppl. 6:69-74, 1975.

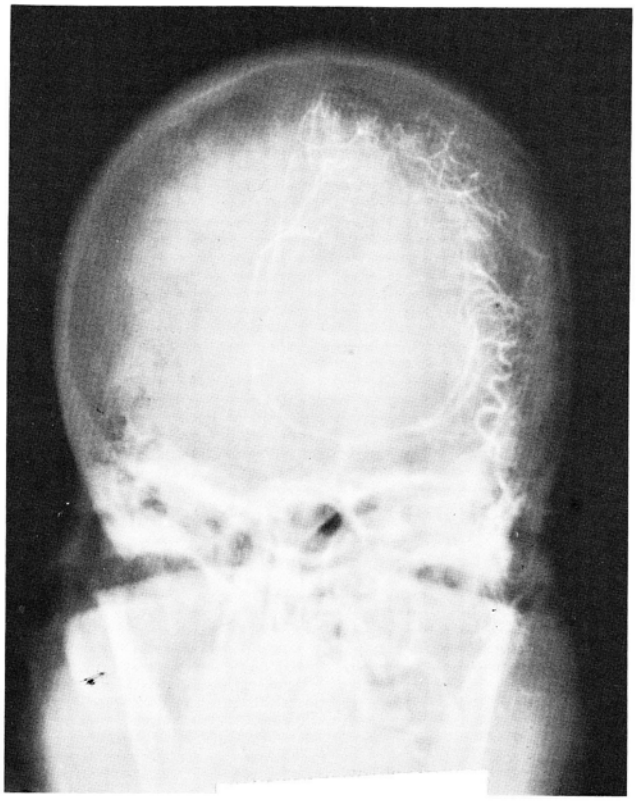
12. Post-Irradiation Necrosis of the Brain

Contributed by **H. M. Zimmerman, M.D.**, New York, New York

The patient was a 51-year-old woman in April 1975 when she complained of eye pains, diminishing vision and headaches. A tumor had been removed from the neck three years previously. On examination, there was anosmia, disorientation and left optic atrophy. The brain scan showed increased uptake in the left frontal area.

Dr. Taveras: The frontal projection shows a rounded shift of the anterior cerebral artery and splaying of the anterior and middle cerebral vessels, which is typical of a frontal mass lesion. The lenticulostriate arteries are stretched upwards, and there appears to be lateral displacement of the vessels over the insula. In the lateral projection, there is evidence of rounding of the pericallosal artery and downward displacement of the supraclinoid portion of the internal carotid siphon. There is no evidence of elevation of the branches of the anterior cerebral artery as they course forward towards the tip of the frontal lobe. The Sylvian triangle is lower than usual, and there is elevation of the pericallosal artery, which seems to be separated from the upper margin of the Sylvian triangle. The elevation of the pericallosal artery could be due to ventricular dilatation or could be due to elevation of the corpus callosum by tumor (Figs. 1 and 2).

Fig. 1—Rounded shift of the anterior cerebral artery.

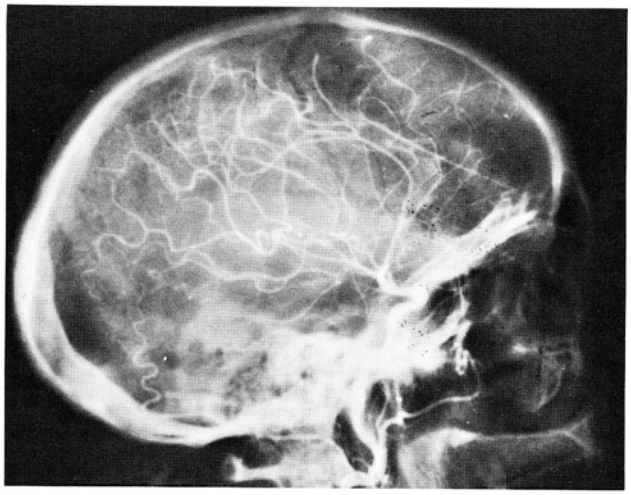


The CT scan demonstrates the presence of an ill-defined area of diminished absorption occupying almost the entire left frontal lobe and producing deformity of the left lateral ventricle in its anterior portion. There is a midline shift of a rather marked degree. Following the intravenous injection of radiopaque contrast, there is an irregular increase in the density of the previously radiolucent area in the frontal lobe. There is no solid mass visible but rather a number of areas have increased in density. The appearance at the level where this cross section was taken does not suggest that there is cystic degeneration of this tumor mass (Figs. 3 and 4).

In the lateral angiographic film, there is at least one vessel in the middle cerebral territory that shows segmental narrowing, and there is at least one, possibly more, in the anterior cerebral, presenting a beaded appearance.

Regarding the possible histology of this lesion, we must consider an infiltrative tumor that is involving both the middle cerebral and the anterior cerebral vessels. Again, as in the previous case already discussed, the possibilities are either a glioblastoma or reticulum cell sarcoma-microglioma. Because of the history of a mass in the neck removed three years previously, the possibility of a lymphoma must be considered. However, the lymphomas do not usually invade the brain with large masses, but rather they involve the meninges and infiltrate the brain through the perivascular spaces. Invasion of the central nervous system in this manner appears to be more common than is recognized. The cases of Hodgkin's disease that I have seen have first involved the bone and/or the meninges and secondarily invaded the brain. The presence of anosmia and a left optic atrophy always suggest

Fig. 2—Rounding of the pericallosal artery with downward displacement of positions of the carotid siphon.



the possibility of a meningioma that has grown backward to compress the left optic nerve. Looking at the solarized copies of the arteriogram submitted for review, there is an apparent increase in the density of the bone along the planum sphenoidale and an apparent loss of the bony outline in the region of the cribriform plate. This would be in favor of meningioma. However, the vessels along the inferior aspect of the frontal lobe are not elevated, and if the tumor arose from this area, one would have to postulate that it infiltrated from that point. I have seen cases of Hodgkin's disease behave in this manner. There is also some density of the bone in the region of the dorsum sella and sphenoid sinus, but this could be an artifact due to the copying of the film. We must raise the possibility of a sphenoid sinus carcinoma with extension upward and diffuse meningeal involvement. This would account for the vascular narrowing. A meningeal sarcoma may also diffusely invade the leptomeninges and produce vascular changes like the one shown in this case.

In summary we have here evidence of a large infiltrative left frontal mass with pronounced midline shift and focal narrowing of vessels in the middle and anterior cerebral artery branches. There appears to be increase in density of the bone in the floor of the anterior fossa and possibly dorsum sella and middle fossa and sphenoid sinus as well. However, because this is a solarized copy of an arteriographic lateral view, I cannot be sure of this finding. The possibilities include lymphoma-microglioma, malignant glioma, sphenoid sinus or nasopharyngeal carcinoma with diffuse brain and leptomeningeal involvement, and meningeal sarcoma.

Dr. Taveras' Impression:

1) **NASOPHARYNGEAL TUMOR**
2) **SPHENOIDAL SINUS TUMOR**

Radiologic impression submitted:

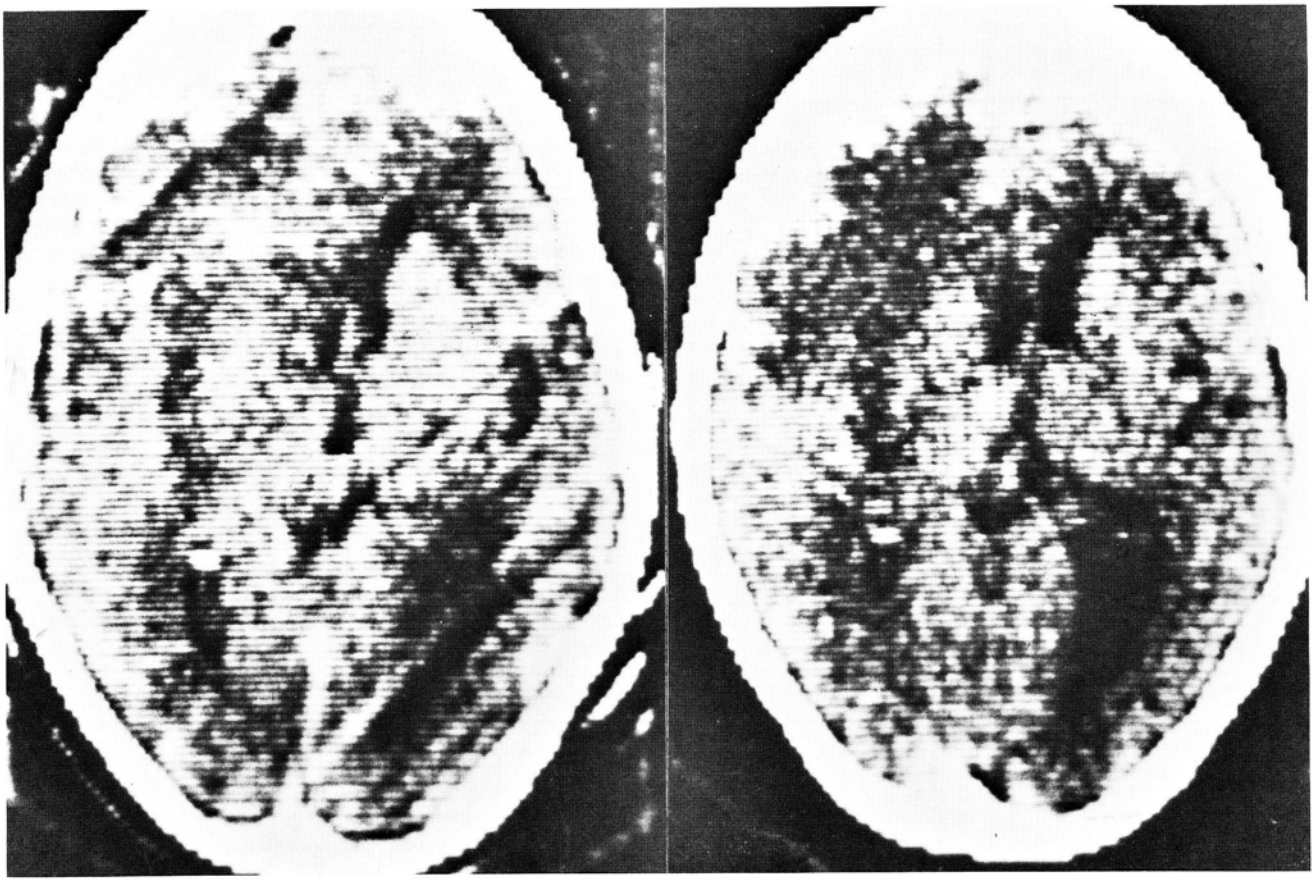
Metastatic tumor	26
Glioma	21
Meningioma	14
Fronto-parietal tumor	10
Benign lesion	14
Others	8

