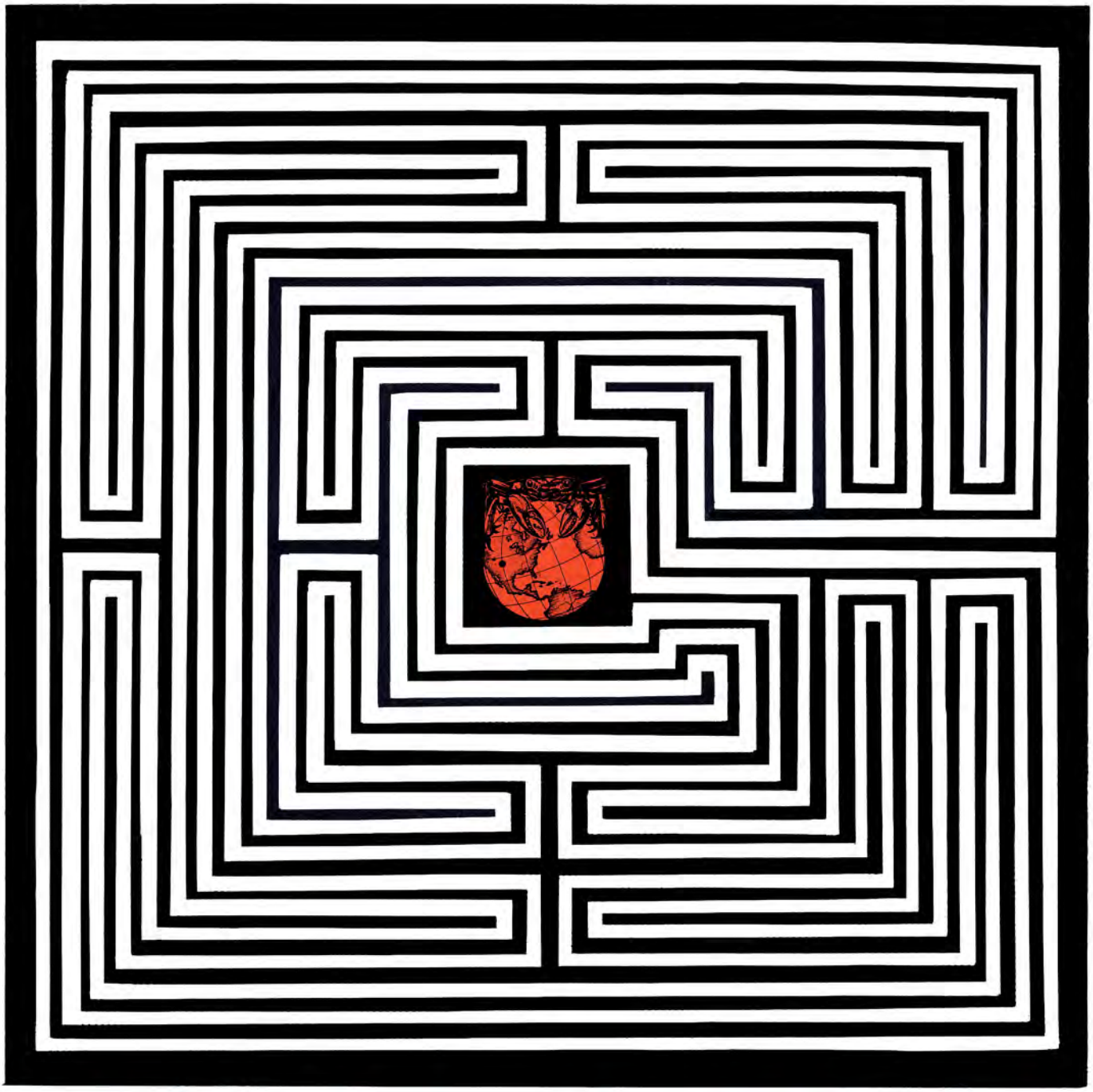

CANCER SEMINAR

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PENROSE CANCER HOSPITAL «» COLORADO SPRINGS, COLORADO

Sisters of Charity

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VOLUME FOUR AUGUST, 1969 NUMBER TWO

Juan A. del Regato, M.D., *Editor*

CONTENTS

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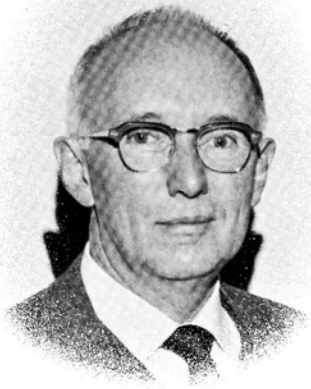
Manuel Viamonte, Jr., M. D.

Averill A. Liebow, M. D.



John L. Pool, M. D.

J. A. del Regato, M. D.

THORACIC TUMORS

This CANCER SEMINAR, on tumors of the lung and mediastinum, closed the second decade of annual seminars in Colorado Springs and their continued success among radiologists, pathologists and surgeons.

On this occasion, the participants in this educational exercise were rewarded by the perspicacity of one of this country's outstanding research radiodiagnosticians, Dr. Manuel Viamonte, Jr., Professor and Chairman, Department of Radiology, University of Miami School of Medicine. The discussions were highlighted by the didactic presentations of Dr. Averill A. Liebow, Professor and Chairman, Department of Pathology, University of California School of Medicine at San Diego. To Dr. Liebow, a widely recognized authority in pulmonary pathology, we owe also the care given to and the good quality of the photomicrographs and captions which illustrate this issue. Our third guest was Dr. John L. Pool, Attending Surgeon, Thoracic Service, Memorial Cancer Center, and Assistant Clinical Professor of Surgery, Cornell University Medical College, New York; his discussion of the cases revealed unusual insight and experience from which we all benefited.

The growing participation in this annual CANCER SEMINAR has made it more difficult each year to satisfy the demand for sets of slides by interested pathologists. We have done our best to provide most participants with sets, at least one such set for each group of participants in one institution. We are aware that we have not been always just or successful in our judgment. Those who attend the CANCER SEMINAR will find us desirous to make amends for past errors . . . we beg to be forgiven.

We wish to thank again all those who have contributed cases for study (the few cases chosen and the more numerous that were rejected) our guest speakers and all those who participated by mail or in person in the proceedings. Their contribution makes these annual events a most enjoyable experience.

J. A. del REGATO, M.D.
Colorado Springs, Colorado
August, 1969

1. *Thymoma*

Contributed by A. S. Blauw, M.D. Roswell, New Mexico

THE PATIENT was a 63-year old woman in October, 1967, when a routine roentgenogram revealed the presence of a mass in the right costophrenic angle; there were no symptoms. In 1960, she had had a "branchial cleft cyst" removed from the neck. There were no abnormalities on physical examination; the hemoglobin was 12.2 gm%, there were 7,200 white cells per mm3; the differential count was normal.

Dr. Viamonte: Frontal and lateral views of the chest reveal a 5x7.5x8 cm lobulated mass in the right paracardiac region. Calcium within the mass is not detected. The heart does not appear to be enlarged. The thoracic aorta is minimally dilated and tortuous. Segmental atelectasis is observed lateral and cephalad to the mass and is probably related to lung compression. The remainder of the lungs appears to be normal.

The mass has a lobulated outline in its cephalic and dorsal portion. This finding suggests an extracardiac tumor, probably non-cystic. The history of a removal of a branchial cleft cyst from the neck may suggest a possible relation of this mass to a pharyngeal pouch branchial abnormality. The thymus gland is derived embryologically from the third pharyngeal pouch on each side as are also the lower parathyroid glands. It migrates caudally into the anterior mediastinum. Occasionally, thymic tissue may not descend and remain in the neck. In other instances it may migrate further downward and reach the diaphragm. Thymomas may develop in ectopic thymic tissue in the neck because of failure to descend, low in the mediastinum close to the diaphragm because of too long a descent, or anywhere in the medastinum.

Solid masses of this size occupying the right cardiophrenic angle suggest the following possibilities: thymoma, teratoma, mesenchymal tumors (lipoma, fibroma, lymphangioma, hemangioma, chondroma), sarcoma, ectopic parathyroid tumor, lymphoma, hernia of abdominal content through a foramen of Morgagni and pericardial tumor.

Dr. Viamonte's impression: 1) THYMOMA, 2) MESEMCHYMAL TUMOR

Roetgenologic Impressions Submitted by Mail

Pericardial cyst	36
Lymphosarcoma	25
Thymoma	5
Mesothelioma	4
Others	16

Dr. Viamonte: A pericardial cyst was a good possibility; I ruled it out on the basis of the outline of the mass. Pericardial cysts usually have a curved contour, a rather well circumscribed demarcation. Lymphosarcoma is a possibility; thymoma was our first choice; I have never seen mesothelioma in this location but I gather that this can also be considered.

Dr. Regato: Dr. B. L. Pear, of Denver, also submitted an impression of thymoma; Dr. E. Salzman, of Denver, offered mesothelioma.

Operative findings: On October 10, 1967, a right thoracotomy was done. The right lung appeared normal but a mass 10 x 8 x 5 cm in diameter was found in the right cardiophrenic angle, with moderate adherence to the pericardium and with numerous blood vessels coursing the surface. On cross section the tumor was pink in color and it was contained in a soft fibrous capsule.

Dr. Liebow: The clue to the diagnosis of thymoma in this case lies in the presence of two cell types. The first consists of predominantly lymphocyte-like cells in large masses, among which are scattered larger cells with pale

Fig. 1—Mass in the right paracardiac area.

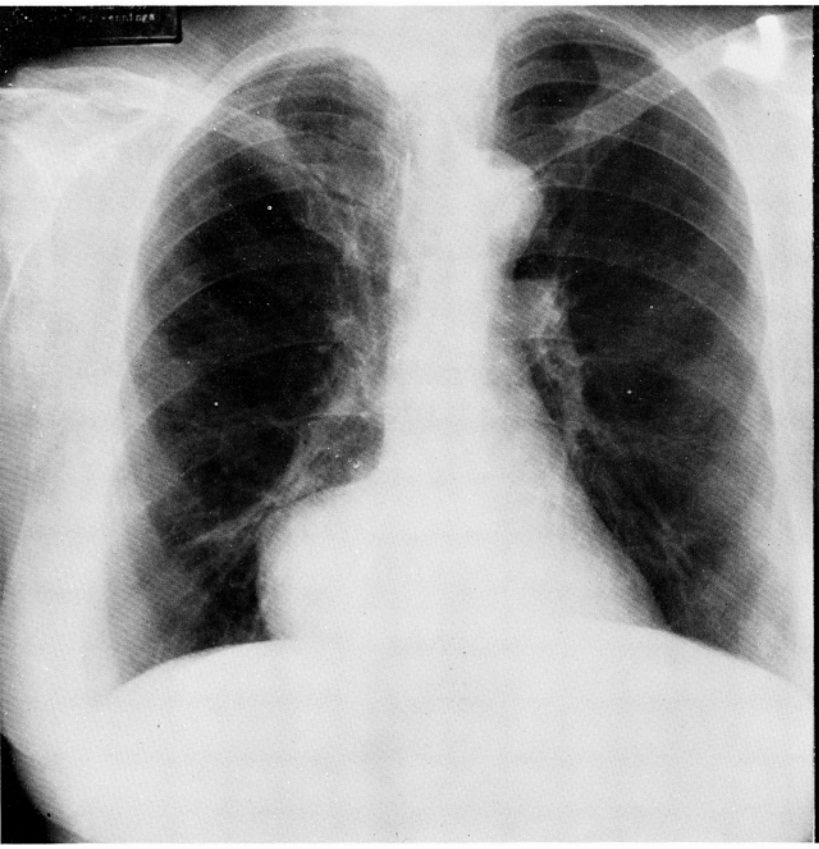
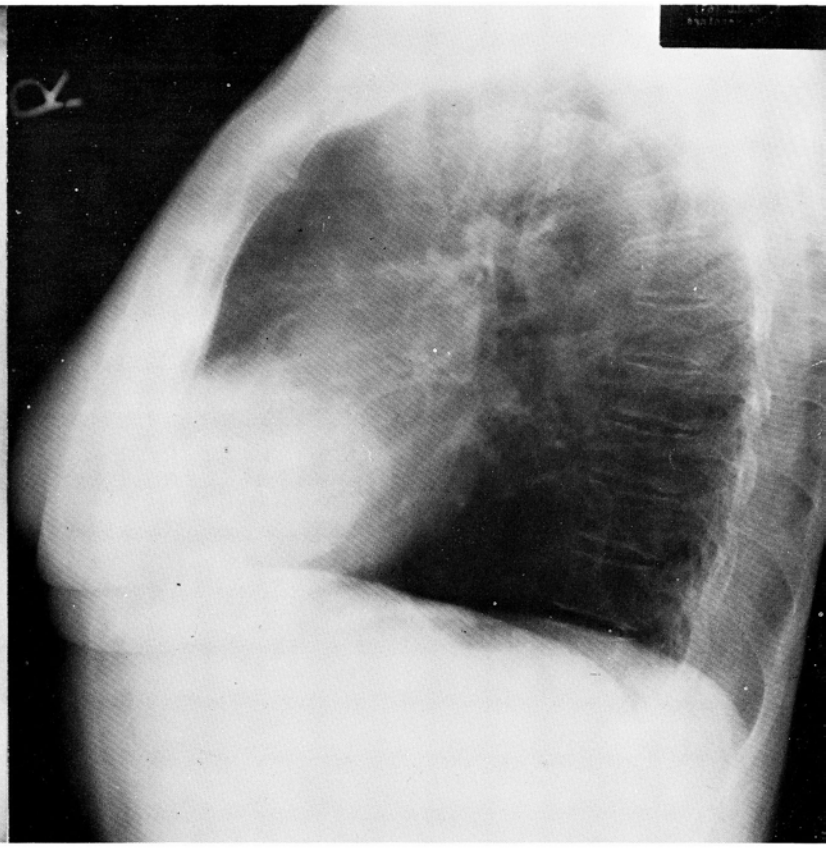


Fig. 2—Lateral view of the mass showing no calcifications.



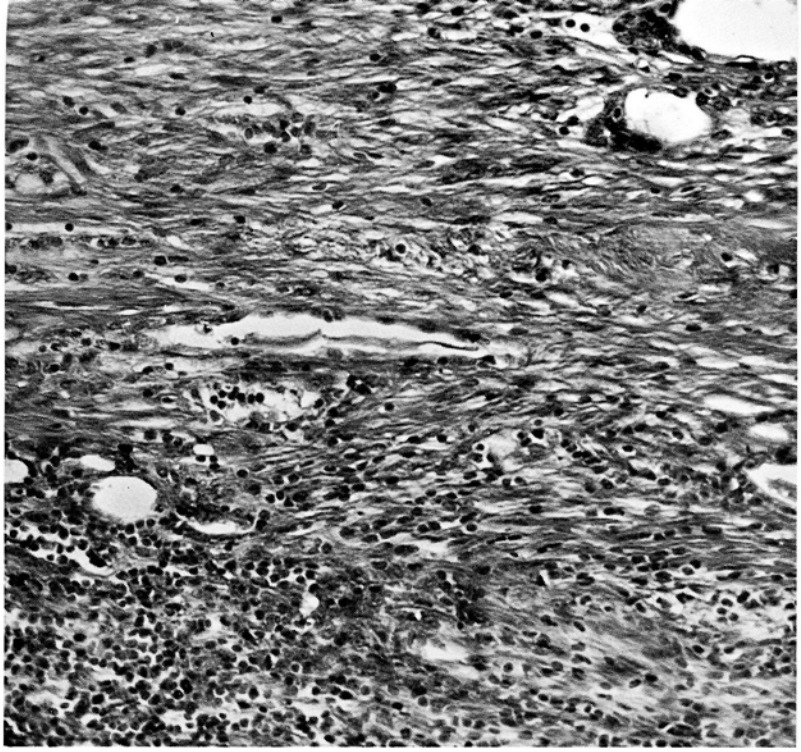


Fig. 3—Thymoma: In upper portion of the Photomicrograph, an epithelial-like component is dominant. Some of the "reticular epithelial cell" derivatives line spaces. In the lower portion of the photomicrograph, cells of lymphocytic type predominate (X 200).

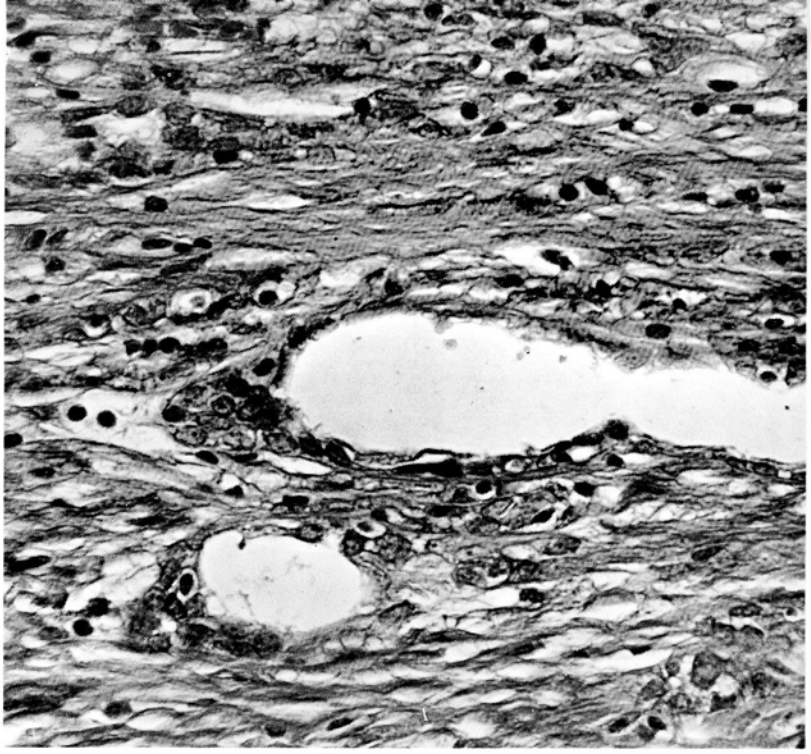


Fig. 4—Detail of reticular epithelial component (X 400).

cytoplasm and huge vesicular nuclei that contain prominent nucleoli. These are not Reed-Sternberg cells, however. Germinal centers are not present. The "starry sky" appearance somewhat resembles Burkitt's lymphoma. The second cell type consists of much larger, spindle-shaped cells, arranged in masses. Certain of these, having become somewhat taller and shorter, line oval spaces. There is no universal agreement on the nature of these cells. They are probably derived from what von Mollendorff called "reticular epithelial" cells. This extremely confusing term implies that the cells are of epithelial origin. There is no evidence, however, that they are related to the squamous epithelium of Hassall's corpuscles. Masses of cells of similar type can be seen condensed about Hassall's corpuscles in the atrophic thymus of persons past the age of forty. Some believe that these are either mesothelial or lymphangio-endothelial cells that become associated with the developing thymus as it reaches the thorax and extends into the anlagen or the pleural or pericardial cavities. This opinion is based on the presence of the spaces within such tumors that are lined by flattened cells resembling endothelium or mesothelium. (Hubbell and Liebow).

Thymic tumors with the structure of the present case represent the most common type of thymoma. Grossly they have a characteristic appearance in which the two types of tissue of which they are composed have a gross representation. The epithelial-like tissue is white or pale pink. It is prominent in the capsule and extends into the substance of the mass in the form of trabeculae, above which there project the darker tan or pink translucent masses of the lymphoid tissue. One or the other component may predominate in various tumors.

As in the present case, many of these tumors are entirely silent clinically, and many also occur in patients more than fifty years of age. As they enlarge, and presumably because of their weight, they tend to sink to positions far lower in the anterior mediastinum than that of the normal thymus gland, even close to the diaphragm as in the present case. As in the present case, they tend to extend partly over one or the other of the lung fields in the PA projection. The history of a branchial cleft cyst in this patient is of interest. The thymus is derived from the third bronchial pouch, and it is possible that these two conditions may have been related.

Myasthenia gravis is only rarely associated with thymomas of this characteristic type. In fact only 15% of persons with myasthenia gravis have actual thymic tumors, and then they are more likely to be composed of masses of large, pale, granular epithelial-like cells. Thirty percent of patients with myasthenia, however, have abnormalities of the thymus, usually consisting of hyperplasia and the presence of many germinal centers resembling those of ordinary lymphoid tissue. These are not present in the normal thymus.

Radiographically the present case presents one feature that may be helpful in differential diagnosis of tumors of the anterior mediastinum. This is the presence of one rather straight border that in certain projections gives the lesion a box-like appearance. Most other tumors tend to be rounded.

Dr. Liebow's diagnosis: THYMOMA

Histopathologic Diagnoses Submitted by Mail

Malignant lymphoma		106
lymphocytic	31	
lymphoblastic	18	
poorly differentiated	6	
Burkitt's	14	
reticulum-cell	3	
histiocytic	2	
well differentiated	2	
Hodgkin's	5	
Thymoma		14

Dr. Liebow: Most participants considered this to be a malignant lymphoma; I should like to stress two things: most lymphomas are not located in the anterior mediastinum and, particularly, not so low; secondly, there is here a double component of the epithelial-like plus the lymphocyte-like cells.

Dr. Regato: Dr. J. H. Coffey, of Fargo, offered a diagnosis of malignant lymphoma, lymphocytic type; Dr. T. H. McConnell, of Dallas, preferred lymphoblastic type; Dr. J. M. Woodruff, of Denver, saw it as poorly

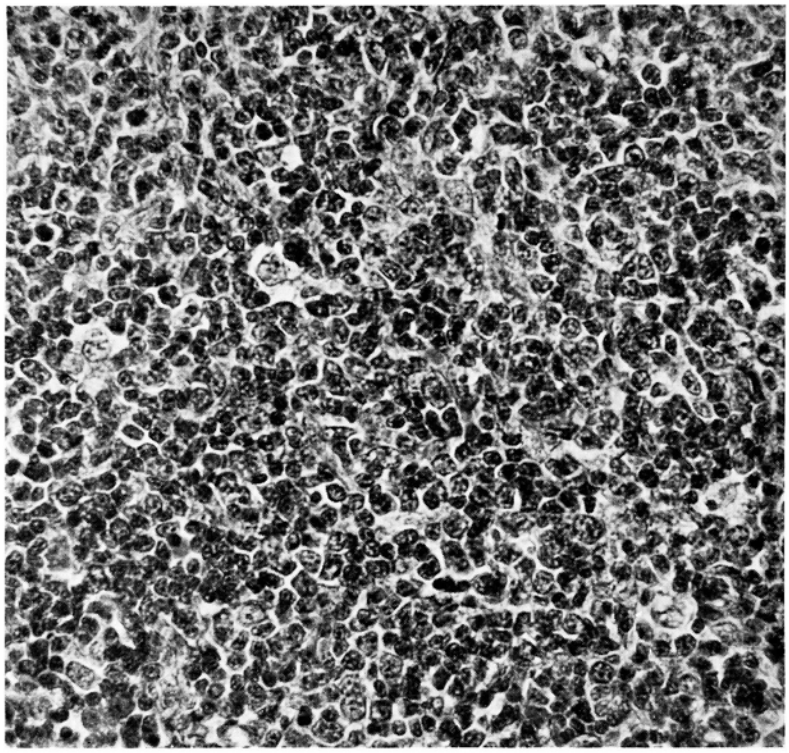


Fig. 5—Predominantly lymphocytic portion of the thymoma. The larger cells with relatively abundant cytoplasm are reticuloendothelial cells. Only a few mitoses are present (X 400).

differentiated, while Dr. J. B. Frerichs, of El Paso, considered it well differentiated; Dr. L. Lowbeer, of Tulsa, called it lympho-histiocytic. Dr. S. H. Choy, of San Francisco, diagnosed it as Burkitt's lymphoma. Dr. M. Wheelock, of Miami, preferred thymoma.

Subsequent history: The patient was interviewed in the last week of October, 1968. She is well except for mild asthma. She is working as a nurse.

Dr. Pool: In cases of this sort, while we lean heavily on our colleagues in radiology and pathology, we are the ones who have to make the final decision as to how to deal with such a patient and more particularly with the family. I would like to comment briefly on the diagnostic aspect. You could list thirty diagnoses that could simulate this radiographic view. For the surgeon it is quite important to know that the diagnosis of hernia through the foramen of Morgagni has been completely excluded before the operation, because you might want to approach the lesion through upper laparotomy. Now a word about thymoma: I notice that Dr. Liebow very carefully avoided an adjective, benign or malignant, in his discussion. Our pathologists will usually add such an adjective. We recently reviewed 53 thymic tumors of which 40 were thought to be malignant, 9 of these were totally removed at surgery and 7 survived beyond the five-year period, five beyond the ten-year period, without evidence of recurrence. Whereas only 4 of 31 in which the lesion could not be completely removed lived five years.

R.L. Annala, M.D., Ruidoso, New Mexico: I took care of this patient. We lost her to follow-up until approximately one week before this meeting. She sent a chest roentgenogram which I got yesterday; it is not unlike that which was shown; there is no evidence of tumor; the bony rib cage is normal, the heart and great vessels appear normal, with some tortuosity of the aorta. The lung fields show some moderate emphysematous changes.

Dr. Viamonte: Some thymomas may have some flattening seen in either the frontal or lateral projection. As far as a diagnosis of hernia through the foramen of Morgagni, a barium enema certainly would be helpful as would be also a diagnostic pneumopoeritoneum. If the omentum is the only one that herniates, it is pretty difficult to make sure what one is seeing.

Dr. Liebow: This is one of the benign forms, but it must be admitted that if it were not removed completely, it can recur. Ordinarily, this occurs not as a mass, but rather as a seeding upon the surfaces; this happens even in those that appear to be benign. However, only in the rarest instances do tumors of this sort invade into the lung and even more rarely do they extend below the diaphragm, even when they recur. Those that are obviously malignant histologically always raise the question as to whether or not we are dealing with a true lymphoma originating in an unusual position in the anterior mediastinum. The most common example is the so-called Lowenhaupt tumor which is an anterior mediastinal lesion that looks exactly like Hodgkin's disease, or is difficult to distinguish from Hodgkin's disease; it has a different history; it tends to maintain itself within the anterior mediastinum and then to extend upwards and downwards, but only rarely to extend in the ordinary manner of Hodgkin's disease. There is still a difference of opinion as to the true nature of that lesion.

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2. *Osteosarcoma (?) of the Atrium and Pulmonary Trunk Invading the Lung (Sarcomatosis?)*

Contributed by: T.H. McConnell, M.D., G. Noteboom, M.D. V. Stembridge, M.D., and J.C. Ogle, M.D. Dallas, Texas

THE PATIENT was a 53-year old woman in January, 1961, when she gave a history of recent progressive dyspnea and chest pain. Examination revealed the following signs: systolic murmur along the left sternal border, a split second sound and right ventricular hypertrophy. The EKG showed right axis deviation; the hemoglobin was 18.6 gm%; the platelets 130,000 per mm^3. The prothrombin time was 100%; clotting time was 7 min. 25 sec.

Dr. Viamonte: Frontal and lateral views of the chest reveal a 2.5 x 3 x 3.5 cm. spherical mass, with irregular contour, and uniformly calcified, in topography of the main pulmonary trunk. The heart does not appear to be

enlarged and has a normal configuration. The vasculature in the lower two-thirds of the right lung appears decreased. A semi-lunar calcification is observed at the level of the left pulmonary artery. Stippled calcifications are noted in the hilar regions and scattered through the medial aspect of the right lung.

The systolic murmur along the left sternal border and split second sound suggests the supravalvular location of this large mass. The physical findings suggesting right ventricular hypertrophy and the electrocardiographic demonstration of right axis deviation suggest the obstructing effects of this mass which probably occupies part of the lumen of the pulmonary trunk. The hemoglobin of 18.6 grams % in the absence of dehydration, of a right-to-left shunt, of a ventilation-perfusion imbalance, and of an erythrocytemic tumor (hypernephroma, cerebellar hemangioblastoma, uterine leiomyoma, ovarian, adrenal and liver tumors and benign nephropathies) suggest polycythemia vera.

Clinical manifestations of the disease appears most often between the ages of 40 and 60. The male to female ratio is 1.3 to 1 or 2 to 1. Most of the symptomatology is related to the increased blood volume, the associated vascular disease, and the tendency to hemorrhage and thrombosis. The most common clinical manifestations are referable to the cardiovascular system. Complaints such as dyspnea on exertion, ankle edema, angina pectoris, palpitations, and headaches are present in about two-thirds of the patients when first seen. The increased blood volume and viscosity place an added load on the heart with the result that enlargement of the heart, congestion, and thrombosis of the pulmonary vessels and evidence of cardiac decompensation may develop. The frequent occurence of thrombosis appears to be related to the presence of the vascular disease secondary to the increased blood viscosity, decreased blood flow and increased number of platelets. However, in this patient, the platelet count was only 130,000 mm^3. Platelet counts, however, may range from 100,000 to 1.5 millions per cubic mm. The incidence of thrombosis has been reported to be from 22% to as high as 40%. Thrombosis probably may occur in any vessel but appears to be most common in the coronary, cerebral, mesenteric, pulmonary, retinal, peripheral arteries of the leg, and portal veins.

A thrombus in any vessel of the blood, especially if present for a long time may calcify. Thrombosis of major pulmonary vessels may be compatible with a long survival. Angiocardiography could have confirmed our diagnostic impression. Other possibilities of a calcification in this region would be: 1) Calcified adenopathy. 2) Calcified cardiac tumor. They can be ruled out by the appearance of the mass, the probably associated calcification in the left pulmonary artery, and by the clincial history.

Dr. Viamonte's impression: OSSIFIED THROMBUS IN PULMONARY TRUNK

Roentgenologic Impressions Submitted by Mail

Hamartoma	28
Osteoma	25
Calcified thrombus	18
Calcified tumor	13
A-V malformation	6
Osteosarcoma	4
Others	7

Dr. Viamonte: I have never seen a hamartoma in this location and I would not think of that diagnosis; this very heavily calcified mass would be against the possibility of non-calcific type of hamartoma excepting perhaps the so-called hamartochondromas. Osteoma and calcified thrombus or osteosarcoma are all possibilities. This is a very heavily calcified tumor and it may well have bone within it. I doubt that one would get an AV malformation at this location. The topography of the lesion is in the pulmonary trunk; it may be related to the heart but it is above the pulmonary valve and in the pulmonary trunk.

Fig. 1—Frontal roentgenogram showing calcified lesion over pulmonary trunk.