Dr. Taveras: There is no basis for us to say that this is a metastatic tumor. With the amount of infiltration and edema, glioma is a definite possibility if it were not for the fact that we have increased bone density. Meningioma is a good diagnosis because of the bone changes, but the benign form would be most unusual for this. Fronto-parietal tumor is an impossibility because it would not be parietal; it is all in the frontal region. This is only a location diagnosis.

Dr. del Regato: Dr. Ritsuko Komaki of Mil-

Fig. 3—Ill-defined area of diminished absorption of almost the entire left frontal lobe and midline shift.

Fig. 4—After injection of contrast material; irregular increase in the density of radiolucent area.



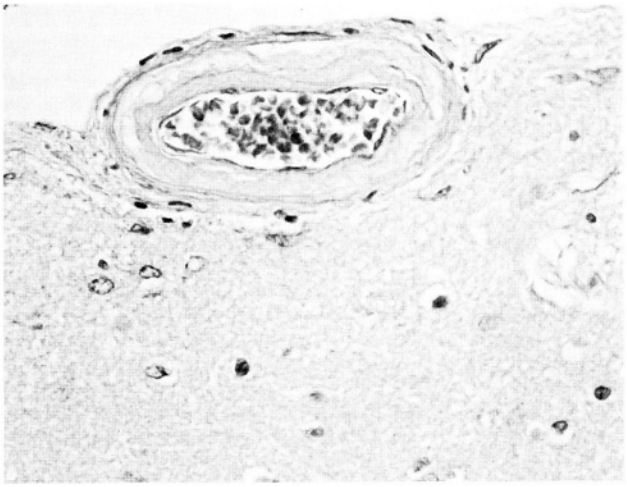


Fig. 5—Thickened arteriole in slightly thickened leptomeninges. H and E stain; x450.

waukee also diagnosed a nasopharyngeal tumor. Dr. John L. Kestel of Waterloo, Iowa recognized a central parietal mass and wondered about the possibility of its being a metastasis. Dr. Lawrence Gold of Minneapolis suggested a hemangiopericytoma.

Operative findings: In April, 1975 a craniotomy was done. The brain appeared discolored and swollen.

Dr. Zimmerman: Our neurosurgeon was handicapped in this case because he was not informed of many of the details prior to operation. These came out later, partly as a result of my diagnosis of a frozen section I was asked to look at during craniotomy. We have since attempted to get a microscopic preparation of the tumor that was said to be in the nasophrynx, but to date we have received no response. Either the slide has been lost or misplaced. At any rate, the neurosurgeon was not told of a diagnosis of a tumor in the nasopharynx of this patient made three years previously in Italy. When the patient appeared at Montefiore Hospital, she had the lesion in the brain that Dr. Taveras just described.

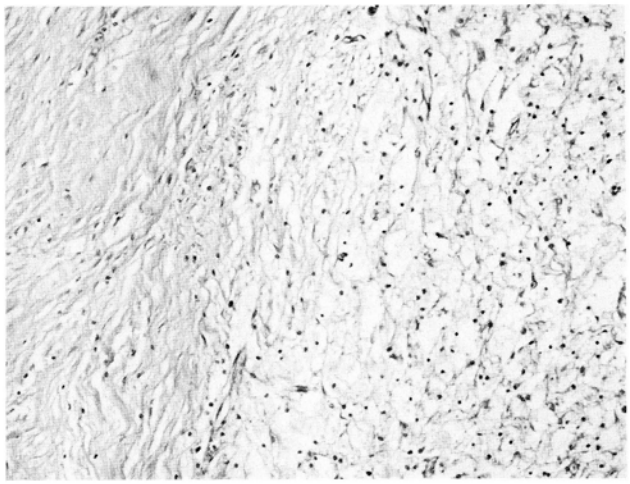
On the basis of a history of diminishing vision and headaches, coupled with the roentgen findings, a craniotomy was performed. At operation the changes were interpreted to represent some form of primary intracerebral neoplasm. These changes consisted of cerebral swelling with discoloration. A large biopsy specimen was removed for frozen section diagnosis, and this failed to disclose any evidence of tumor. The leptomeninges were slightly thickened, and many of the meningeal vessels were prominent by virtue of their thick walls (Fig. 5). Adhesions between the pia-arachnoid and the underlying cortex were extensive. Scar tissue replaced the subpial parenchyma, which otherwise was the seat of an extensive encephalomalacia (Fig. 6). Where neither fibrosis nor softening was present in the cerebral cortex, the architecture was nonetheless disorganized, and here and there darkly stained particles of ferrocalcium and iron were scattered. Up to this point, the picture suggested cerebral infarction of long standing. In other parts of the specimen, many thick-walled vessels with perivascular fibrosis were noted. An occasional lymphocyte and polymorphonuclear leukocyte also made their appearances. The encephalomalacia and interstitial edema were dominant features (Fig. 7). A reactive protoplasmic astrocytosis, not astrocytoma, was part of a reparative or healing process. In some fields, the fibrosis was enormous and collagenous connective tissue mush in evidence.

What produces this microscopic picture? It is not that of the usual demyelinating disease, such as multiple sclerosis, because both the necrosis and fibrosis are far too extensive. There is also a peculiar spongioform appearance due to interstitial edema that is part of the lesion and is unlike the picture usually present in multiple sclerosis. Then there are foci of coagulative necrosis in which neurons are shrunken and hyperchromatic and have evidently been caught in the process of dying. This too is not what is usually seen in a demyelinating process.

Nor is this the picture of cerebral infarction for some of the same reasons: liquifactive and coagulative necrosis, formation of dense scar tissue, and the presence of old, intermediate and relatively fresh lesions in the same fields that indicate a progressive process.

Then my attention was focused on rather significant vascular changes that demanded an explanation in terms of etiology. These changes consist of angionecrosis with considerable fibrinoid deposits (Fig. 8). In some vessels, lumens are obliterated, and undoubtedly this led to infarction. Other vessels merely have thickened walls but are surrounded by perivascular rings of fibrosis. The Virchow-Robin spaces are obliterated by the fibrous tissue. In the parenchy-

Fig. 6—Radiation necrosis in subpial layers of cerebral cortex. Dense collagenous connective tissue scar is on left, and encephalomalacia is on right. H and E stain; x180.



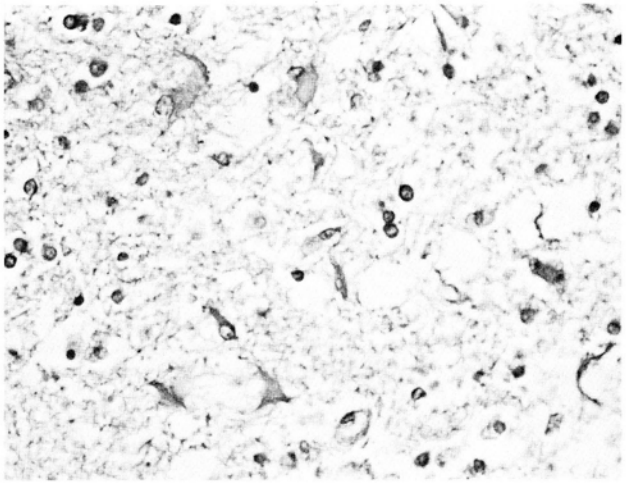


Fig. 7—Encephalomalacia and edema in radiation necrosis. Note large protoplasmic reactive astrocytes. H and E stain; x450.

ma, in addition to the fibrosis, there is astrocytic proliferation.

We had the temerity on the basis of these microscopic preparations to suggest to the neurosurgeon in the case that his patient had received heavy x-irradiation to the head and that the biopsied lesion was that of radiation necrosis. This diagnosis took him completely by surprise, and he was rather skeptical. He questioned the patient and her family closely and learned for the first time of the presumable nasopharyngeal tumor for which a total x-ray dosage of some 10,000 rads had been given to the rhinopharynx in two series about two and a half years previously.

This is not the first or only case of radiation necrosis that I have seen. Two of my colleagues, one a radiotherapist and the other a neurosurgeon, each have had patients who were treated with little more than 5,000 rads of x-rays for chromophobe adenomas of the pituitary gland and who developed radiation necrosis about two years later. Both patients had subsequent biopsies of their temporal lobes that revealed lesions indistinguishable from those I have shown you in the present case. Reports on radiation necrosis are appearing sporadically in the recent literature. By the way, in our present case there is no evidence of tumor recurrence in the nasopharynx, nor is there any evidence of an intracranial metastatic focus. The radiotherapy may have cured the primary tumor, but it led to cerebral injury.

Dr. Zimmerman's Diagnosis:

RADIATION NECROSIS

Histopathologic diagnoses submitted:

Astrocytoma	25
Degenerative process	4
Encephalomalacia	3
Infarct	3
M. S.	1
Chordoma	1
Others	10

Dr. Zimmerman: Astrocytosis, yes, but astrocytoma, no. The degenerative process — how right. Encephalomalacia is right. It is an infarct-like lesion, but it is not really an infarct because it is radiation burn. It is not multiple sclerosis, and chordoma is purely a fanciful diagnosis.

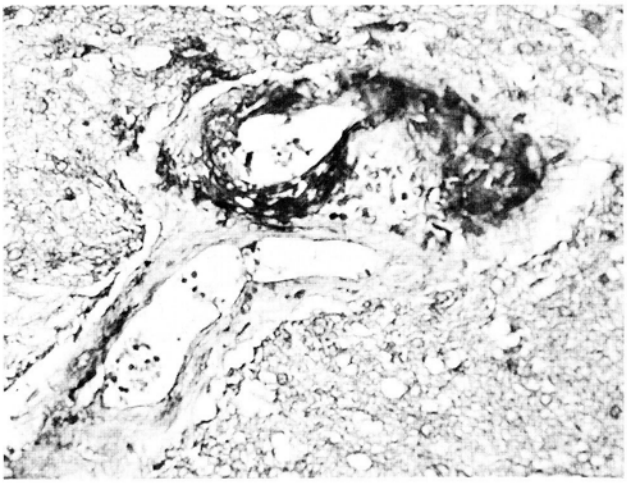
Dr. del Regato: Dr. Henry Azar of Tampa saw only encephalomalacia with gliosis. Drs. Magda and J. Kepes also saw reactive gliosis in areas of demyelinization. Not having the pertinent details of history, none of the experts or other participants suggested "radiation" necrosis.

Subsequent history: Following operation it was found that the patient had been irradiated for a nasopharyngeal tumor in February-March 1972 in Catagna, Italy. A total dose of 4900 rads was said to have been received by the tumor in 41 days; there was additional irradiation of supraclavicular lymph nodes. Apparently, there had been a recurrence, and radiotherapy was repeated in September-October 1972 when an additional dose of 5,000 rads was received in 42 days.

Dr. Henry Azar, Tampa, Fla.: Frankly, I cannot say that this is a case of radiation necrosis. Perhaps the changes are compatible, but I question a straight diagnosis of radiation necrosis when we know that secondary vascular sclerosis can occur in a field of outstanding inflammation, degeneration, encephalomalacia and so forth. In all fairness, I would like to submit that there are vascular changes, changes perhaps suggestive of radiation effect but not enough to come up with a diagnosis of radiation effect.

Dr. Kjellberg: I have had some experiences in the use of proton beam irradiation, largely of the pituitary; we have done over 800 procedures with this form of irradiation in which the deliberate intention was to produce focal radionecrosis. For the most part, these have been patients with pituitary tumors, although some

Fig. 8—Angionecrosis with fibrinoid change in radiation necrosis. H and E stain; x280.



with normal pituitaries, but in which the intention was to produce focal radionecrosis. More recently, we have tried to irradiate some arteriovenous malformations, and the early impressions are favorable responses. In the course of doing this, we have become somewhat familiar with and definitely interested in radionecrosis because we do not regard this as a complication but rather a therapeutic goal. I have struggled with this prospect for about 15 years.

The histopathologic certainty of many of the effects is hard to come by. I found your expositions most illuminating, but I have also been involved in these cases often enough to hear the kind of dialogue that emerged from the floor. As a bystanding neurosurgeon, I think that perhaps these topics have not been explored in enough depth or breadth so that widespread understanding of them is readily available. However, I am pleased to see that this seems to be changing somewhat. It is a very interesting subject.

When a radiation dose is referred to, we realize that we have to pay special attention to it. Rate of delivery is normally thought of as something like 200 rads a day, five days a week for a number of weeks, such as four to seven. Our irradiation is delivered at a rate of 5,000 to 15,000 rads in one hour or less. The intensity is considerably higher than average. A real translation of units is required in order to use rads in describing both kinds of irradiation. Also, the field size of irradiation makes a big difference. We use fields between 7 mm to 5 cm in diameter. These are things that I have had difficulty in learning, but I continue to be interested. I think that the kind of discussion generated by this case brings about further interest and more information.

Dr. James Cox, Milwaukee, Wisc.: I too am impressed with Dr. Zimmerman's diagnosis. If the biopsy that Dr. Zimmerman looked at was in the base of the skull adjacent to the irradiated area, I think the findings would be quite understandable. I do not see why the changes in the cranial falx could be attributed to the irradiation, particularly in view of the angiographic findings discussed by Dr. Taveras.

Dr. Taveras: The changes that we saw in the skull bone in the films of the angiogram involve the walls of the sphenoid sinus and the floor of the anterior foci; this is the usual place where you would get sclerosis of bone in association with nasopharyngeal carcinomas that invade upwards and permeate bone with or without destruction. In general the increase in density of the bone appears after radiation therapy and is not usually seen originally. I was saying, therefore, that maybe the tumor did not arise in the nasopharynx but perhaps in the sphenoid sinus. Very often that is something impossible to decide. We see the tumor and the changes in the bone; we do not know whether the tumor started in the sphenoid or in the nasopharynx.

Dr. J. Cox, Milwaukee, Wisc.: Are there not vascular changes much above those structures in association with the brain?

Dr. Taveras: When they irradiated this tumor, evidently their field was very high, and the changes that we see go all the way up to the corpus collosum. I am attributing that to edema.

Dr. del Regato: This woman was treated twice to a considerable dose. That in itself is enough to give all kinds of difficulties, but a great deal depends, as Dr. Kjellberg has suggested, on the size of the field and the area that was irradiated, and we know nothing about it.

Dr. Kjellberg: There is one other point of observation: the blood flow seems to influence the extent of the radiation change. On the upstream side of blood flow, the area is much more resistant to radiation change than it is on the downstream side. With the proton beam we sought to superimpose isodose curves on the degree of radiation change; the changes were graded from total necrosis to marginal change and simple edema without any cellular change. Doses of a few hundred rads, far lower than you would ever blame any radiation for, may cause edema. I do not really know the significance of this observation, but I hope to learn someday. Perhaps some of the toxic materials that are part of the evolving irradiation change the flow downstream and induce further changes as a result of some kind of toxic effect resulting from the destruction of cells.

Dr. J. Kepes, Kansas City, Kans.: The brain and spinal cord are very frequently the intended target of irradiation in brain tumors. However, one thing that has always impressed me about radiation myelopathy and cerebral changes due to irradiation is that most of the cases we have seen were those in which the brain was an incidental target, rather than the intended target.

Dr. Zimmerman: The cases that I have seen with hypothalamic radiation necrosis were incidental to irradiation that was intended for a chromophobe adenoma. Radiation effects are tremendous. I think it is extremely important to know about which species of animal you are talking. Someone tried to irradiate frogs and used 50.000 rads; the frogs licked their chops, did perfectly well, and nothing ever happened. You can give enormous doses without seeing any effects on tissue cultures. In the intact animal of whatever species, the effect is quite different, and that may have something to do with the absorption of material that passes into the circulation and later damages blood vessels. The only time you see fibrinoid necrosis, other than from irradiation, is in hypertensive episodes.

It is also important to know how long after irradiation you examine your specimen. In man it takes at least two years before the effects become evident; in all the cases that I have seen,

at least two years have elapsed between the end of irradiation and the time when a radiation necrosis has developed.

The diagnosis here is made from a combination of all things. Fibrinoid degeneration occurs very rarely in any condition other than this kind of a lesion. When all the changes seen here are added up, I honestly believe there is no other possible diagnosis that could be entertained.

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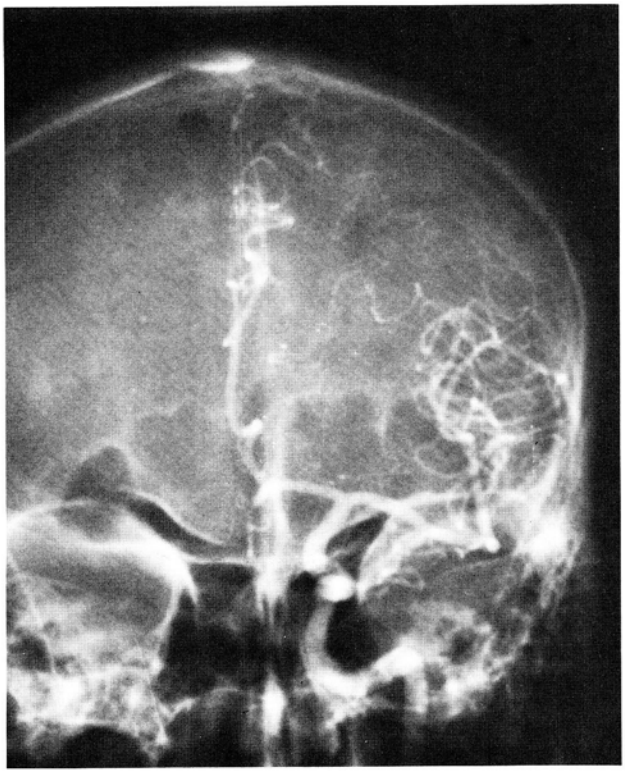
13. Metastatic Cerebral Carcinoma

Contributed by **E. V. Grayson, M.D.**, Hollywood, Florida

The patient was a 65-year-old man in January 1975 when he complained of incontinence; he had suffered trauma to his forehead two months previously, and there had been loss of appetite and decreased mentation. On examination he was semicomatose, dehydrated and disoriented; there was rigidity of the neck and extremities. The Babinski was negative on left and questionable on the right. Laboratory procedures showed no abnormalities.