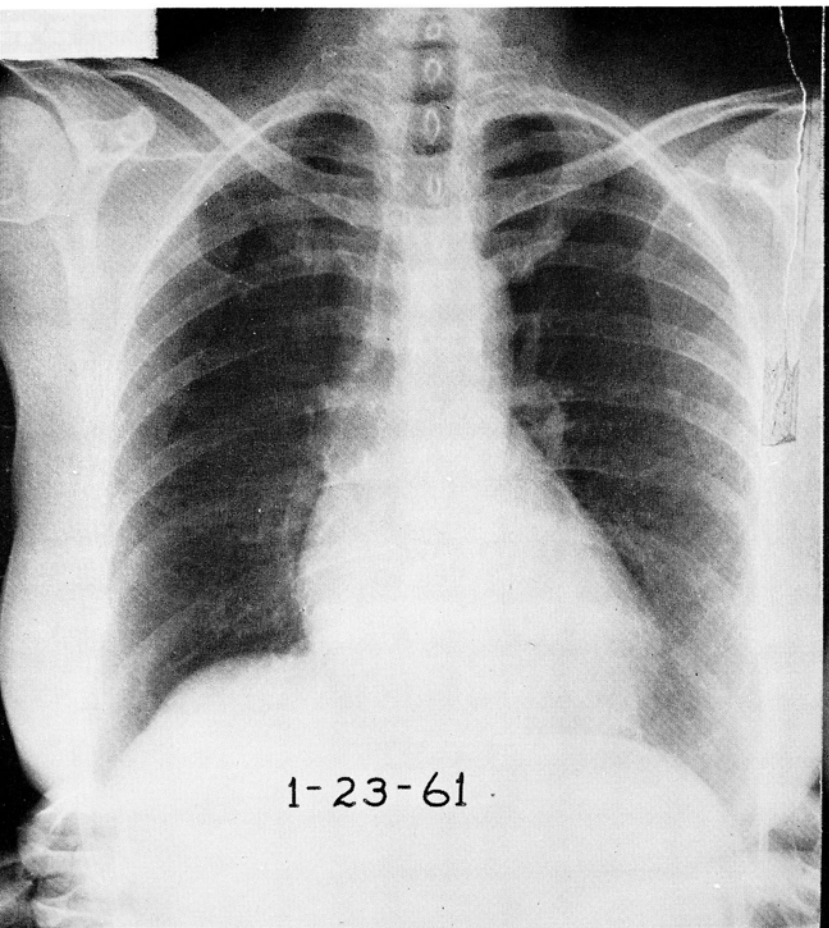
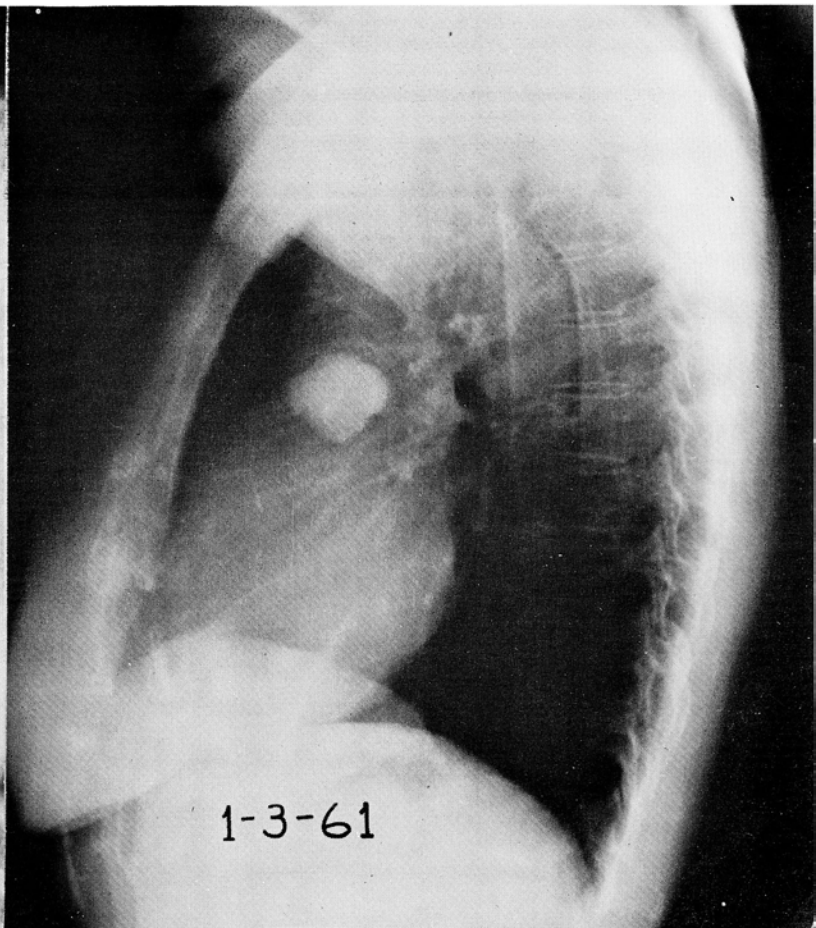


Fig. 2—Lateral view of calcified mass in January, 1961.



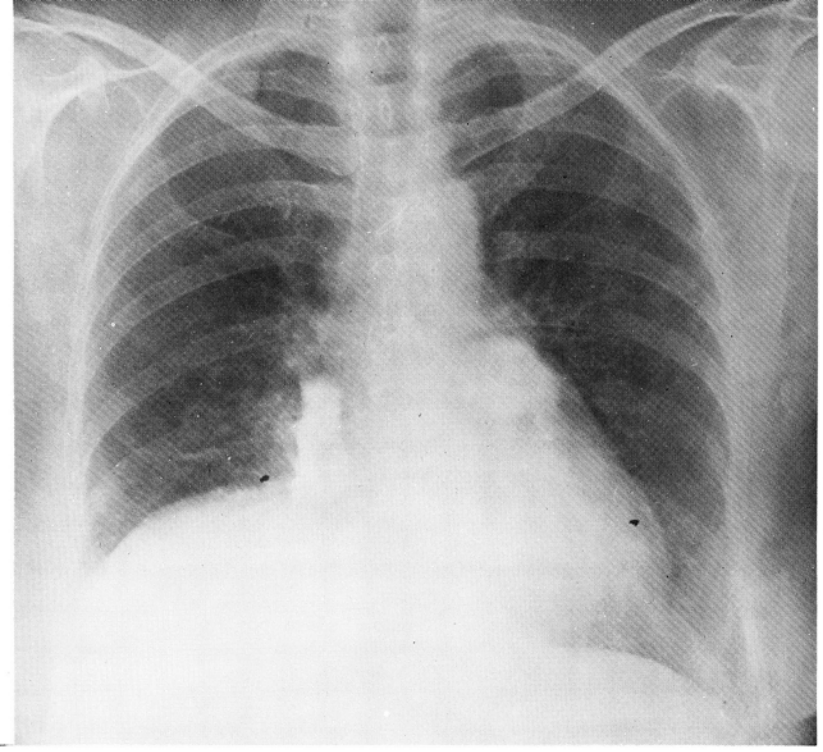


Fig. 3—Frontal roentgenogram, in September, 1962 showing calcified foci of recurrence.

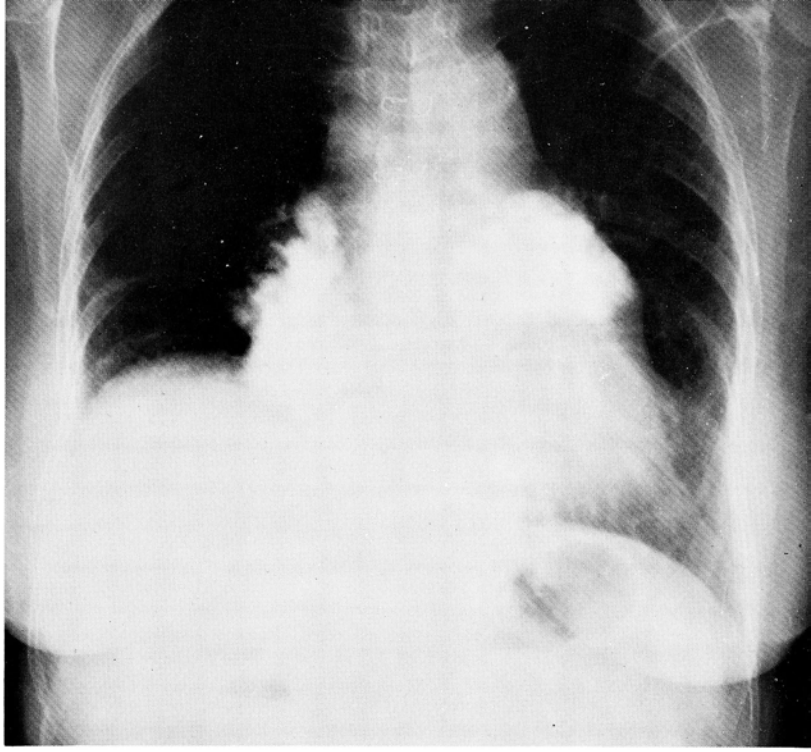


Fig. 4—Increased calcification in July, 1963.

Dr. Regato: Dr. M. Daves, of Denver, and Dr. P.J. Hodes, of Philadelphia, also offered calcified pulmonary artery thrombus.

Operative findings: On February 1, 1961, a thoracotomy was performed. An almost entirely calcified tumor was found in the main pulmonary artery extending into the right pulmonary artery. Sharp dissection was needed to separate the tumor from the artery; a portion of the pulmonary valve was sacrificed.

Dr. Liebow: The histological structure of the tumor corresponds to that of a typical bone. There appears no evidence of malignancy. It involves the adventitia of the pulmonary artery, but without destruction of the media. In many places it is separated from the latter by a homogeneous hyaline material. This does not have the appearance of amyloid when examined under polarized light, nor does it give a positive Congo red reaction. It is therefore considered to be simply hyalinized connective tissue. On one aspect the tumor extends to, but does not invade, regularly arranged, striated myocardial muscle fibers, that from their thinness and strap-like appearance suggest tissue of the atrium. In some places the tumor is separated from this muscle by a layer of osteoid tissue.

Various possibilities for the orgin of bone within various tissues should be considered. Ossification of amyloid, which can occur in various locations, including the lung, is not supported by the evidence in the present case. There are no signs that the lesion was originally a granuloma, although in such lesions there can take place not only calcification but also ossification, and there are also no elements to indicate that the osteoma is part of a teratomatous lesion. The best conclusion, therefore, appears to be that the tumor arose by transformation of connective tissue.

From the clinical point of view it is most difficult to explain the patient's polycythemia. Even if there had been restricted inflow into the vascular bed of the lung, as suggested by both clinical and electrocardiographic signs of right heart strain, there should be no significant degree of desaturation of the blood.

Dr. Liebow's dignosis: OSTEOMA, involving atrium of the heart.

Histopathologic Diagnoses Submitted by Mail

Osteoma	37
Osseous metaplasia, ossification, calcifcation, ectopic bone	69
Hamartoma	18
Osteosarcoma	5
Choristoma	3
Others	9

Dr. Liebow: Osseous metaplasia was considered by most and the various mechanisms of this have been discussed, osteoma by many and hamartoma only by few. If one looks into the original article, written by Albrecht in 1904, the term hamartoma had a different use than it has now. Albrecht said that all the benign lesions were hamartomas in the sense that they represented an embryonic rest which then proliferated as if the Creator, in making an organ, had a little bit of tissue left over and dabbed it onto the lung. This was his idea about all benign tumors. Since then the term has been limited to structures which are complex and which might represent an embryonic rest although the evidence of a true embryonic origin is just as poor as it is for a benign tumor. In the more limited sense, lesions which are composed largely of cartilage but with bronchial intrusions, sometimes fat and sometimes bone formation commonly in the periphery of the lung, have this term applied to them. I have never seen one in the mediastinum. "Choristoma" seems inappropriate here, since there is no sign that the tumor represents a mixture of "complex elements of varying histological structure of an organ or tissue in an ectopic location".

Dr. Regato: Dr. J. Rosai, of St. Louis, proposed ossified hamartoma. Dr. D. Mulkey, of Denver, preferred organizing thrombus. Dr. R.D. Schultz, of Sioux Falls, offered benign ossification.

Sections of this lesion were examined at the Armed Forces Institute of Pathology (accession 1138847); Dr. William C. Manion wrote: "It is our opinion that this is a

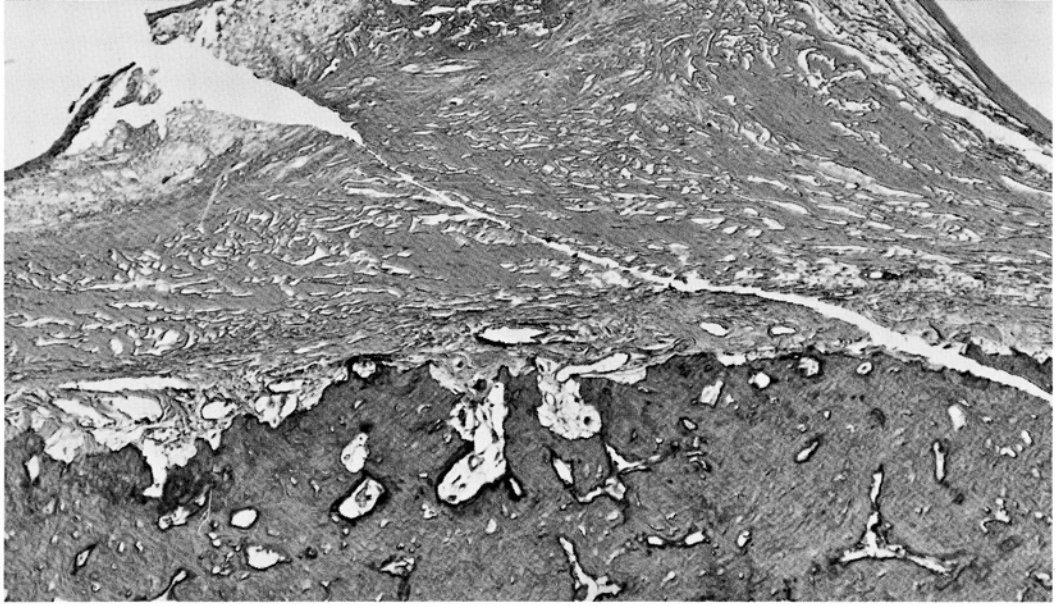


Fig. 5—Osteoma of mediastinal connective tissue: Hyaline, almost acellular tissue, intrudes between pulmonary artery (at the right), and the right atrium. At bottom of the photomicrograph, there is well differentiated osseous tissue (X 200).

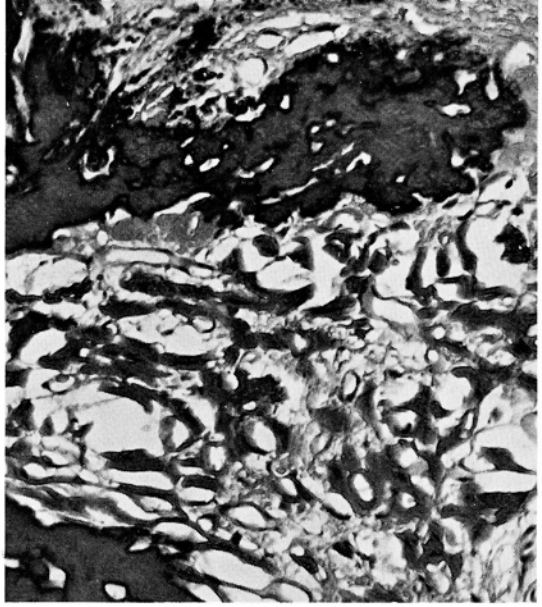


Fig. 6—Hyaline connective tissue, osteoid and atypical bone (X 400).

fibrosarcoma with metaplastic bone . . . The orthopedic branch suspects that this is metaplastic bone produced by cells that normally form elastica, hence an 'ossifying elastoma' . . . The cellular areas look like fibroblasts . . . It is not unusual to find small areas of osseous metaplasia or calcification in tumors arising in the pulmonary valve area".