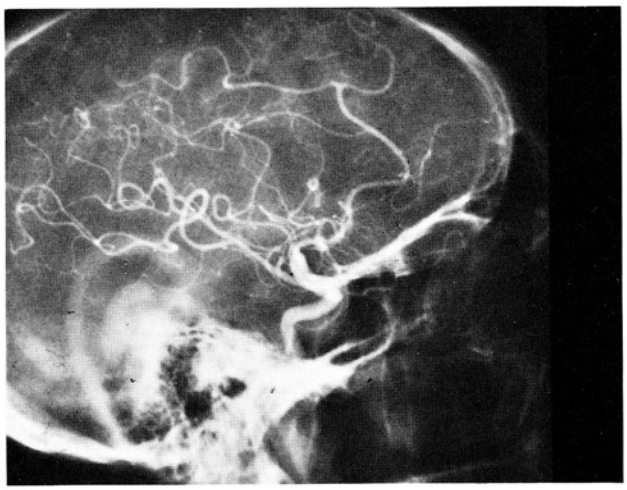
Dr. Taveras: The frontal view demonstrates the presence of a slight midline shift of the anterior cerebral artery. The horizontal portion of the anterior cerebral artery is slightly elevated. The supraclinoid portion of the siphon is essentially normal in position. The intracavernous portion of the internal carotid artery is slightly displaced laterally. The middle cerebral vessels in the region of the Sylvian fissure show slight downward concavity of most of the vessels going from the Sylvian fissure to the surface of the brain, suggesting a mass in the opercular region. The angiographic Sylvian point may be slightly displaced medially (Fig. 1).

Fig. 1—Midline shift of anterior cerebral artery.



In the laterial view of the arterial phase, there is evidence of downward displacement of the anterior portion of the Sylvian triangle and a slight separation of the branches of the middle cerebral artery in the opercular region. There are no abnormal vessels (Fig. 2) on that film. The lateral view in the venous phase shows enlargement of the sella turcica (Fig. 3). There appears to be a double floor with one side being more depressed than the other. The dorsum sella appears to be totally destroyed. When one looks at the sella turcica in the frontal projection, there is definite depression of the left side of the floor of the sella turcica. This suggests that the mass is intrasellar in location and that the enlargement of the sella turcica and destruction

Fig. 2—Evidence of downward displacement of the anterior portion of the Sylvian triangle.



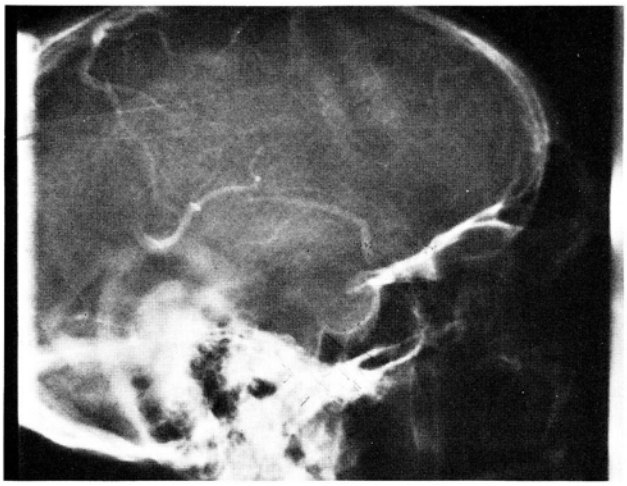


Fig. 3—Venous phase showing enlargement of the sella turcica.

of the dorsum is not due to generalized increased intracranial pressure. In general, when the dorsum is destroyed secondarily to increased intracranial pressure, the floor is demineralized throughout, and there would not usually be depression of one side of the floor of the sella.

I feel, on the basis of the findings in the region of the sella turcica, that we are dealing here with an intrasellar tumor with moderate suprasellar extension and extending somewhat more to the left because of the depression of the left side of the floor of the sella turcica. There is also evidence of a suprasylvian mass anteriorly placed in the frontal parietal operculum, and there appears to be no connection between the mass in the sella turcica and the suprasylvian mass. Certainly, the horizontal portion of the middle cerebral artery is not in any way elevated, and I am not able to establish a connection between the pituitary adenoma, which is apparently off center in location extending towards the left side, and the suprasylvian mass. Extensions of pituitary adenomas are usually in continuity, and only extremely rarely would they be separated from the initial mass in the sella turcica. The so-called pituitary carcinoma is an entity that is not accepted by everyone, and the term invasive adenoma of the pituitary would appear to be a better one.

In summary, we have an intrasellar mass that is fairly typical in terms of its configuration and a left opercular or suprasylvian mass. It would appear to me that there is no connection between these two masses, and therefore, I am forced to make two diagnoses. The suprasylvian mass may well be intracerebral in location, although it is fairly superficially placed, and I would consider a glioma or metastatic lesion here as a good possibility. Coincidence of a pituitary adenoma with a glioma is uncommon, but it does occur. Another possibility to consider would be a metastatic lesion to the pituitary gland and to the suprasylvian region. Direct metastases to the pituitary gland are rare, but they do occur, and it would be a definite possibility here. The enlargement of the sella turcica with depression on the left side of the floor is more in favor of a slowly developing tumor, rather than a rapidly growing metastatic process leading to the findings described in the history, namely that the patient was semicomatose, dehydrated and disoriented.

Dr. Taveras' Impression:

1) **PITUITARY ADENOMA**
2) **Another tumor, or**
3) **Something else!**

Radiologic impressions submitted:

Glioma, astrocytoma (suprasylvian, midbrain)	33
Metastatic tumor	16
Chromophobe adenoma	9
Subdural empyema	6
Others	14

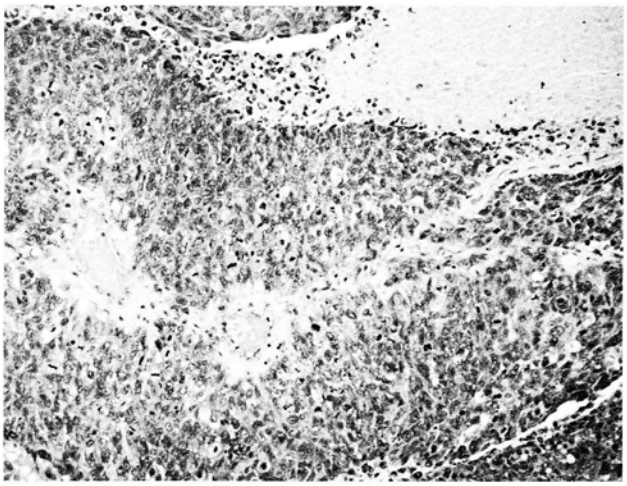
Dr. Taveras: Suprasylvian location, yes, but I see absolutely no reason for the midbrain. I think that the tumor in the frontal region could well be metastatic, but it could also be primary. I agree with chromophobe adenoma, but that is only half a lobe; there are two lesions here. I do not know why anyone would diagnose subdural empyema.

Dr. del Regato: Dr. Joel Tew of Chicago suggested a glioma. Dr. S. Chandra Mouli of Chicago offered a diagnosis of chromophobe adenoma. Dr. James Cox of Milwaukee suggested a chromophobe carcinoma, which would explain the two lesions.

Operative findings: On February 21, 1975 a left fronto-parietal craniotomy was done. The cerebral convolutions appeared flattened. A tumor measuring 3 x 2 cm was found in the lateral aspect of the frontal lobe near the optic nerve; it was curetted and suctioned.

Dr. Zimmerman: My diagnosis, as I'm sure was the case for all the pathologists in this room,

Fig. 4—Nests of epithelial cells clustering around blood vessels in this metastatic carcinoma of pulmonary origin. H and E stain; x150.



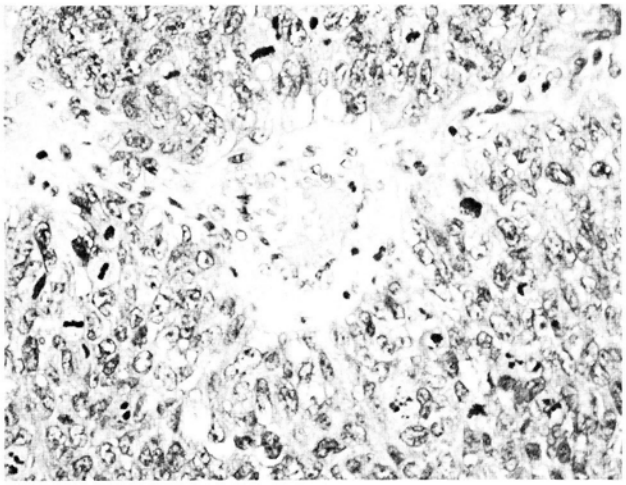


Fig. 5—Numerous epithelial tumor cells in mitotic division. The epithelial nature of the tumor is clear. H and E stain; x375.

was made simple by being informed that there were two neoplasms. Dr. Taveras had a much more difficult problem than we, not having been so informed.