Subsequent history: The patient recovered postoperatively and appeared well in June, 1962, one year after operation, when she was admitted for a cholecystectomy; the roentgenogram of the chest revealed a 2.5 cm calcified mass at the angle of the right atrium. In July, 1963, the lesion had progressed and produced chest pains and heart failure; a thoracotomy was done to remove the large recurrent calcified tumor but this could not be carried out. In May, 1965, the patient expired. The pulmonary artery, the aorta and the vena cava were found incorporated and constricted within the tumor; an arm of the tumor extended to the pleural space and liver.

Autopsy sections were again sent to the A.F.I.P. and Dr. William C. Manion wrote: "Our experiences with tumors of this site have revealed the tendency to form both cartilage and bone and all the other cases that we have seen have turned out eventually to be malignant. We would agree . . . now that from the findings in the lung, the diagnosis of osteogenic sarcoma was most likely".

Dr. Pool: I would like to say a word about the most common intracavitary tumor of the heart; namely, the myxomatous group of tumors which may be fibromyxomatous or lipomyxomatous. These, of course, are most prominent in the left atrium and then right atrium but can occur in the ventricle and can be attached in such a way as to pass through the pulmonary valve. They can also be multiple. I tried to find out whether such lesions have ever been reported as showing any calcification and I could find no such report.

T. H. McConnell, M.D., Dallas, Texas: When we first saw this tumor it was diagnosed as an organizing thrombus with osseous prosoplasia. We sent the slides to the Armed Forces Institute of Pathology; Dr. Manion's opinion was that this was a fibrosarcoma with osseous metaplasia. This patient expired; the tissue which has been submitted for everyone's consideration is autopsy tissue and I am sorry that it does not demonstrate the more aggressive areas of this tumor. We sent autopsy tissue to the A.F.I.P. Their opinion is that this is an osteosarcoma.

Dr. Regato: Dr. McConnell, Dr. Berthrong had seen some of the original material that you submitted. We thought that it would be best to submit to this large audience the tissue from an area close to the origin rather than that in which it appears in the lung.

M. Berthrong, M.D., Colorado Springs, Colo.: I knew we would catch hell for this one. We picked the block from the autopsy material that represented best the lesion as it was in 1961. It seemed hardly fair to show slides of a peripheral lung lesion together with that roentgenogram. The extension into the peripheral lung of a highly undifferentiated osteogenic sarcoma was present in the autopsy material.

Dr. McConnell: I might add that I found several cases in the literature of roughly similar neoplasma occurring in the same area with bone formation.

Dr. Viamonte: I was puzzled by the polycythemia and I thought it would be nice to relate the 18.2 gms% of hemoglobin, the decreased vascularity and the calcification. Could any explanation be given for the polycythemia of the patient?

Dr. McConnell: We are unable to explain it.

Dr. Viamonte: In the *British Journal of Radiology*, 1966, there is an article where calcification of tumor thrombus of the left pulmonary artery was described secondary to metastatic renal carcinoma; thrombi may calcify but apparently metastasize also. I wonder how we got some tumor in the right atrium when apparently the primary site was in a pulmonary vessel.

Dr. Liebow: There are interesting conditions in the lungs, which I like to call "*sarcomatosis*", which seem to follow the branches of the pulmonary artery and also the bronchial tree. I don't know why, it is a very puzzling thing. We must have seven to ten of these. They seem to extend directly along the walls of these structures as if some stimulus were gradually converting the tissue to what is rapidly proliferating and quite clearly malignant. Sometimes it looks like chondrosarcoma; sometimes like an ordinary fibrosarcoma.

Dr. Regato: In all fairness to you, Dr. Liebow and also to Dr. Berthrong, the fact was that some of the blocks that had been submitted by Dr. McConnell showed the tumor within lung tissue; this would have given away the diagnosis.

L. Lowbeer, Tulsa, Okla.: Is this supposed to be a primary extraskeletal osteosarcoma? Or has an attempt been made for a skeletal survey to find out if there is a primary tumor somewhere? If this turned out to be an osteosarcoma it is not really surprising because there are a number of instances in which in some areas the metastasis or the primary tumor is extraordinarily acellular. Several years ago a case was presented in this seminar which was diagnosed as a meleorheostosis but later turned out to be a multicentric osteosarcoma and was so published in England. In cases of this type, there are areas of extraordinary acellularity or complete absence of cells with osteosclerosis but next to it in other areas there are portions of extreme cellularity.

Dr. Regato: Dr. Lowbeer is right; a case diagnosed here as a case of meleorheostosis was later published in England as a case of multicentric osteosarcoma; they are entitled to their opinion but nothing is final. Information that I have from Dr. McConnell is that one arm of the tumor extended into the pleural space and to the liver, but he didn't say clearly whether there were significant isolated metastases from the tumor.

Dr. McConnell: When this tumor was first diagnosed, an extensive roentgenologic search for another lesion was carried out and none was located. At the time of autopsy, the entire neoplasm was contiguous. There were no metastases. The tumor was a locally invasive one which had incorporated all of the mediastinal contents, had invaded through the diaphragm and was invading the liver but there were no lymphatic or hematogenous metastases.

Dr. Regato: The point being that if there are metastases you do not need a pathologist to know that it is malignant. It is when there is no metastases that you need him.

Dr. Liebow: In view of the histological structure represented in the available material, the subsequent course is indeed surprising, even though the progress of the lesion was slow. The subsequent course suggests that this tumor should be considered one of the "sarcomatoses" that can involve the lung and associated structures. These can be derived from undifferentiated connective tissue, or cartilage, or smooth muscle. They seem to extend along the broncho-arterial rays and perivenous tissues in the septa, more or less in continuity with involvement of both lungs to which, however, they can remain confined.

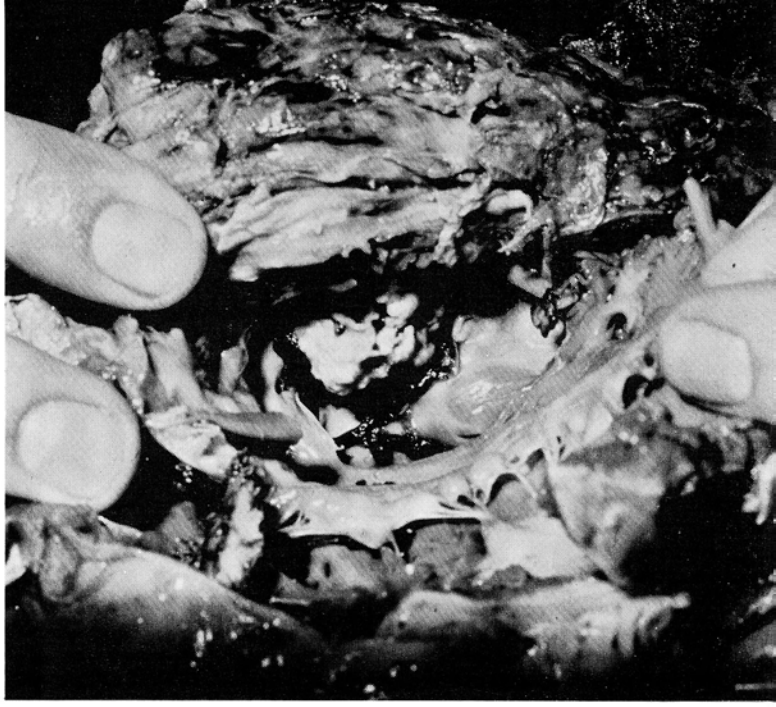


Fig. 7—Post mortem view of intravascular calcified mass.

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3. *Malignant Mesothelioma of the Mediastinum*

Contributed by Mark C. Wheelock, M.D., Miami, Florida

THE PATIENT was an 18-year old girl in July, 1966, when she gave a history of chest pains, cough, expectoration and loss of 20 pounds in weight over a period of 12 months. Examination revealed a short systolic murmur at the left cardiac border, a triple cardiac rhythm and a split second sound at the pulmonic valve. The EKG showed a T-wave inversion and non-specific ST-T wave changes in the precordial leads.

Dr. Viamonte: Frontal and lateral views of the chest of this teenager reveal an extensive mediastinal tumor surrounding the heart and great vessels and occupying the anterior-superior mediastinum. The slight posterior esophageal displacement may be related to the invasion of the middle mediastinum or to posterior displacement of the middle mediastinal structures by the large mediastinal tumor. There is a left pleural effusion and hypovascularity of the right upper lobe.

Cardiomegaly and pericardial effusion can be ruled out because the widening of the mediastinum extends cephalad and lateral to the aortic knob, (beyond the plane of the pericardial attachment). Also, the shadow of the left pulmonary artery appears to be medial to the lateral border of the mediastinal shadow (hilus overlay sign).

Tumors surrounding the heart and occupying the anterior mediastinum in this age group are usually: 1) Thymoma. 2) Lymphoma. 3) Metastatic carcinoma. The hypovascularity of the right upper lobe suggests the possibility of embolic occlusion of pulmonary arterial branches.

The most important clinical manifestation of cardiac metastasis are progressive intractable heart failure, dyspnea, anginal pain, cardiac murmurs (particularly if they change in nature), arrhythnia, bundle branch block, obstruction to the orifice of the great veins and pericardial effusion. The latter occurs in 1/3 of metastatic tumors affecting the heart and is often bloody. Embolism may occur from tumors involving the endocardium. With the possible exception of malignant melanoma, no particular type of malignant tumor seems to tend to preferentially metastasize to the heart. Of the group of carcinomas, those of the breast, lung, and stomach most commonly produced metastasis to the heart.

The radiographic findings, the clinical history suggesting implantation, extension, invasion, and penetration of the heart and neighboring structures and the patient's age should make us suspect a malignant thymoma, or a lymphoma. An angiocardiographic study is most informative in this type of situation.

Dr. Viamonte's impression: 1)MALIGNANT THYMOMA, 2) LYMPHOMA (sic)

Roentgenologic Impressions Submitted by Mail

Rhabdomyosarcoma	25
"Lymphoma" (sic)	9
Malignant thymoma	5
Cardiac tumor	4
Mycotic pneumonia	3
Others	30

Fig. 1—Anterior Mediastinal mass surrounding heart with left pleural effusion.

Dr. Viamonte: I have never seen a rhabdomyosarcoma creeping above the brachiocephalic arteries. They usually are confined to the heart. They may invade the pericardium; the fact that this tumor is extending into the superior mediastinum would make me consider this an unlikely possibility. In this case, there was a decreased vascularity in the right lung, indicating that there is a decrease in pulmonary blood flow suggesting an embolic component. Widening of the mediastinum with decreased pulmonary vasculature would suggest the possibility of a mediastinal tumor that has invaded the heart with tumor emboli or thrombi that cause the decreased vasculature.

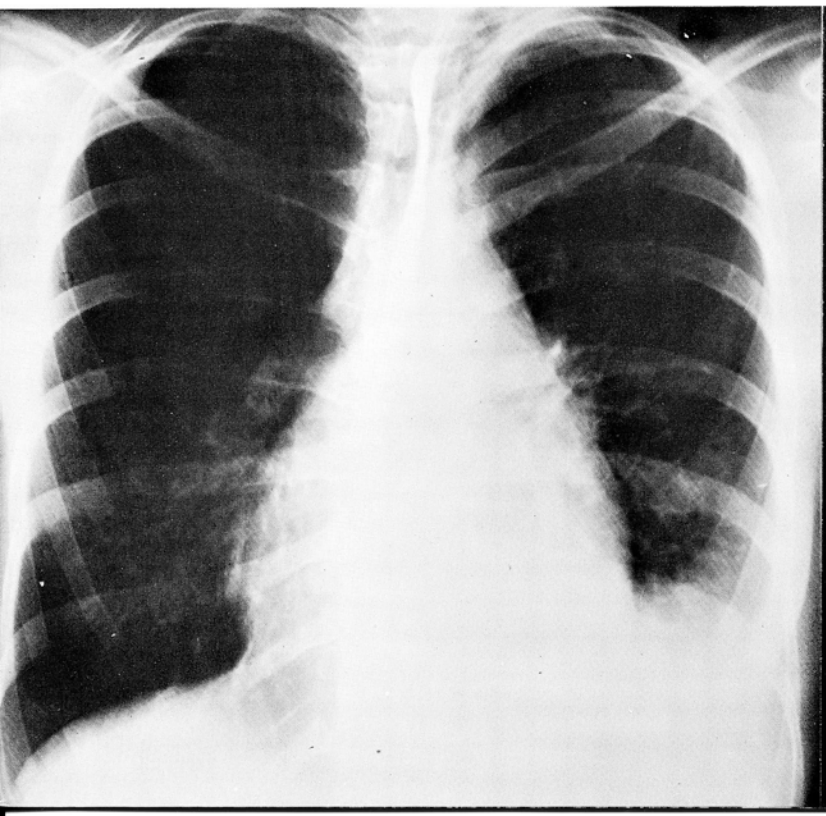
Dr. Regato: Dr. C. H. Taggart, of Colorado Springs, offered calcified atrial myxoma; Dr. L.O. Martinez, of Miami, preferred malignant thymoma.

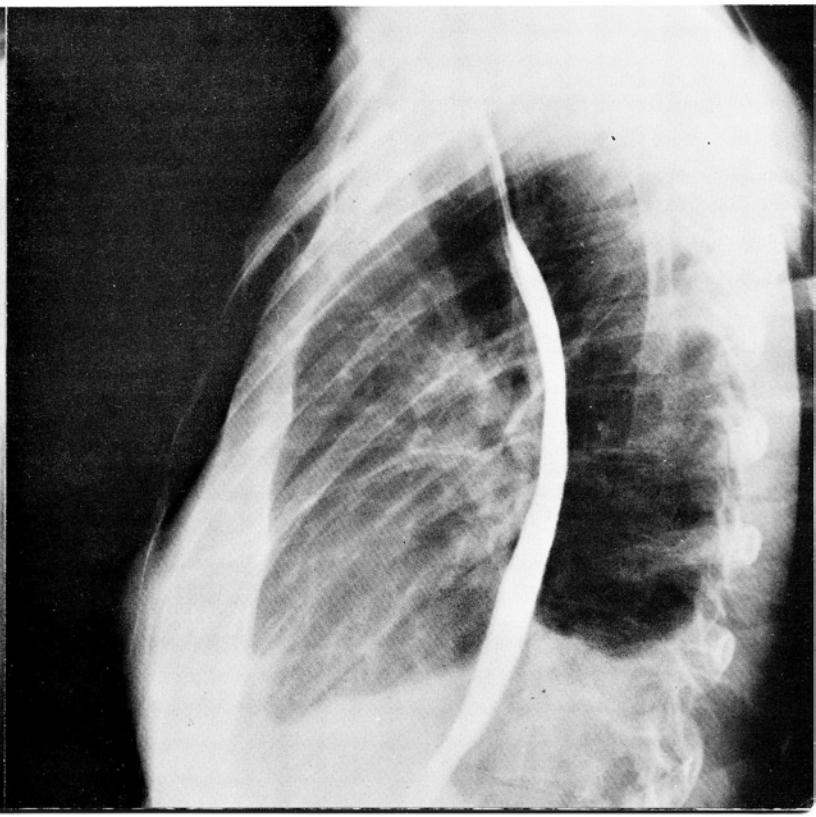
Subsequent history: The patient developed a sudden pain in the left leg followed by progressive respiratory distress and evidence of cardiac failure. In spite of medical measures the patient expired on July 27, 1966. At autopsy, the trachea, the bronchial bifurcation, the aortic arch and the efferent vessels were found matted in a fibrous mediastinal mass which extended to the sternum. The atrial septum was infiltrated by the fibrous tissue; the right ventricle was enlarged. The lungs showed marked passive congestion, focal hemorrhagic infarcts and organizing thrombo-emboli; the liver showed lobular hyperhemia. The thyroid, pancreas, spleen, kidneys, adrenals and bone marrow were found normal.