What we see in the first slide of this case is a chromophobe adenoma of which we were unaware because this tumor was not represented in the microscopic slide we received for diagnosis. In the next projection slide that I prepared, there are tumor cells under fairly high magnification that infiltrate the brain tissue and are associated with hemorrhage and necrosis. The malignant cells are of epithelial type (Fig. 4). They form nests that cluster around blood vessels, each nest of cells being separated from another by necrotic tissue. This is the picture of a metastatic epithelial neoplasm. Under higher magnification, the tumor is seen to contain many cells in mitotic division (Fig. 5). Many of the mitoses are bizarre, as befits a highly malignant neoplasm. The cells have distinct walls, and this confirms the initial impression of an epithelial type of tumor.

Now one may ask, where is its origin? This is not easy to be sure of. When faced with a highly malignant metastatic epithelial neoplasm in the brain, the average pathologist thinks first of the lungs as its site of origin. Well, it often is the lungs that is the primary site of such a tumor, and it probably is so in this case. However, in reality the lungs themselves receive metastatic tumors from many parts of the body and sometimes pass them on to the brain. The lungs may act as filters for circulating epithelial and non-epithelial tumor cells and may serve merely as a way-station for these cells on their way to the brain. For this reason, a tumor in the lungs seen by x-rays is not conclusive evidence of its bronchogenic or pulmonary origin.

This leads me to another comment. Over the years we have learned that cerebral metastases are often more easily diagnosed as to their sites of origin than are even the tumors in their primary sites. That is probably because the brain is a "privileged" immunological site and doesn't alter the metastatic cells in a way to obscure their histologic appearance. Many a diagnostically difficult tumor yields to diagnosis when studied in its brain metastasis.

From what I see in this case, I would guess that the primary site is the lung, but I would like to know whether an x-ray of the chest was made. Now we are told there was a tumor in the lung. I had guessed as much, and from the diagnoses submitted by many of you, it is obvious that there is no disagreement.

Dr. Zimmerman's Diagnosis:

METASTATIC CARCINOMA (Lung)

Histopathologic diagnoses submitted:

Metastatic carcinoma	45
Others	9

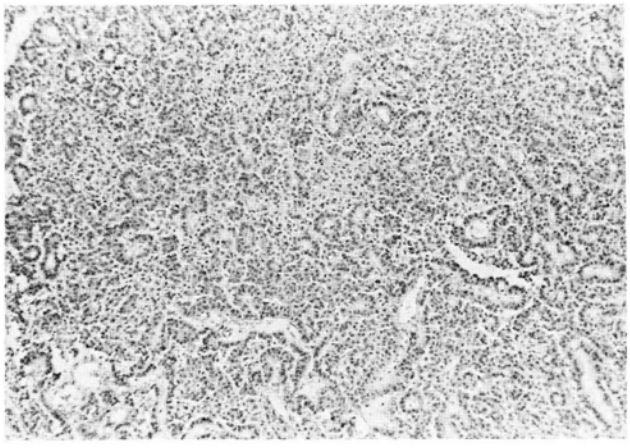
Dr. Zimmerman: I am disturbed by the suggestion that a chromophobe adenoma in the pituitary was a carcinoma of the pituitary in order to get a unified diagnosis. In some 450 chromophobe adenomas of the pituitary that we examined minutely, there were only two instances that I would be willing to call carcinoma.

Dr. del Regato: Dr. Daniel Collins of Milwaukee suggested a pituitary tumor with metastasis. Most experts suspected a pulmonary primary for what they diagnosed as metastatic carcinoma.

Subsequent history: Three days after craniotomy, on February 14th, 1975, the patient expired. Autopsy revealed the presence of a pituitary adenoma and a carcinoma of right upper pulmonary lobe with extension to the pleura and metastases to the brain, adrenals and bone marrow (Fig. 6).

Dr. Kjellberg: I have some special interest in pituitary adenomas. In the Armed Forces Institute of Pathology series of about 1,000 pituitary tumors, one of the remarkable facts is that only half of them were symptomatic enough to have been recognized during life. The ones not recognized were not necessarily small tumors;

Fig. 6—Pituitary adenoma found at autopsy.



they averaged 2 to 4 cm in their longest dimension, so persons can harbor such lesions and remain absolutely asymptomatic. They may have full life expectancies and die of some other cause. Occasionally, an incidental pituitary adenoma may be found in association with another disease. In a study of 1,000 allegedly normal pituitaries, a gentleman named Costello found almost 20% contained some tissue that would be classified histologically as a pituitary adenoma; these cases were mostly in old patients. With age there seems to be an increasing frequency of microadenomas in the pituitary. Of course, some of those microadenomas will develop into macroadenomas, but that still does not mean that they are functional or clinically recognizable. It makes it a little easier to accept a chromophobe adenoma diagnosis along with another one.

From the clinical point of view, there are a number of puzzling things about this case that I think would be appropriate to clinical or surgical evaluation. I find some things troubling in trying to make them fit together, such as head trauma leading to incontinence in a patient who can give a history. That makes me think that there has to be further information. I do not understand how a semicomatous and dehydrated patient would have normal laboratory findings. Another puzzling thing was that the amount of shift in the angiogram did not remotely account for the amount of coma. That much shift is very easily tolerated, and there had to be some other explanation. There was no evidence that the pituitary adenoma was very large, but massive pituitary adenomas, almost totally obliterating the third ventricle, can occur without particularly altering the patient's alertness or state of consciousness.

Another thing that confused me was the operative findings; this tumor was on the lateral aspect of the frontal lobe near the optic nerve. I was certainly eager to see some explanation other than the pituitary account for most of the symptoms. Pituitary tumors almost never metastaize. As far as I know, the only pituitary tumors that metastasize are those in Cushing's disease.

Dr. Zimmerman: Even in Cushing's disease, they do not metastasize. We have seen one pituitary adenoma that had been operated upon, and some two years later, there was a mass in the cauda equina region of the cord; they excised a chromophobe adenoma.

14. Malignant Lymphoma of the Spinal Cord

Contributed by **H. A. Azar, M.D.,** Tampa, Florida

The patient was a 38-year-old man in July 1974 when he complained of lumbosacral pain that was followed by fecal and urinary incontinence. On examination there was paresis of the lower extremities and a T9 sensory level. The lumbar puncture brought clear fluid, and there were no cells.

Dr. Taveras: The first film shows widening of the spinal cord in the upper thoracic region and apparently also in the lower cervical area. The appearance is typical of an intramedullary lesion producing cord enlargement, either intramedullary tumor or a syringomyelia (Fig. 1).

The second film shows a nodule in the upper lumbar region over the cord and associated apparent slight nodularity, which could be produced by enlarged blood vessels or by tumor nodules. It should be noted that there is a silver clip above this nodularity, which indicates that the patient probably had previous surgery (Fig. 2).

The apparent vascularity suggests the possibility of a vascular nodule, such as may be seen in hemangioblastoma associated with a syringomyelia in the cervical and upper thoracic regions. This association has been seen in patients with Von Hippel-Lindau's Syndrome. The silver clip may have dropped from the cerebellum from previous surgery, and on that basis one would have to suggest that there was either a previous posterior fossa operation or that there was an upper cervical operation above the area shown by the myelogram. The silver clips usually drop from a higher location, more commonly from the posterior fossa. Ependymomas of the fourth ventricle rarely extend down towards the spinal cord directly, but seeding occasionally is found in the more malignant forms. The other possibility is an astrocytoma of the upper cervical spinal cord with downward growth of the tumor and a nodule presenting on the surface lower down.

Dr. Taveras' Impression:

INTRAMEDULLARY TUMOR:
1) **EPYNDYMOMA**
2) **HEMANGIOBLASTOMA WITH SYRINGOMYELIA**

Radiologic impressions submitted:

Ependymoma	21
Astrocytoma	23
Syringomyelia	10
A V M	7
Hemangioblastoma	6
Others	13

Dr. Taveras: I entirely agree with ependymoma, which is a good possibility. That the patient had a hemangioblastoma, then a syringomyelia higher up would be a good diagnosis. I think that all of these diagnoses are somewhat in the ballpark, and I can live with any of them.

Dr. del Regato: Dr. R. Byhardt and Dr. L. T. Hill of Milwaukee also offered ependymoma. Dr. Edward Grayson of Hollywood, Florida also suggested hemangioblastoma.

Operative findings: In March 1974 a laminectomy was done with marsupialization of a cyst.

Dr. Zimmerman: If you want to learn all I know of the condition represented by this case, you would be strongly advised to read the 1975 issue of **Acta Neuropathologica,** Supplement 6, which is a report of an international meeting on malignant lymphomas. In Vienna of that year, Professors Jellinger and Seitelberger and I conducted this meeting on many aspects of lymphomas.

In the first slide of the spinal cord in this case (Fig. 3), there is shown a malignant lymphoma with involvement of a blood vessel wall. As Dr. Taveras indicated in discussing a previous case, vascular mural involvement occurs in malignant lymphoma as well as glioblastoma multiforme. In both conditions, the vessel walls seem thickened. When that happens, the vascular lumens become constricted and even occluded, and infarction may result. This is evidently what happened in the present case where there is a myelopathy in the nature of an infarct-like lesion with massive necrosis. The tumor cells are arranged in collar fashion around blood vessels, infiltrate the vessel walls, and occlude some of

Fig. 1—Widening of the spinal cord in upper thoracic and cervical area.