Dr. Liebow: A tumor composed of rounded or spindle-shaped cells invariably present difficulties or uncertainties in interpretation, and therefore a variety of diagnoses. In the present case the bulk of evidence suggests that the lesion is a mesothelioma.

While some other cells appear rounded, and thus suggestive of lymphosarcoma, it is quite possible that these represent spindle-shaped elements that have been transected. In certain fields in the parietal body wall there are foci where true lymphocytes have accummulated about lymphatics. It is evident here that the cells of the tumor are considerably larger, and have coarser, more reticular nuclear structure. The presence of sharply de-

Fig. 2—Slight posterior esophageal displacement.





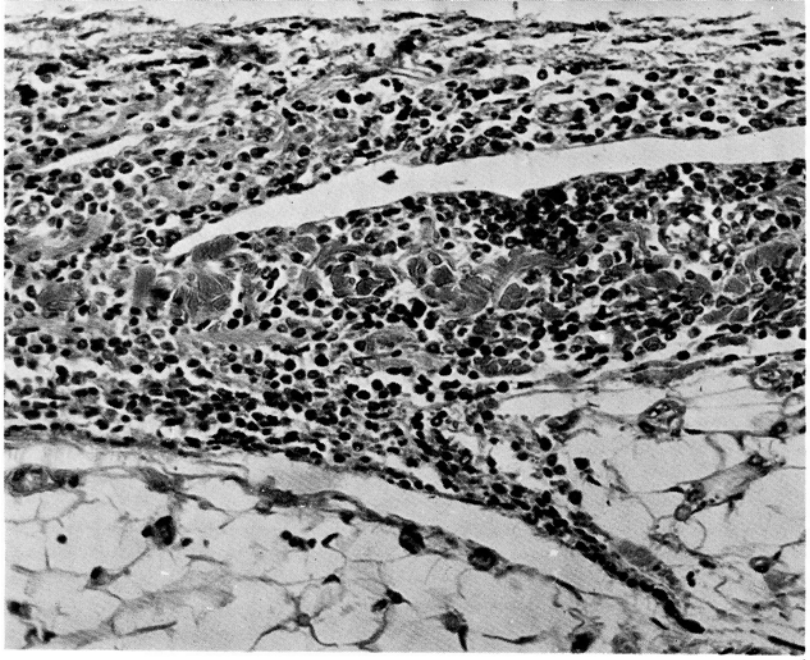


Fig. 3—Mesothelioma: Portion of pleural space lined by flattened cells. Similar cells but of more rounded shape lie deeper within the parietal pleura and extra-pleural tissue (below). These cells are larger than the lymphocytes which are also present (X 200).

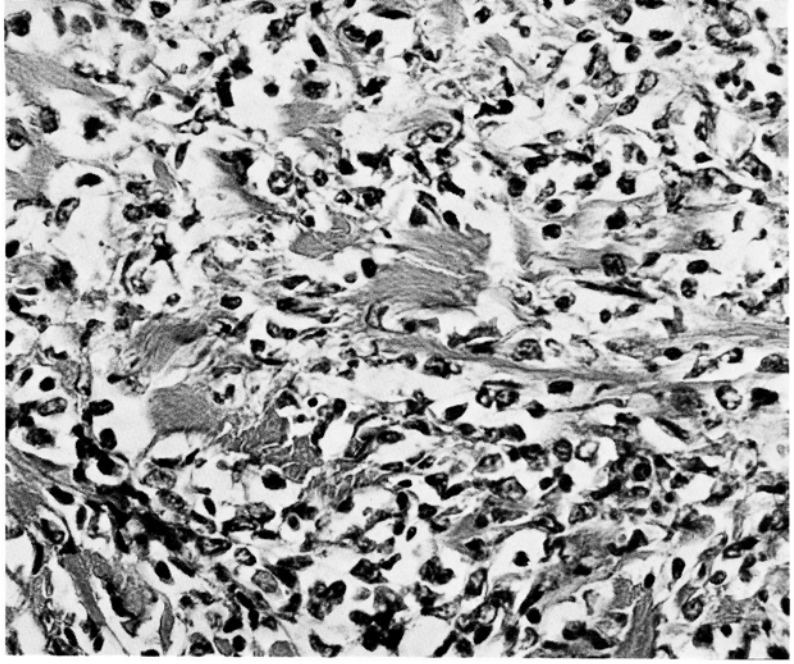


Fig. 4—Larger spindle shaped and rounded cells of the mesothelioma within the clefts of hyalinized tissue (X 400).

lineated masses of hyaline connective tissue that occur in irregular bands is entirely compatible with what is found in many mesotheliomas, particularly those of fibrous type. Most suggestive that the lesion is a mesothelioma is the presence of spaces among masses of cells that probably represent residual isolated parts of the original pleural cavity. Where the actual pleural surface is preserved, it appears that the lining cells of the pleural space are closely similar to those that compose the cell masses of the tumor. The fact that only material in close relation to the trabeculae of fibrous connective tissue stains with Alcian is somewhat against the diagnosis of mesothelioma.

Malignant diffuse mesotheliomas in their most characteristic form have both spindle-shaped and epithelial-like components. In the present case the former are predominant. The arrangement of reticulum is haphazard, and while individual cells are enveloped in some fields, compacted bundles often are surrounded by reticulum fibers. Against the diagnosis of reticulum cell sarcoma are the sharply defined, collagenous bands. Rhabdomyoblastoma is more difficult to distinguish, since such hyaline masses can be found in these tumors. This is a reasonable possibility, especially if the wall of the heart is involved. We have encountered three such cases arising in the right atrium in which the bulk of the tumor lay within the substance of that chamber with involvement of adjacent pericardium, which became fused into a single mass. There was evidence of diffuse seeding of the lung, with miliary hemorrhagic metastases and sanguineous pleural effusions. Against this diagnosis, however, is not only the presence of spaces within the tumor, but also the similarity to the pleural lining cells.

Dr. Liebow's dignosis: RETICULUM-CELL SARCOMA

Histopathologic Diagnoses Submitted by Mail

Leukemic infiltrate	37
granulocytic	21
Reticulum-cell sarcoma	21
Malignant lymphoma	20
Embryonal rhabdomyosarcoma	17
Mesothelioma	15
Others	21

Dr. Liebow: I would consider this to be a tumor with granulocytic infiltrate. I do not see any evidence of granules in these cells, to suggest a granulocytic origin. The main thing against a reticulum cell sarcoma was the fact that mitoses are so few and likewise for malignant lymphoma of another kind. Rhabdomyosarcoma is a very good consideration, particularly in a young patient; mesothelioma should be the first to be considered from the point of view of pathology. It should be stated that this patient is much younger than most individuals with pleural mesothelioma. The electrocardiographic changes might be related to involvement of the myocardium.

Dr. Regato: Dr. D. Dawson, of Colorado Springs, offered a diagnosis of reticulum-cell sarcoma. Dr. P.B. Visconti, of Denver, called it a case of acute granulocytic leukemia. D. P.C. Dyke, of Denver, preferred embryonal rhabdomyosarcoma. Dr. K.R. Holloman, also of Denver, offered mesothelioma. Sister Joseph Ignatius, of Cincinnati, suggested pulmonary reticulosis and Dr. M. Wheelock, of Miami, who contributed the case, made a diagnosis of malignant thymoma.

Dr. Pool: I think the clinician was faced with a problem in trying to differentiate this left pleural effusion. I certainly agree with Dr. Viamonte that the radiographic evidence and obliteration of the aortic arch is against a pericardial effusion. I was impressed with the symptomatology of cough and pain suggesting involvement along the trachea and major bronchi which in older people can be seen in metastatic breast cancer, lung cancer and in fibrous mesothelioma. The only point against mesothelioma is the absence of pericardial effusion; perhaps if this were a pleural mesothelioma secondarily invading the mediastinum, that would not be a necessary factor.

M. Wheelock, M.D., Miami, Fla.: We had quite a discussion at the time we went over this case. The primary lesion was a big mass over the anterior pericardium, an extensive infiltrating, proliferating tumor which did go into the heart at different areas but not over the epicardium. There were not the masses in the heart such as described for a rhabdomyosarcoma. This had to be a lesion going in from the outside into the heart; much of the epicardium was not involved. These were huge masses; I held out for reticulum cell sarcoma. Gould thought it was a mesothelioma until he saw the sections. There we had the Hassel's corpuscles. This is what we interpreted as the thymus. We could not see any of the papillary proliferations that you see in the usual mesothelioma.

Dr. Liebow: I have never seen invasion of the myocardium by a thymic tumor. Now the question arises how much of the lesion is represented by the first slide that you saw. Is what you saw just a small bit of thymus that was left or was it a component of the tumor itself? Was a large part of the tumor composed of the tissue we see here?

Dr. Wheelock: That's right.

Dr. Liebow: I think that if that is the case then the diagnosis of thymoma is much more reasonable than I thought from seeing the material that was actually submitted.

M. Berthrong, M.D., Colorado Springs, Colo.: We made sections of everything that Dr. Wheelock saw. Almost all of the material looked like the slides that you got. There was some thymus and I thought it was surrounded by tumor but we didn't have enough of that block to make slides for everybody. What was in the Seminar slide represents most of the tumor as submitted to us.

Dr. Liebow: In the material that you saw was there very little thymic tissue?

Dr. Berthrong: Very little and what I saw I thought was being invaded. There still may be some doubt as to the origin of this tumor, particularly because of the involvement of the heart, the young age of the patient, and because of the way in which it was disseminated.

Dr. Wheelock: Just direct invasion but no metastases.

Dr. Regato: This shows you the intricacies of preparing a case that would be suitable for the Cancer Seminar. We have to get enough material for 300 slides and they must all be comparable; we cannot always offer material that became available when the patient died. It is fairer to present the clinical information, roentgenograms and surgical material as of the time when the patient was seen. Details of autopsy findings should be revealed later, to everyone, simultaneously.

Dr. Liebow: The idea of thymoma certainly deserves consideration. It differs from the characteristic tumor type such as that of the first case discussed in this seminar.

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4. *Hemangioma-Hemangiopericytoma of the Upper Mediastinum*

Contributed by M.R. Abell, M.D. and W. Martell, M.D., Ann Arbor, Michigan

THE PATIENT was a 16-year old boy in May, 1967, when he gave a history of numbness and pain of the left shoulder of 8 weeks duration. Examination revealed decreased reflexes and muscular strength of the left arm and a deep mass fixed in the supraclavicular region. Laboratory work-up was non-contributory.

Dr. Viamonte: The frontal chest roentgenogram of this teenager discloses an 8 x 11 cm superior mediastinal mass displacing the trachea to the right. The mass appears to be intrathoracic and to extend into the base of the neck, (the upper and lateral margin of the mass is indistinct and the cervical portion of the trachea appears displaced to the right). The lungs, heart and bony thorax appear to be normal.

A left subclavian arteriogram discloses the uniform, profuse, hypervascular nature of this mass, which displaces caudally the left subclavian artery. Tumor vessels are observed within the mass.

The fixation of this mass on clincial examination, hyporeflexia, and hypotonia suggest a malignant tumor with involvement of the brachial plexus. Hypervascularity as the one observed in this tumor is usually seen in primary vascular tumors.

Tumors of the blood vessels can be divided into benign and malignant. Benign lesions are the hemangiomas. Microscopically they can be divided into seven basic types: capillary hemangioma, cavernous hemangioma, hemangioendothelioma, hemangiopericytoma, venous angioma, arteriovenous angioma and sclerosing angioma. The malignant vascular tumors are the angiosarcomas. They include Kaposi sarcoma.

Angiographic findings such as seen in this case, we have seen in three patients with hemangiopericytomas.

Hemangiopericytomas have been sited in many and varied sites in the body. Widespread sites are not surprising when one considers these tumors as being of capillary origin. Radiologically the tumor usually presents purely as a soft tissue mass. Although calicification has been noted pathologically, it is usually not observed radiographically. By angiography, they may present as a highly vascular tumor with appearance suggesting arteriovenous fistula. In some cases of hemangiopericytomas, however, no tumor vessels have been seen and a diffuse capillary blush has been obtained. Large draining veins may be seen. Although the angiographic appearance may on occasion be highly suggestive of the precise diagnosis of hemangiopericytoma, the diagnosis must rest on histologic findings. The tumor arises from the pericytes which lie around the capillary vessels and are thought to be modified smooth muscle vessels. Many hemangiopericytomas are benign and several cases have been recorded of local spread and some with late metastases. Various authors have stressed the impossibility of assessing the degree of malignancy on histological grounds. The incidence of metastasis in hemangiopericytoma is 25 out of 197 cases (Stout, 1956). Up to 1964, nineteen cases of primary thoracic hemangiopericytoma had been published. This tumor has no predilection for age or sex. It was congenital in three of Stout's patients. In cases of thoracic hemangiopericytoma the age range was from fifteen to seventy-five years with an average of forty-six years. Tumor size, in general varies greatly from a few cm to the occupation of half of the pelvis or pleural space.

Dr. Viamonte's impression: MALIGNANT HEMANGIOPERICYTOMA

Roentgenologic Impressions Submitted by Mail

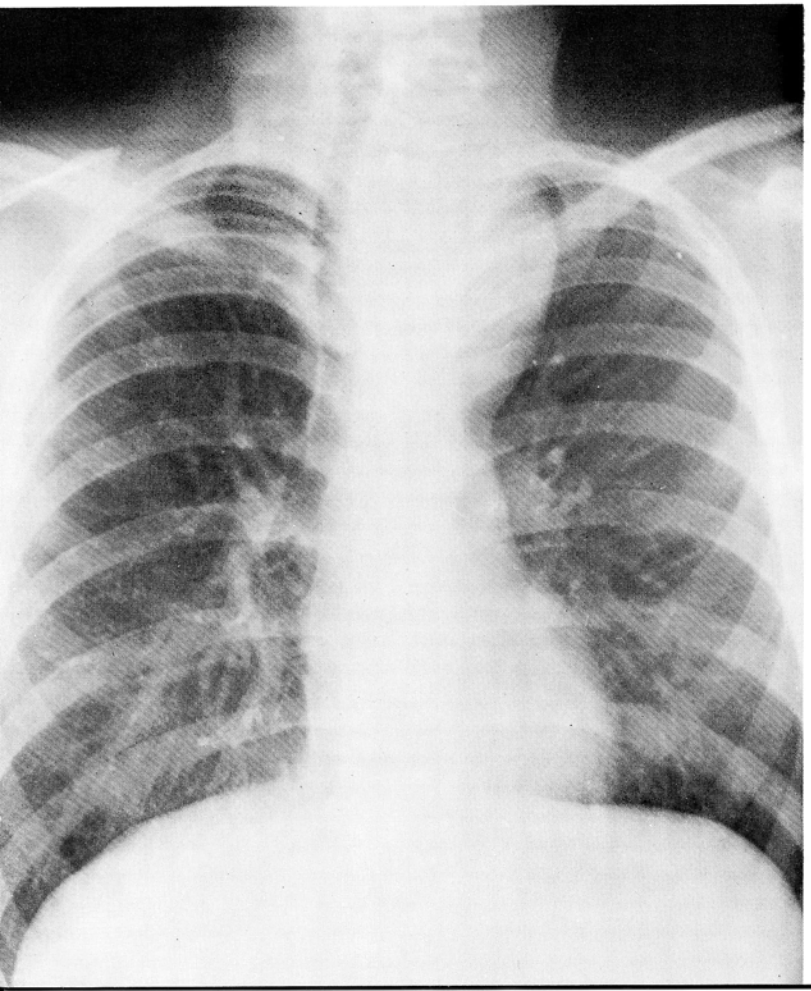
Chemodectoma	28
Carcinoma of thyroid	18
Hodgkin's	7
Various malignant tumors	15
Hemangioma	5
Hemangiopericytoma	4
Others	3

Dr. Viamonte: Chemodectoma or non-chromaffin paraganglioma is a definite possibility as well as hemangioma and carcinoma of the thyroid. Radiographically we had the impression that this tumor was primarily intro-thoracic and extending into the base of the neck. I am not aware of a uniformly vascular carcinoma of the thyroid. Hodgkin's disease is not, in my experience, a highly vascularized tumor. I believe that we have to consider, on the basis of the clincal and radiographic impression, a malignant primary vascular tumor, probably hemangiopericytoma.