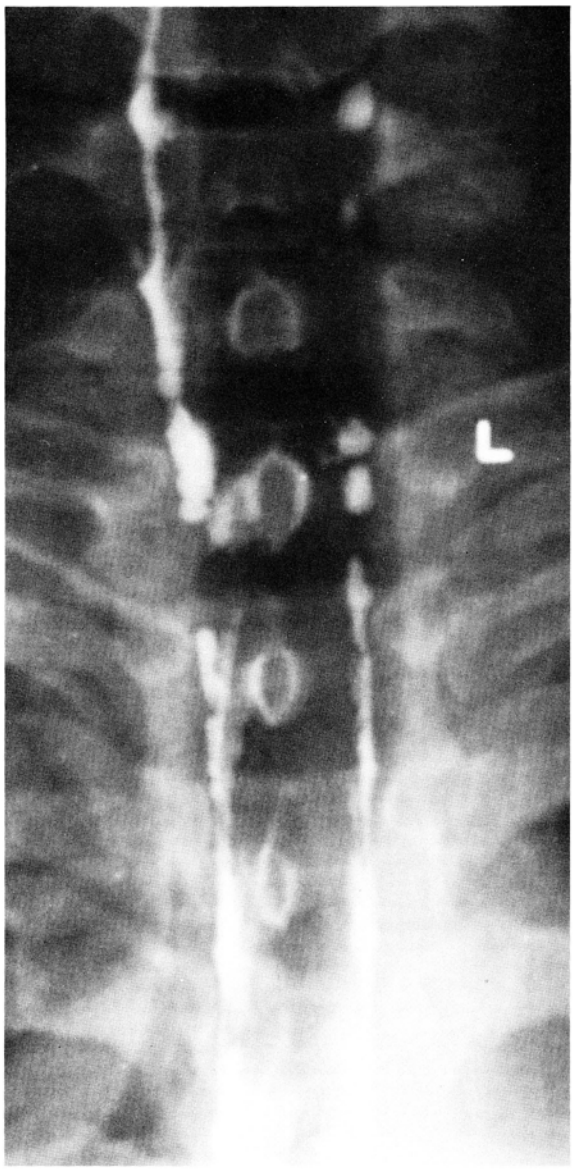
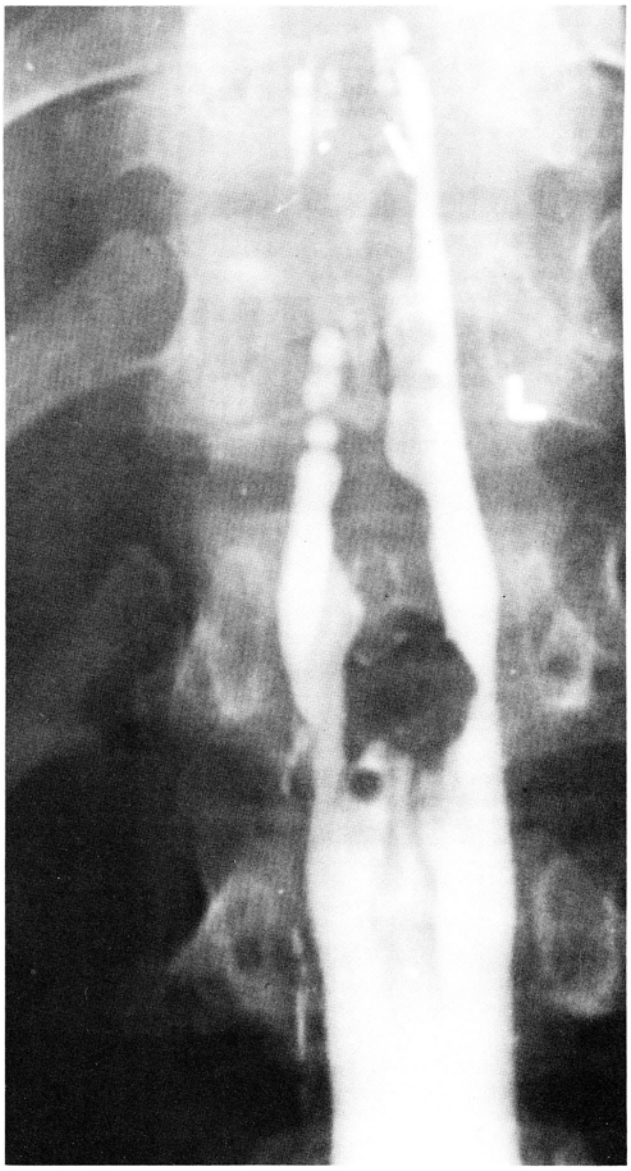


Fig. 2—Nodule in the upper lumbar region over the cord.



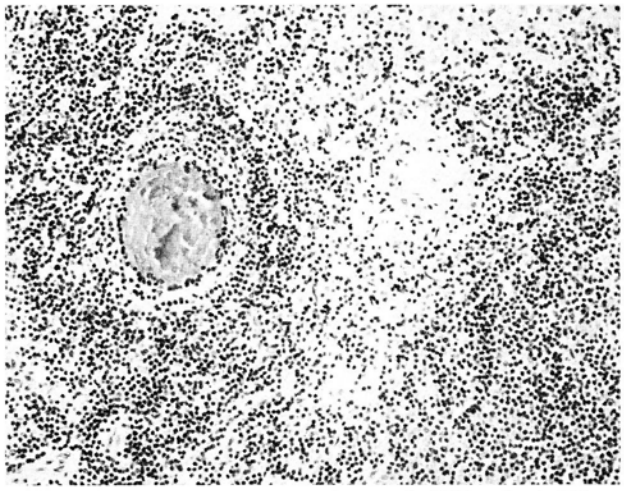


Fig. 3—Intraspinal perivascular and diffusely infiltrative malignant lymphoma (lymphosarcoma) with vascular mural involvement. H and E stain; x180.

these vessels. This leads to ischemic necrosis of the spinal parenchyma. The necrosis, the infiltrating tumor cells, the edema and the frequent hemorrhages are what has produced an expanded cord to yield the picture of an intramedullary neoplasm. The tumor in this case is neither an ependymoma nor an astrocytoma. In the next projected slide, there can be seen massive necrosis in the spinal cord, and only the margin just beneath the pia-arachnoid is still preserved intact. The subpial intact portion forms a sort of cylinder, encasing the central liquified spinal parenchyma.

In the next slide, there are shown focal collections of lymphocyte-like cells related to blood vessels whose walls are infiltrated. The perivascular Virchow-Robin spaces are filled with these cells. There is extensive necrosis of the spinal cord with here and there a remnant shadow of an anterior horn cell (Fig.4). Inevitably, the tumor cells are found infiltrating the adjacent parenchyma. Under high magnification, the lymphocyte-like neoplastic cells are indeed identifiable as of lymphocytic origin (Fig. 5). They are quite uniform in size, shape and staining intensity, but occasional cells have bizarre shapes and resemble those of reticulum cell sarcoma. In sections stained for reticulin, it is seen that the tumor cells produce a fine reticulin meshwork (Fig. 6). This reticulin fiber deposit occurs intramedullarly and not alone in the spinal leptomeninges. I can only agree with Dr. Kepes that when tumor cells of any kind invade the meninges, they stimulate a proliferative reaction on the part of the connective tissue normally present in these coverings. It is therefore important to demonstrate proliferated reticulin well within the spinal parenchyma, as in this case, for it to have diagnostic validity. Only when you find excessive amounts of reticulin in places where there normally is none is this significant.

The spinal nerve roots are also involved in the lymphomatous process (Fig. 7). The distribution of the tumor cells in this location is comparable to that in the cord itself. The leptomeninges are infiltrated, but perivascular tumor cell deposits are also present.

Based on the experience with a considerable number of cases of spinal cord involvement by malignant lymphoma, I have reached the conclusion that this condition is not one of primary or exclusive cord involvement. The cord is always implicated, either as the result of an extracranial systemic lymphomatosis with spinal cord metastasis, or in consequence of a primary cerebral malignant lymphoma with secondary extension to the cord. In the latter case, tumor cells from the cerebral lymphoma reach the ventricular system or the subarachnoid space and are seeded in the spinal meninges, from which they extend along the Virchow-Robin spaces into the cord parenchyma.

Several years ago, I prepared a table of incidence of brain tumors in my series of over 5,000 cases. Of the ten most common intracranial tumors in this series, malignant lymphomas ranked eighth in frequency with 168 cases (3.2 per cent). Almost half of these tumors were primary in the brain; the others were part of a systemic disease in which the nervous system was also involved. At the same time, I had over 600 tumors that involved the spinal cord, of which 57 cases were malignant lymphomas. All of these, as I indicated previously, involved the cord either as part of a generalized systemic lymphomatosis or from seeding from above.

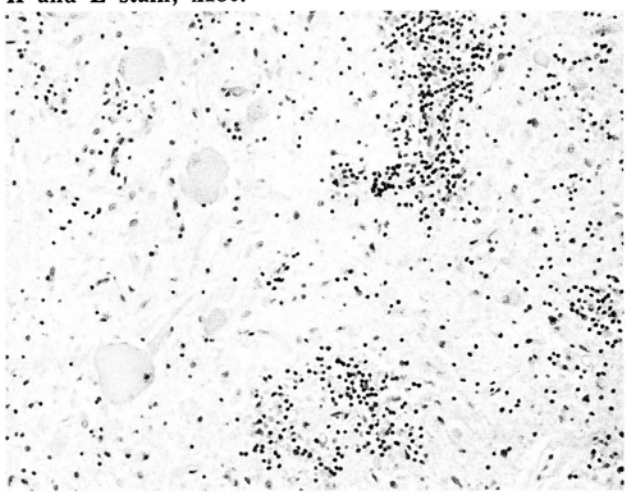
Dr. Zimmerman's Diagnosis:

MALIGNANT LYMPHOMA (Lymphosarcoma)

Histopathologic Diagnoses Submitted:

Malignant lymphoma	37
Leukemia	6
Microgliomatosis	9
Myeloma	2

Fig. 4—Myelomalacia in malignant lymphoma. Note "axonal" change in degenerating anterior horn cells. H and E stain; x180.