Dr. Regato: Dr. B.L. Pear, of Denver, offered chemodectoma. Dr. E. Salzman, of Denver, preferred neuroblastoma.

Operative findings: The patient was thought to have a thyroid tumor and on May 19, 1967, an excision of the cervical mass and the cervical laminectomy were done; the tumor had to be freed of cervical roots and of the spinal dura. After histopathologic findings were reported a new intervention was carried out on May 31, 1967: this time a midline thoracotomy was done, the tumor had to be separated from the trachea and esophagus; it was removed in continuity with the sterno cleido-mastoid muscle, the C-6 and C-7 nerve roots had to be sacrificed. The blood loss was over 5,000 cc. The specimen measured 10 x 9 x 6 cm and presented a grossly encapsulated rubbery, multinodular tumor with a sausage-like appendage; it was tan-white in color and presented focal areas of calcification and of hemorrage.

Fig. 1—Superior mediastinal and lower cervical mass displacing the trachea.



Dr. Liebow: Histologically as well as radiographically this tumor appears to be clearly related to vessels, and possesses features both of hemangioma and hemangiopericytoma. In some respects the tumor is similar to that of case 3. It is composed predominantly of spindle-shaped cells, and there are within it, again, masses of hyaline connective tissue. However, in this instance vascular spaces are unquestionably lined by cells of the tumor, and the appearance in part is that of any cavernous or capillary hemangioma. In other portions, however, the cells are arranged about vessels in regular interlacing cords and there results an "organoid" pattern, somewhat reminiscent of chemodectoma. In the reticulum stain the cells are grouped in columns or masses, although occasionally individual cells are surrounded by fine argyrophilic fibers. Calcification is present focally, largely within the thick capsule.

There is an additional feature of interest in that large vessels within the capsule are composed of masses of muscle fibers, in oblique or predominantly longitudinal arrangement. These in many places are separated by large accumulations of acid mucopolysaccharide, which stains intensely with the Alcian stain. The significance of this change is not clear. One possibility is that if the tumor is functioning as an arteriovenous fistula, which as Virchow pointed out seems, indeed, to be the case in many hemangiomas, the blood flow might be very large, with turbulence that could be responsible for medionecrosis.

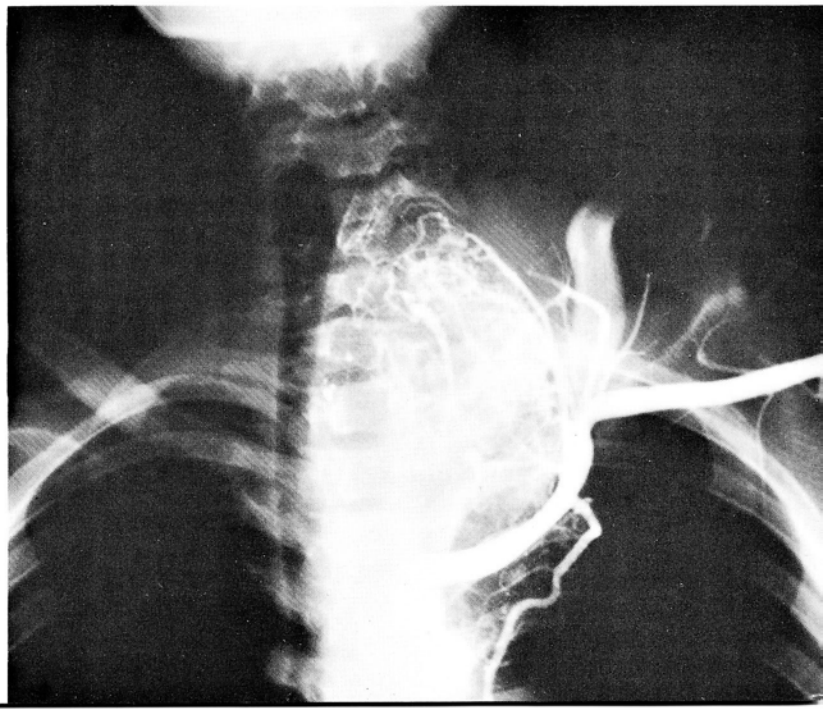
The vascularity is clearly evident in the angiogram. The location of this lesion also is entirely compatible with hemangioma-hemangiopericytoma. Such tumors are commonly invasive and may metastasize.

Dr. Liebow's diagnosis: HEMANGIOMA - HEMANGIOPERICYTOMA

Histopathologic Diagnoses Submitted by Mail

Hemangiopericytoma	52
Thymoma	35
Chemodectoma	9
Hemangioendothelioma	6
Sarcomas (various)	14
Paraganglioma	7
Others	8

Fig. 2—Left Subclavian arteriogram revealing increased vasculature.



Dr. Liebow: Hemangiopericytoma is well supported, particularly by the reticulum stains, in certain fields of this lesion. Again, the question of thymoma was raised and some of the aspects of the slide would support this diagnosis. Hemangioendothelioma is surely a component of the lesion, but the important components here really are the pericytes which indicate an entirely different diagnosis. While there are some histological resemblances, the biological and cytological relationships between chemodectoma and hemangiopericytoma remain to be elucidated. Spindle cell types of thyroid carcinoma exist, but these have a highly malignant appearance, a feature not manifest in this tumor.

Dr. Regato: Dr. W.J. Frable, of Richmond, Virginia, made a diagnosis of hemangiopericytoma. Dr. R.M. Sherwin, of Colorado Springs, offered spindle-cell type thymoma. Dr. P.C. Dyke, of Denver, preferred chemodectoma and Dr. R.D. Schultz, of Sioux Falls, non-chromaffin paraganglioma.

Subsequent history: Following operation the patient received radiotherapy to the neck through fields 10 x 12 cm in diameter. In July, 1968, the patient appeared well except for residual weakness of the left arm and a persistent Horner's syndrome; there was no evidence of recurrence. On September 5, 1968, she was admitted for investigation of further trouble in the neck.

M.R. Abell, M.D., Ann Arbor, Mich.: In September, 1968, he had a weakness of the right arm; the myelogram revealed a block at level of C7. A laminectomy was done; a neoplasm was present and they removed most of it. It presents the same histologic appearance as the more cellular hemangiopericytoma. At this time there is no evidence of recurrence of the intro-thoracic mass and there are no pulmonary metastases, so the occurrence has apparently been restricted primarily to extension within the canal system. We considered paraganglioma also at the time: the chromaffin stains were negative. Many blocks of tissue showed simply a hemangiomatous component which we thought were benign with areas of dystrophic calcification and bone. We thought that this was a malignant hemangiopericytoma developing in a pre-existing hemangioma.

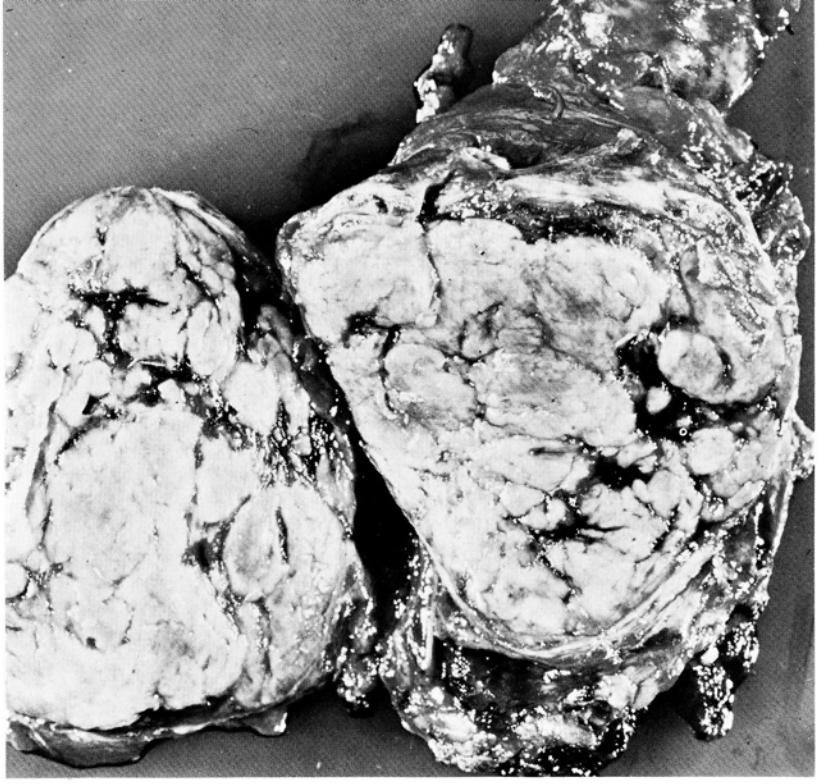


Fig. 3—Gross appearance of mass removed from trachea and esophagus.

Dr. Pool: The blood vessel study and the roentgenogram showed a malignant tumor. I did not think it could be carcinoma of the thyroid because in an adolescent it does not present, as far as I know, as so large a neoplasm. I would like to emphasize the importance of biopsy in planning treatment because some tumors in this area might do better with pre-operative irradiation. It is worthwhile to get a good representative piece of tissue and wait, if you have to, to do your surgery. Also, it is worthwhile to have tried to excise, or to have excised, a hemangiopericytoma. I can report a personal experience of a patient with a retroperitoneal hemangiopericytoma invading two transverse processes who is alive eighteen years after resection. These tumors seem to have a tendency to invade the vertebrae.

Fig. 4—Hemangioma-hemangiopericytoma: At the right, elongated and flattened cells line spaces filled with erythrocytes. At the left, whorls and spirals of elongated cells interpreted as pericytes occur in masses (X 200).

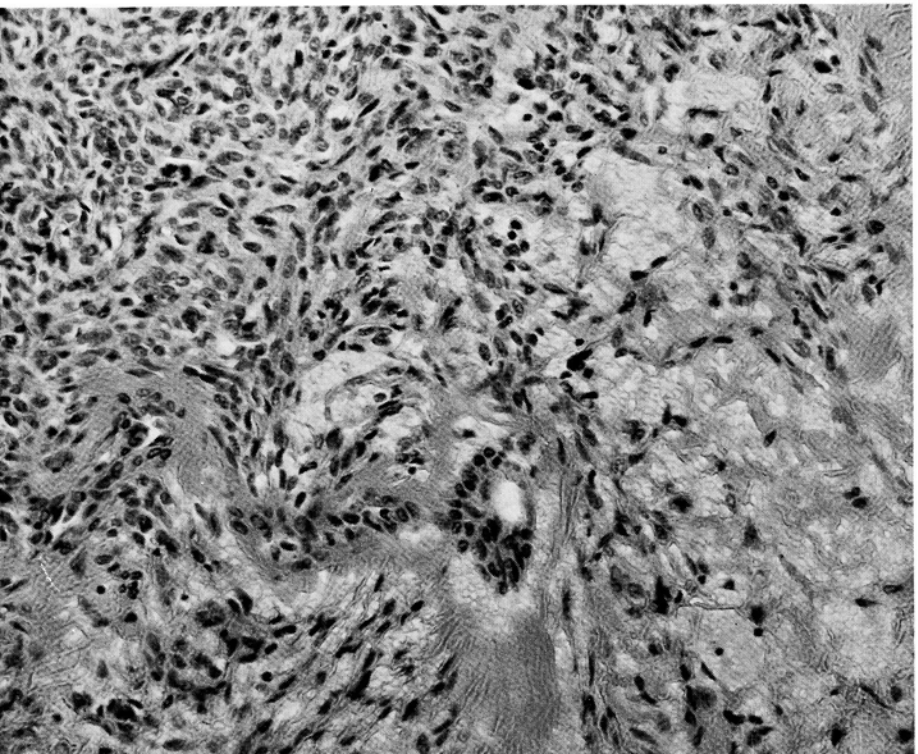
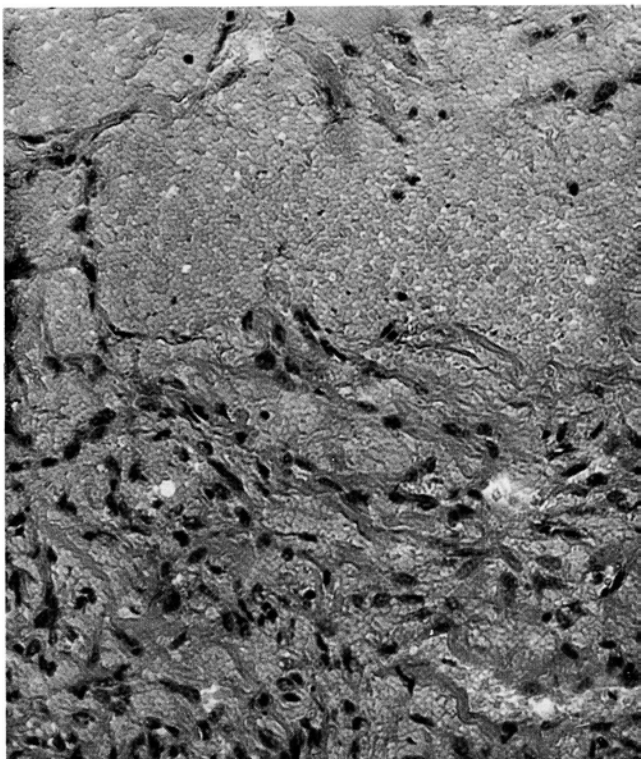


Fig. 5—Detail of the hemangiomatous component shown in Fig. 4 (X 400).



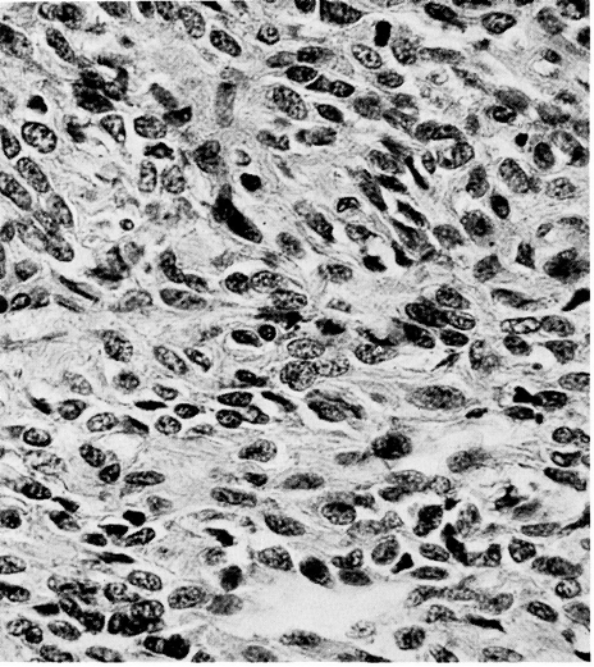


Fig. 6

Fig. 7

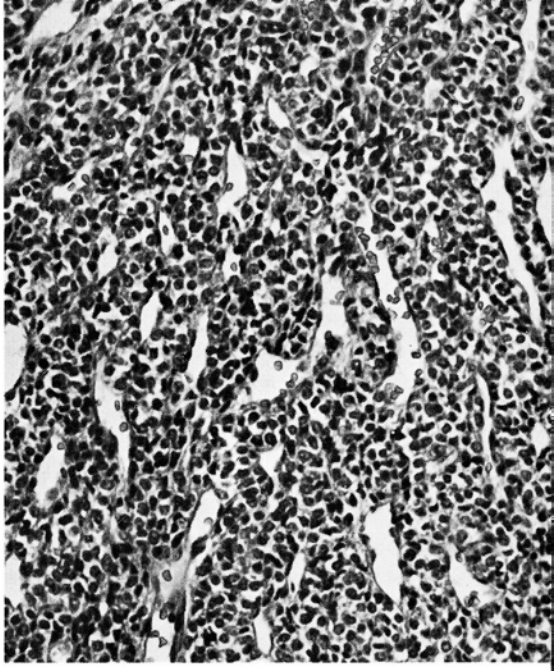


Fig. 8

Fig. 6—Detail of the variable pericytes, one of which is in mitosis (X 400).