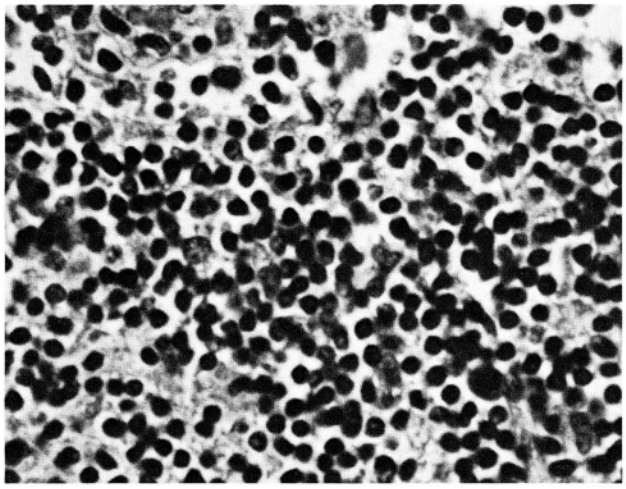


Fig. 5—Lymphosarcoma. Most tumor cells have a uniform appearance as to size and staining properties. H and E stain; x720.

Dr. Zimmerman: I do not like the term microglioma. I do not know why a tumor in the cord or brain is called microglioma, and when it is in the liver, bone marrow or spleen, it is called something else; yet it is the same tumor. I have just sent to the publisher a volume that will be appearing sometime this year with the lead article by Professor Fugita of Kyoto, Japan. He writes an extensive article, raising the fundamental question of whether or not there really are microglia at all; his evidence is so interesting that it reinforces my distaste for a diagnosis of microglioma. I think there are reticulum cell sarcomas or lymphosarcomes rising from the perivascular tissues in the brain as they do in other organs.

I do not know that leukemia can necessarily be predicted. Most of the 168 cases I have studied in the brain did not have leukemia. A primary tumor of malignant lymphoma variety can exist without leukemia. Of course, if one prefers to call it microglioma, that is acceptable even though I myself do not like the term. Myeloma can only be diagnosed if it is known that the marrow in the spinal column is involved. You saw no bone marrow change here at all, and I do not really believe this is a myeloma, although myeloma is one type of malignant lymphoma in my classification. I think plasmacytomas, myelomas, reticulum cell sarcomas, lymphosarcomas and Hodgkin's disease all belong to the group of malignant lymphomas.

Dr. del Regato: Dr. Henry Azar of Tampa made a diagnosis of microgliomatosis. Dr. Edward L. Lee of Tampa offered lymphocytic lymphosarcoma. Dr. R. Hackett of Gainesville, Florida suggested Hodgkin's.

Subsequent History: Following operation the patient's condition became worse; he was put on prednisone and eventually required a tracheostomy. On October 29th, 1974 he died. Autopsy revealed microgliomatosis of the pons, medulla oblongata and spinal cord.

Dr. H. Azar, Tampa, Fla.: The autopsy was performed by Dr. Francas, who has become a local expert on microgliomatosis.

Dr. Kjellberg: I have wondered about the term syringomyelia as suggested by a few radiologists. As far as I can tell, this is only a cyst of the spinal cord; yet the term is so euphonious that people opt to use it.

Dr. Zimmerman: It is the wrong term. There is a hydromyelia from an infarct of the central cord.

Dr. Kjellberg: Evidently, they can occur with or without tumors. The term is sometimes used to refer to either one. It seems that we would confuse ourselves less if we would simply use the term cyst of the spinal cord substance. I think that therapy for this lesion would include exploration and biopsy, frozen and permanent

Fig. 6—Spinal malignant lymphoma revealing a meshwork of proliferated reticulin fibers. Wilder silver carbonate stain; x450.

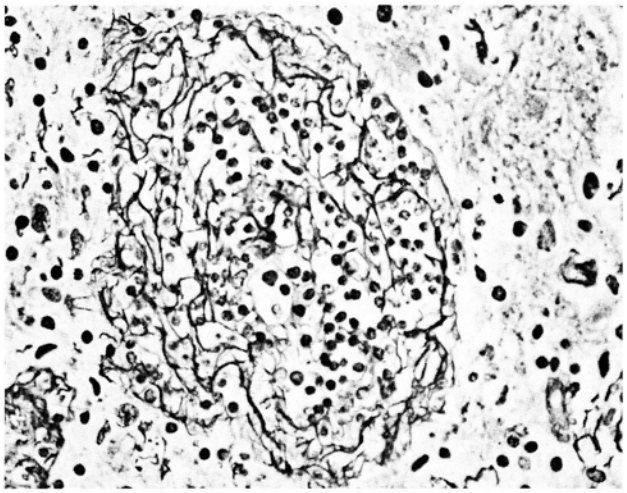
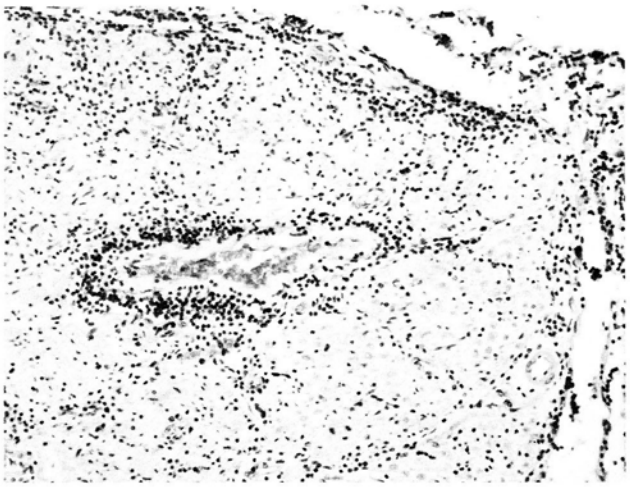


Fig. 7—Malignant lymphoma in and around spinal nerve root. H and E stain; x180.



sections. In the course of diagnosing spinal cord lesions. I think it is probably well worthwhile to use microsurgical technique. There are reports of some exceptionally good total surgical removals of intraspinal tumors by the use of the microtechnique, but it is a very difficult procedure. It is reasonable to drain a cyst, and I think vigorous support in the post-operative period will be called upon for many patients. I was curious whether post-operative consideration for x-ray therapy had been entertained in this patient.

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15. Epidural Malignant Lymphoma of the Spine

Contributed by **J. D. Cox, M.D.** and **B. K. Chun, M.D.**, Milwaukee, Wisconsin

The patient was a 16-year-old boy in March 1972 when he received a trauma on the sacrococcygeal region while playing hockey; pain persisted and became associated with difficulties in the movements of the left leg. On examination the knee and ankle reflexes of the left leg were weak and diminished muscular strength. Laboratory examinations were all within normal limits.

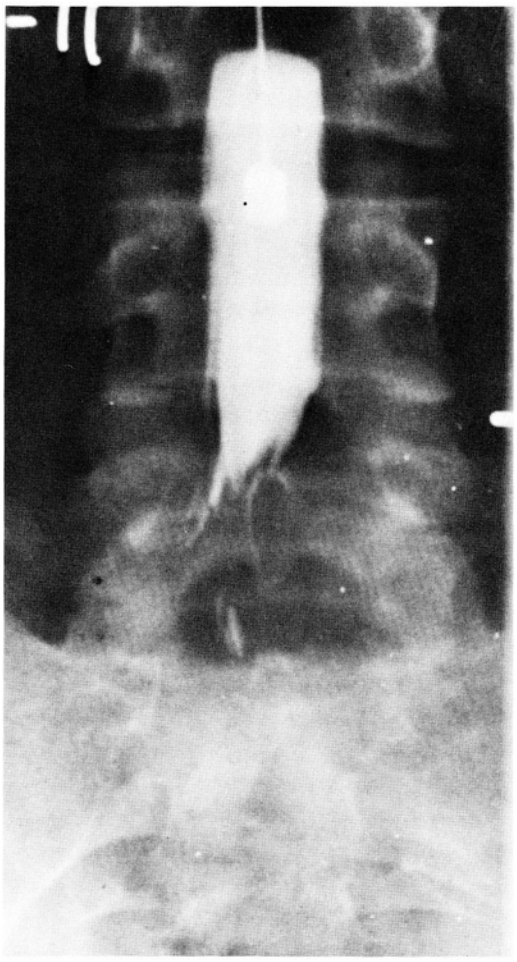


Fig. 1—Frontal projection of myelogram, typical of extradural effect with contrast material pushed to the right.

Dr. Taveras: The appearance in the frontal projection is typical of an extradural effect. That is, the column of contrast material is pushed to the right, and the diameter of the oil column as it approaches the defect becomes narrower. The roots are definitely displaced to the right. A small drop of pantopaque is seen to have gone beyond the block and has extended down to the lumbosacral junction. This drop of pantoqaque is also displaced to the right (Fig. 1).

In the lateral projection, the appearance is not particularly typical of any specific process. It simply demonstrates a block, which is not seen to involve the central or the dorsal sides specifically (Fig. 2). I cannot see any bone destruction, but there is demineralization of the left first sacral pedicle, and the posterior margin of the vertebral of L5 and S1 is somewhat less well-defined than the L4 and L3 vertebral bodies. However, this is a solarized copy, and the film was made for a myelogram and not a film made specially for bone detail.

Regarding the nature of the lesion, we are dealing with an epidural mass, which is in all likelihood a neoplasm. Among the lesions, we should also list a hematoma, in view of the history of trauma, and an abscess. Both of these lesions are unlikely. In this region, hematoma producing these findings would be most unusual without fracture, and an abscess would probably be more diffuse in its deformity of the pantopaque. This appears to be a rather well-defined mass situated on the left side, and aside from the apparent demineralization of the left sacral pedicle and slight loss of the cortical bone at the posterior margin of L5 and Sl, there is no evidence of bone destruction. I am assuming that these findings could be produced by pressure demineralization. A chordoma is a definite possibility in this region, but the absence of a clear

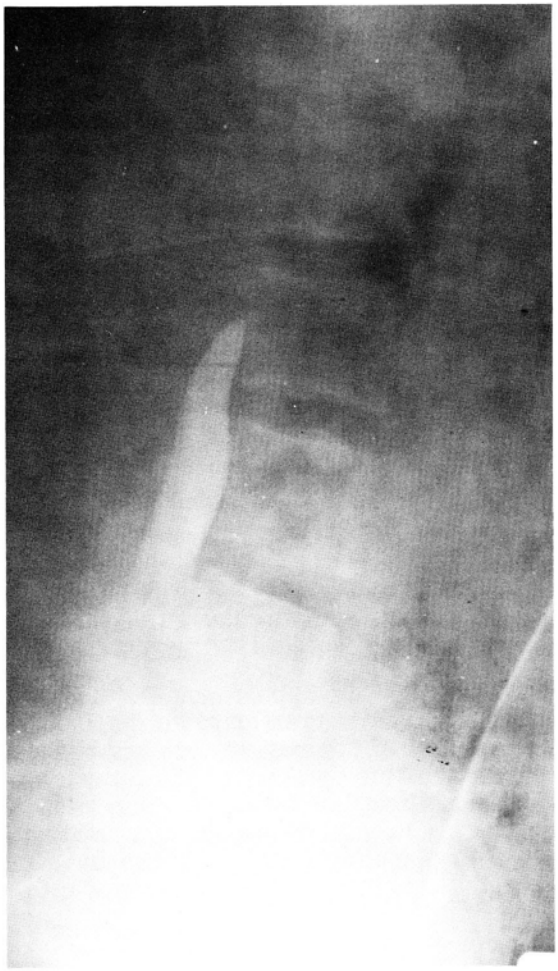


Fig. 2—Lateral projection showing block.

cut bone destruction is against this diagnosis. Among epidural neoplasm in a 16-year-old boy, I would list lymphoma reticulum cell sarcoma as the most likely one.

Dr. Taveras' Impression:

ROUND CELL TUMOR

Radiologic Impressions Submitted

Metastatic tumor	11
Malignant lymphoma	10
Hematoma	22
Ependymoma	8
Others	16

Dr. Taveras: The patient is 16 years old, and he could have had a primary tumor elsewhere. However, it would be wise not to call it metastatic at age 16 unless you knew the patient had neuroblastoma or something like that. Malignant lymphoma, a round cell tumor, is what I think would be the best diagnosis. I see no reason for diagnosing ependymoma, which is an intradural tumor; only rarely would you see extension extradurally, and that would usually be after surgical intervention. I have seen one instance of a patient with a lymph node in the groin that proved to be an ependymoma. Then we did a myelogram, and there was indeed an ependymoma. Such cases are very unusual.

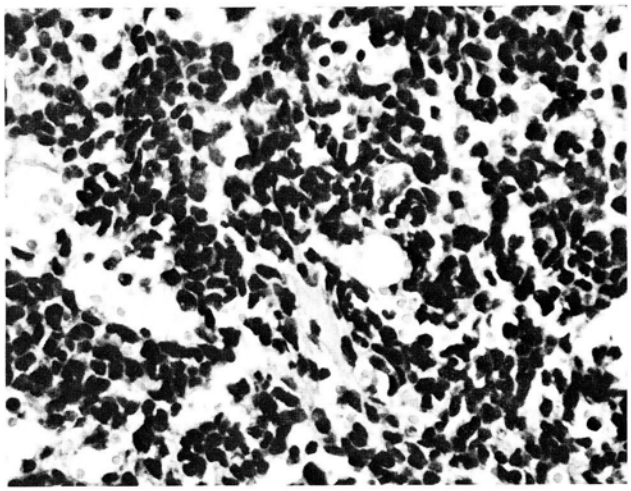


Fig. 3—Epidural spinal lymphosarcoma. The cells are remarkably similar to those of Case 14, figure 5. H and E stain; x450.

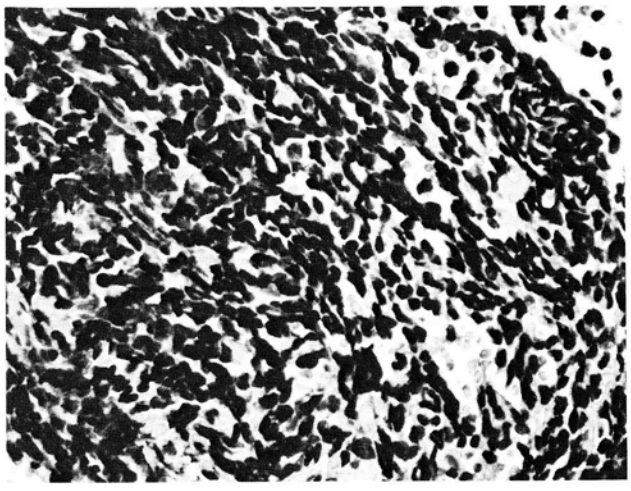
Dr. del Regato: Dr. Harold O. Peterson of Minneapolis recognized a large extradural mass and suggested a malignant lymphoma. Dr. Stephen Greenberg of Tampa was of the same point of view. Dr. August Rymut of Milwaukee offered ependymoma.

Operative Findings: On March 23rd, 1972 a laminectomy was done, and an extradural tumor was found. The removed pieces of tissue were hemorrhagic.

Dr. Zimmerman: The very small bit of tissue that we were asked to look at contains small cells that are round and malignant. This makes Dr. Taveras' diagnosis of a malignant small cell tumor correct.

The tumor is a lymphosarcoma (Fig. 3), but it could be a reticulum cell sarcoma. This differential diagnosis is difficult to make from the

Fig. 4—Same case as illustrated in figure 3 but showing artifactually elongated cells in tissue from spinal epidural space. H and E stain; x450.



tissue available for study. Most cells resemble lymphocytes that form a mass, a tumor, and many cells are in mitotic division. They fail to produce a distinctive histologic pattern. Such perhaps would be expected if, as some of you suggested, this tumor represented a medulloblastoma or a neuroblastoma. Under high magnification, the tumor is seen to be composed of the same type of cells as that present in the previous case (Case 14). The diagnosis in the present case is epidural spinal lymphosarcoma.

It is frequently difficult to determine the nature of the cells in a biopsy of tissue in the spinal epidural space because of artifact. The removal of such soft tissue by forceps that is employed to pull on the specimen results in an elongation of the tumor cells so that they resemble fibroblasts (Fig. 4). Under such conditions of specimen removal, there often results a diagnosis of sarcoma or even fibrosarcoma. The freshly teased specimen is placed in formalin, which fixes the artifact and baffles the pathologist.

Dr. Zimmerman's Diagnosis:

EPIDURAL MALIGNANT LYMPHOMA

Histopathologic Diagnoses Submitted:

Malignant lymphoma	15
Medulloblastoma	13
Hemangiosarcoma	7
Ewing's	6
Small cell sarcoma	6
Ependymoma	12
Others	5

Dr. Zimmerman: Malignant lymphoma is fine. I do not like medulloblastoma for the reasons mentioned, namely that these are intradural tumors and not epidural; following surgery, it is another story. I have yet to find a real medulloblastoma in the epidural space. I think hemangiosarcoma is suggested partly on the basis of this artifact, which I tried to emphasize. I do not like Ewing's sarcoma because I do not see the histological structure, but more importantly, I know of no Ewing's sarcoma without bony destruction. To diagnose a Ewing's sarcoma without bone involvement would be so out of my experience that I just could not do it. Small cell sarcoma is fine, and the same holds true for ependymoma. It is an intradural tumor and not epidural.

Dr. del Regato: Dr. W. J. Kirsch of St. Petersburg diagnosed extradural lymphoma. Dr. Leo Lowbeer of Tulsa offered angiosarcoma. Drs. Magda and J. Kepes preferred small cell tumor with seeding of medulloblastoma and suggested that Ewing's tumor should be ruled out. Dr. F. M. Enziger (A.F.I.P. account No. 1405491) made a diagnosis of malignant lymphoma compatible with soft tissue Ewing's.

Subsequent History: Radiotherapy was administered. A total dose of 5500 rads was received at the level of the spinal cord in 33 days.

On February 29th, 1976 I spoke to the patient's father. The youngster now weighs 250 pounds and was married six months ago.

Dr. Kjellberg: I think this case speaks for itself. The correct diagnosis was made by the correct means, and correct therapy was instituted. The patient is doing very well.

Dr. del Regato, I would like to thank you and the staff for this cancer seminar. I have certainly found it a pleasure and would like to express my gratitude for the privilege of participating.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