Fig. 7—"Organoid" arrangement of pericytes about vascular spaces. There is some resemblance to chemodectoma (X 45).

Fig. 8—Detail of "organoid" component. The masses of pericytes are separated from the endothelial lined channels by thin laminae of connective tissue (X 200).

P.J. Hodes, M.D., Philadelphia, Pa.: I would like to ask Dr. Viamonte what was there about this that made him think of hemangiopericytoma. There did not seem to be enough venous run-off with all of the succulence of this tumor. Would you tell us a little more about the characteristics of pericytoma.

Dr. Viamonte: We happen to have three patients with almost an identical pattern; the vascularity was rather diffuse, uniform. One case was a thoracic one; the other was on the base of the left cervical region. We have other cases that did not show this aggressive large arterial vasculature. One metastasized to the liver and kidney and just showed a capillary blush; recently we had one in the thigh with almost an identical vascular pattern. Sutton has published similar cases and he points out that one can suggest the possibility of hemangiopericytoma on the basis of the uniform increased aggressive vasculature. I base the impression of malignancy mainly on clinical grounds. I have no personal experience of angiography on carcinoma of the thyroid. The large size of the feeding arteries is what I thought characteristic of hemangiopericytoma. From a surgical point of view, it is important, in a patient like this, to know the blood vessels supplying the primary tumor. At the time when excision is planned, it is important to see if there are prominent vessels supplying the tumor, so that the surgeon has some sort of a map of the vascular abnormality that he may encounter; thus, he may be prepared to tie those vessels that are the primary suppliers of blood to the tumor.

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5. *Carcinoma of Ectopic Parathyroid*

Contributed by F.A. Traylor, M.D., H.H. McGee, M.D.
and D.J. Stephenson, M.D., Lakewood, Colorado

THE PATIENT was a 30-year old man in March, 1963, when he noted the sudden onset of pain under the left scapular region with stiffness of the left shoulder. There was a history of "renal calculus." Examination revealed no abnormalities; routine laboratory procedures were reported as normal.

Dr. Viamonte: Frontal and lateral chest roentgenograms reveal a 4 x 6.5 cm right prehilar, smoothly outlined mass with no other chest abnormalities observed.

The differential diagnosis of a large prehilar mass includes anywhere from a benign condition such as giant adenitis, thymoma, bronchogenic cyst, and benign mesenchymal tumors, to malignant neoplasms such as bronchogenic and metastatic carcinoma, lymphoma, etc. However, the history of "renal calculus" should make one suspect the possibility of hyperparathyroidism secondary to an ectopic parathyroid gland or to a non-parathyroid tumor producer of PTH. Tumors containing a PTH-like substance have been found in the kidneys, parotids, adrenals, lungs, and spleen. Most of the lung tumors reported with hypercalcemia or producing PTH-like substances have been squamous cell carcinoma.

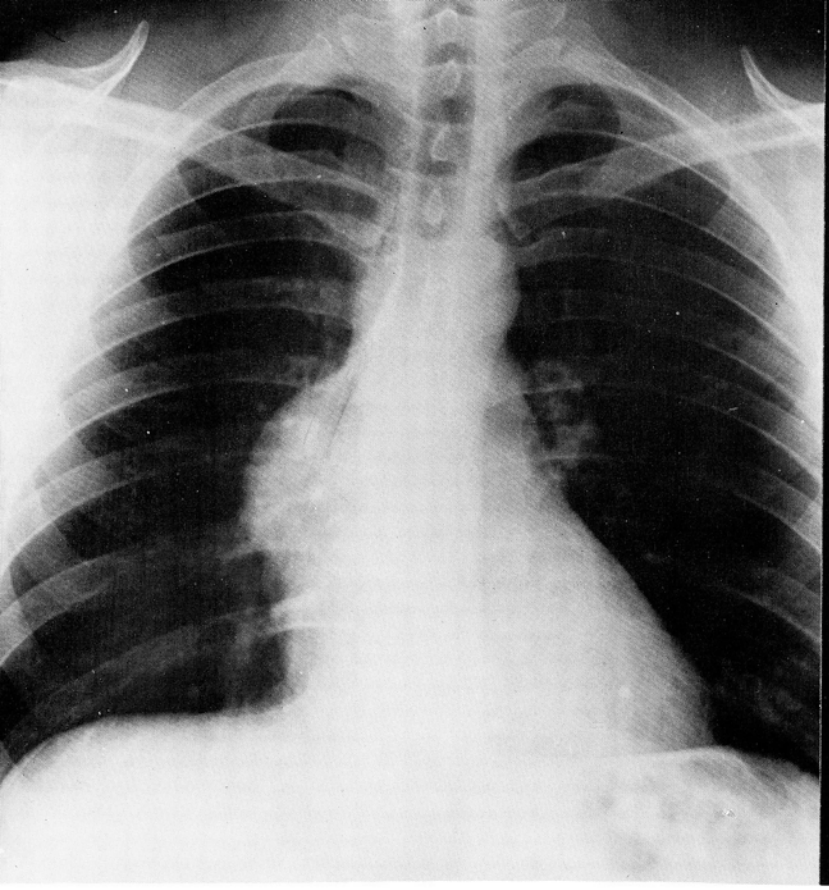

Fig. 1—Right parahilar smoothly outlined mass.

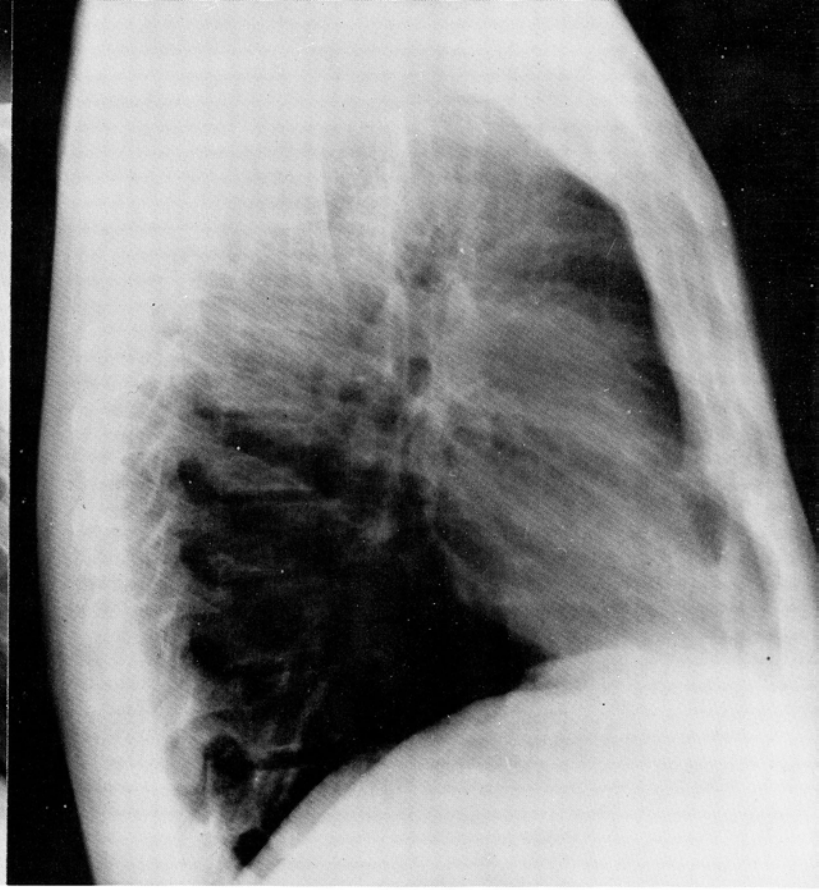

Fig. 2—Lateral roentgenogram showing pre-hilar mass.

Carcinoma of the lung was associated with hypercalcemia in 13% of a series of 119 cases reviewed by Locks (Turkington) and in nine of these no metastasis to bone could be identified at autopsy. Reversion of hypercalcemia to normal after irradiation or surgical extirpation of the carcinoma is the only conclusive evidence of a hormonally active tumor. Hypercalcemia in cancer usually is the result of bone destruction due to metastases, high calcium or Vitamin D intake, adrenal insufficiency, hyperthyroidism, or of a direct action of tumor tissue on calcium metabolism.

Although routine laboratory procedures were reported as normal, we would relate the mediastinal tumor to a PTH-like producing tumor which might explain both the mass and the history of renal calculus. If the patient was a smoker, squamous cell bronchogenic carcinoma is statistically the most likely possibility. If he was a non-smoker, the possibility of some other type of bronchogenic tumor such as the undifferentiated type or a bronchial adenoma may be considered.

Dr. Viamonte's impression: 1) BRONCHIAL CARCINOMA, 2) BRONCHIAL ADENOMA 3) ECTOPIC PARATHYROID TUMOR

Roentgenologic Impressions Submitted by Mail

Carcinoid	26
Aneurysm	12
Parathyroid adenoma	9
Thymic Tumor	8
"Lymphoma" (sic)	8
Others	18

Dr. Viamonte: Carcinoid is a possibility. The fact that the lesion was so confined to the mediastinum certainly makes it compatible with a bronchial adenoma. I think one can rule out an aneurysm. We are trying to relate this mass to a renal calculus and we suspect that the patient had hyperparathyroidism. What might give you a mass like this is perhaps an aneurysm of the azygos vein. The oval shape would be against an aneurysm. A thymus tumor, to the best of my knowledge, has not been reported associated to this syndrome. The same can be said of lymphoma.

Dr. Regato: Dr. E. Salzman, of Denver, offered an impression of parathyroid adenoma; Dr. J.D. Cox, of Colorado Springs, designated it as a mediastinal parathyroid adenoma. Dr. M. Levine, of Denver, also suggested a parathyroid tumor.

Operative findings: On April 5, 1963, a thoracotomy was performed and an anterior and superior mediastinal mass was removed: it measured 11 x 7 x 5.5 cm, and it was irregularly nodular and presented cystic areas.

Dr. Liebow: While the position of the mass is not that of normal parathyroid tissue, there are histological features highly suggestive of a tumor of this organ, as is the history of renal calculus.

One histological feature is particularly indicative of parathyroid tumor: the groups of very tall cells with basal nuclei and elongated bodies of clear cytoplasm that have a more or less radial arrangement about a minute lumen. These correspond to what is demonstrated in Fig. 32 in the Fascicle on Tumors of the Parathyroid Gland. Most of the cell masses, however, are much less regular, in fact often in disarray, and mitoses among them are common. There are also foci of necrosis and hemorrhage. These features suggest malignancy. There are also minute foci of calcification. The position of this lesion is entirely compatible with a tumor arising from ectopic parathyroid tissue (See fig. 2 in Cope).

Dr. Liebow's diagnosis: CARCINOMA of the PARATHYROID, probably of ectopic origin.

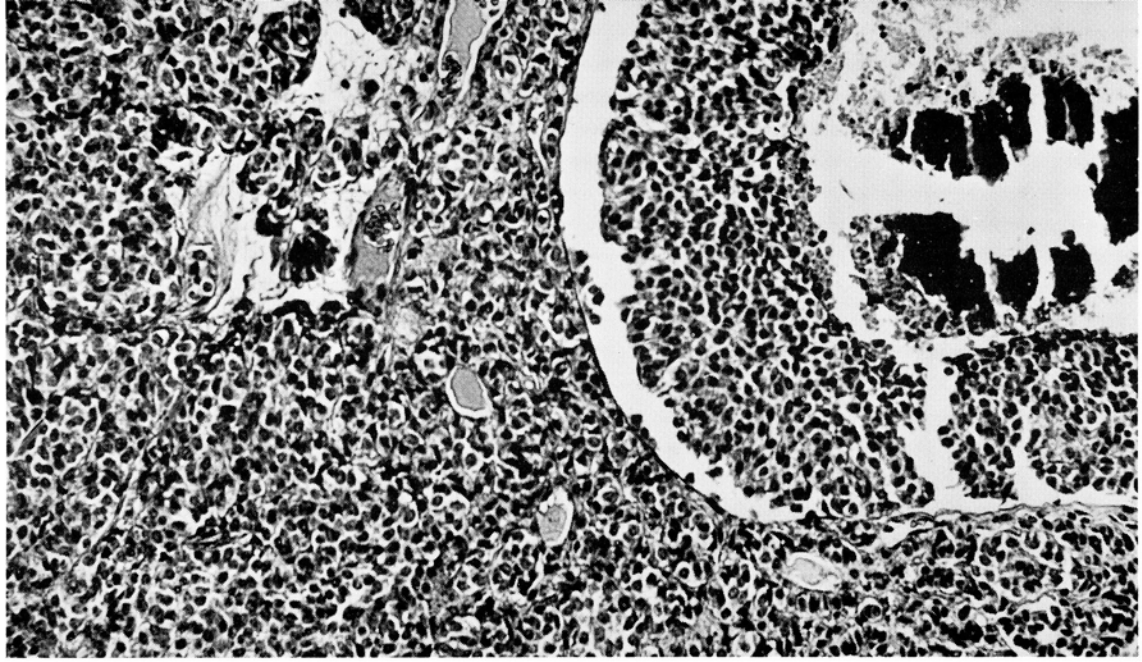

Fig. 3—Parathyroid carcinoma: Irregularly arranged epithelial masses of "chief cell" type. Occasional mitoses are present. Follicular spaces containing a material rich in protein are surrounded by flattened cells (X 200).

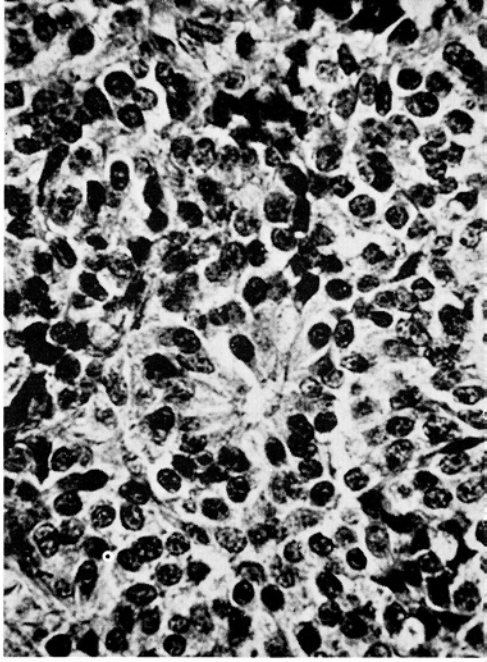

Fig. 4—Acinar arrangement typical of parathyroid tumors. Elongated cells arranged about a small space into which they thrust villous projections resembling cilia. One cell in mitosis is seen in left lower quadrant of the photograph (X 400).

Histopathologic Diagnoses Submitted by Mail

Parathyroid adenoma	45
Parathyroid carcinoma	14
Bronchial carcinoid	27
Neuroblastoma	6
Non-chromaffin paraganglioma	3
Others	25

Dr. Liebow: There is general agreement that the tumor is of parathyroid origin; the distinction between adenoma and carcinoma is a matter of some difficulty. It is true that certain parathyroid adenomas rather closely resemble in arrangement the trabecular pattern of typical carcinoid tumors. The stromal relationships here are very helpful and also the appearance of the acini. The acinar arrangement of very tall cells occur in the parathyroid tumor but not in the bronchial carcinoid. Acini are not found in non-chromaffin paraganglioma; this diagnosis is ruled out not only by the appearance of tissue but also by the stromal relationship.

Dr. Regato: Dr. F.P. Bornstein, of El Paso, made a diagnosis of parathyroid adenoma. Dr. R.E. Stanford, of Denver, offered parathyroid carcinoma. Dr. M.R. Abell, of Ann Arbor, designated it as carcinoid thymoma. Dr. F. Foote, of New York, preferred sympathicoblastoma and Dr. B. Castleman, of Boston, bronchial adenoma.

Subsequent history: The patient did well until November, 1966, when he presented a recurrence of the left shoulder pain. A midline thoracotomy was done on November 7, 1966, and a soft recurrent mass 7 x 7 x 3.5 cm was removed; this was followed by a post-operative radiotherapy. In November, 1967, the patient developed a lumbar pain and gravel in the urine; the serum calcium was 11.9 mg%. In April, 1968, the calcium excretion was found to be 300 mg daily: a parathyroid adenoma 1.5 cm in diameter was removed from the neck and the serum calcium slowly decreased. He has remained well.

Dr. Pool: The clinical picture of hypoparathyroidism can be quite varied and this man, at the time of his first tumor removal, did not have symptoms other than what might be affected from the size of his mediastinal mass. He did not have nausea, for instance. If this were a functional parathyroid adenoma, he should have had some post-operative difficulties, such as tetany, because of the fact that he did not have hypoparathyroidism at the time of resection. An interesting point about mediastinal parathyroid adenomas is that their arterial supply is often from the thyrocervical trunk; the surgeon has the advantage, if he can find this vessel, of tracing it down into the mediastinum in trying to find such a lesion. I wonder if, at the time of his third operation, all four parathyroids were identified; this also raises the question that it is somewhat unusual, but not impossible, to have four parathyroids in the neck and a parathyroid tumor in the mediastinum.

F.A. Traylor, M.D., Lakewood, Colo.: I was only connected with the first operation; the last two operations were done in California. The parathyroid adenomas that were removed in April were removed from the neck. There was not any artery which could be considered to be the thyrocervical trunk during his thoracotomy, in 1963. I got a letter from this patient last week and he tells me that he has had a recurrence of the symptoms of his parathyroid tumor. He has had some pain in the chest, and nervousness, and his internist has found an elevated calcium. His chest roentgenogram is negative.

Dr. Liebow: The question that arises here is whether or not the patient is suffering from an endocrine polyadenomatosis, rather than merely from multiple parathyroid adenomas. If it were a hyperplastic state with diffuse hyperplasia of the parathyroid, one would expect, although one does not always find, a somewhat different histological structure with a predominance of large clear cells which are not present here. If there are multiple parathyroid tumors which have a chief cell structure, then I think it is very pertinent to find out if there are other kinds of adenomas involving endocrines in this patient; this probably will turn out to be the case. The point that was made by Dr. Viamonte about the relationship of the parathormone-like hormone to squamous carcinoma of the lungs surely is important; that is by far the predominant kind of lung cancer in which parathormone-like substances are produced. However, it would be unlikely to have such a tumor as a squamous cell carcinoma in a patient thirty years of age. Even if he were a very heavy smoker, this patient would have had to start smoking at the age of five or ten: not impossible, but unlikely.

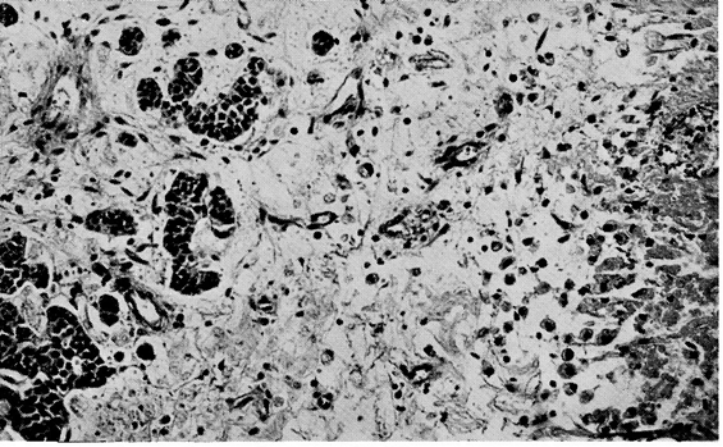

Fig. 5—Focus of necrosis (X 45).

P.J. Hodes, M.D., Philadelphia, Pa.: I am a little bit surprised that this patient has not had radiographs made on the hands or other parts of the body in order to determine whether or not this parathormone business is indeed the case. I would like to add also that the most marked type of bone changes that I have seen have been in patients who have parathyroid carcinomas.

Dr. Traylor: I cannot answer this, I do not know. All his treatment in the last four years have been done in Los Angeles.

M.R. Abell, M.D., Ann Arbor, Mich.: I have to defend my diagnosis of thymoma. The size of this lesion, 11cm, bothers me a bit for a parathyroid tumor in the mediastinum. Also the location: the surgeon said that it was primarily in the anterior superior mediastinum, in the location of the thymus gland. In Cushings' disease, and in some of the polyadenomatoses, the thymomas that develop have a neural, epithelial, and a carcinoid pattern. I would like to suggest that this may be part of the polyadenoma syndrome but this may not be a parathyroid adenoma but a thymic adenoma.

H.J. McGee, M.D., Wheatridge, Colo.: Initially, we also considered this to be a thymoma when the first operation was performed by Dr. Traylor. I believe Dr. Lattes has described a series of thymomas from the anterior mediastinum in which such neuroepithelial rosette-like structures were present. I wonder if Dr. Liebow would comment further on that. Probably, we are dealing with a case of polyendocrine adenomatosis but we think that we have a thymoma as the original lesion and a parathyroid adenoma has occurred subsequently as a separate lesion.

Dr. Liebow: Regarding the significance of certain structures, in particular this interesting acinar relationship that was made here with regard to the actual nature of the thymoma on the one hand and the parathyroid on the other, in the embryo these two tissues are most thoroughly intermingled and indeed they are both derived from branchial cleft tissue. I think this is very important in considering the interrelationships of these; we probably are dealing with differentiations of tissues which are certainly very closely related embryologically.

Dr. Regato: Dr. Lattes wrote: "The differential diagnosis is betwen mediastinal parathyroid tumor and mediastinal carcinoid, so-called bronchial adenoma, in the mediastinum; I vote for the second."

L.I. Gottlieb, M.D., Salt Lake City, Utah: I am a little concerned about the diagnosis of parathyroid adenomas versus carcinomas. Do you feel that an occasional mitotic figure is enough to make a diagnosis of carcinoma versus a benign lesion?

Dr. Liebow: Well, this is not the only point; the failure of encapsulation and the presence of necrosis, I think too, in favor of the diagnosis of carcinoma rather than adenoma. The abnormal serum calcium values confirm the parathyroid nature of the lesion, as does the presence of renal calculi. Recurrence of the tumor is compatible with its malignant histological features. The argument that other lesions called "carcinoid thymic tumors" can produce hypercalcemia seems specious, in view of the histological characteristics of this tumor.

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6. *Rhabdomyosarcoma of the Heart*

Contributed by **D.R. Dickson, M.D.** and **P.A. Riemenschneider, M.D.**
Santa Barbara, California

THE PATIENT was a 68-year old woman in August, 1966, when she complained of dyspnea and a sensation of anterior thoracic pressure. On examination the blood pressure was found to be 130/84; the EKG showed an antero-lateral ischemic pattern; the CBC was within normal limits.

Dr. Viamonte: Frontal and lateral views of the chest reveal a left pre-hilar mass and generalized cardiac enlargement. The anterior mediastinum appears to be involved by tumor. The lungs reveal no abnormalities. Degenerative changes are observed in the thoracic spine.

The radiographic findings suggest a malignant tumor involving the heart. The possibilities are: 1) Thymoma; 2) Bronchogenic carcinoma; 3) Lymphoma; 4) Malignant teratoma; 5) Pericardial tumor (mesothelioma, sarcoma, metastatic neoplasm).

I do not believe it is possible to differentiate a primary mediastinal extracardiac tumor invading the heart

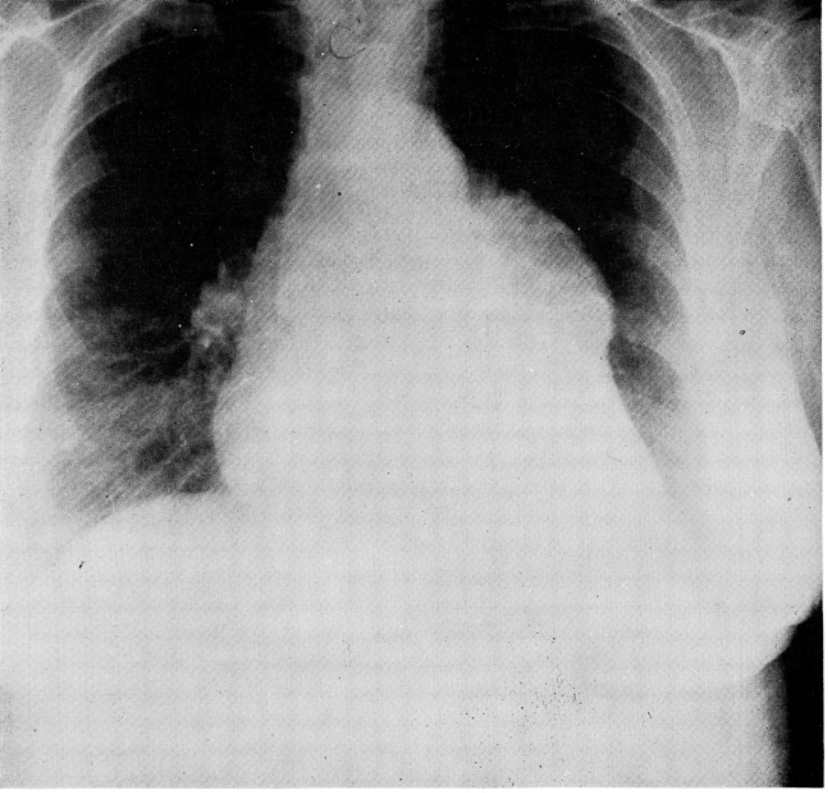

Fig. 1—Left pre-hilar mass.

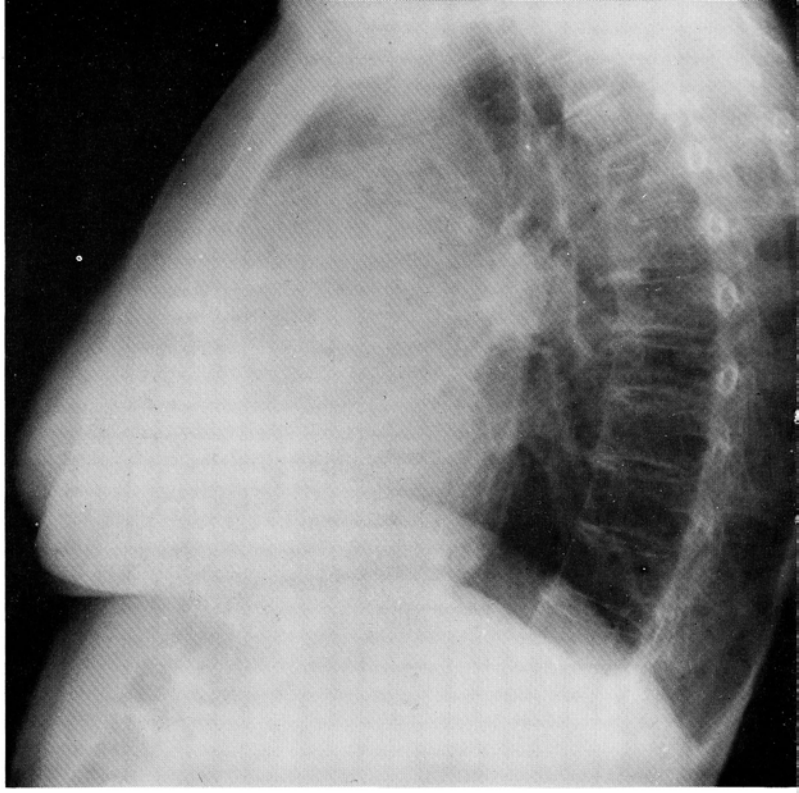

Fig. 2—Mass extending into anterior mediastinum.

from a pericardial tumor extending into adjacent structures. The latter is statistically a less likely possibility. Angiocardiography and mediastinal aspiration biopsy under fluoroscopic guidance are diagnostic radiologic procedures which could be used in such a case to provide a histologic diagnosis.

Dr. Viamonte's impression: MALIGNANT TUMOR WITH CARDIAC INVOLVEMENT

Roentgenologic Impressions Submitted by Mail

Rhabdomyosarcoma	25
Thymic tumor	23
Teratoma	13
"Lymphoma" (sic)	12
Others	10

Dr. Viamonte: Almost any mediastinal tumor which may involve the pericardium or cardiac tumor that extends beyond the confines of the pericardial cavity may present radiographically with this appearance. I do not believe that the clinical history is in favor of any histologic type; all these are likely possibilities.

Dr. Liebow: I wonder why you think that this tumor involves the heart.

Dr. Viamonte: The transverse diameter of the heart is increased and the fact that the tumor is presenting mainly to the left side of the heart implies that it probably is accompanied by either pericardial effusion or by direct invasion of the pericardial cavity. The other possibility is that the patient has cardiac dilatation unrelated to a tumor.

Dr. Regato: Dr. J.C. Lemon, of Denver, offered malignant thymoma. Dr. E. Salzman, also of Denver, submitted lymphosarcoma of the thymus. Dr. N. Goodman, also of Denver, offered pheochromocytoma.

Operative findings: On September 8, 1966, a thoracotomy was done: the lesion was found attached to the arch of the aorta; the pericardium was entered to facilitate the dissection of the tumor, but it was impossible to release it from the pericardium and heart. The removed specimen measured 9 x 8.5 x 4.5 cm; on section the tumor was rubbery in consistency and tan in color.

Dr. Liebow: In this instance the presence of elongated cells, as well as larger cells with foamy cytoplasm containing PAS positive material, taken together with evidence of involvement of the heart, suggests the possibility of primary rhabdomyosarcoma of that organ. The tumor is clearly malignant.

To be considered in differential diagnosis are primary liposarcoma and metastatic clear-cell tumor of the kidney. Results of a fat stain (not available) would clearly be of interest. The PAS-positive material, probably glycogen, would be expected in a renal hypernephroid tumor, but not in the liposarcoma. The stroma that contains large, thin-walled vessels also differs from that of metastases from renal tumor, where the vessels tend to be narrow. Primary cardiac rhabdomyosarcomas, mentioned in connection with case 3, have an appearance identical with that of the present lesion.

There occur in the lung tumors with a stroma similar to that of the present case, that are very rich in glycogen. These are all peripheral in position and have been called "benign clear-cell" or "sugar" tumors. Their origin is unknown. None have been encountered in the mediastinum.

Not only is the radiographic appearance suggestive of involvement of the myocardium in the present case, but so also are the electrocardiographic signs of an antero-lateral ischemic pattern. It is possible, however, that the latter is totally unrelated to the neoplasm, but rather the consequence of coronary artery disease.

Dr. Liebow's diagnosis: RHABDOMYOSARCOMA OF THE HEART

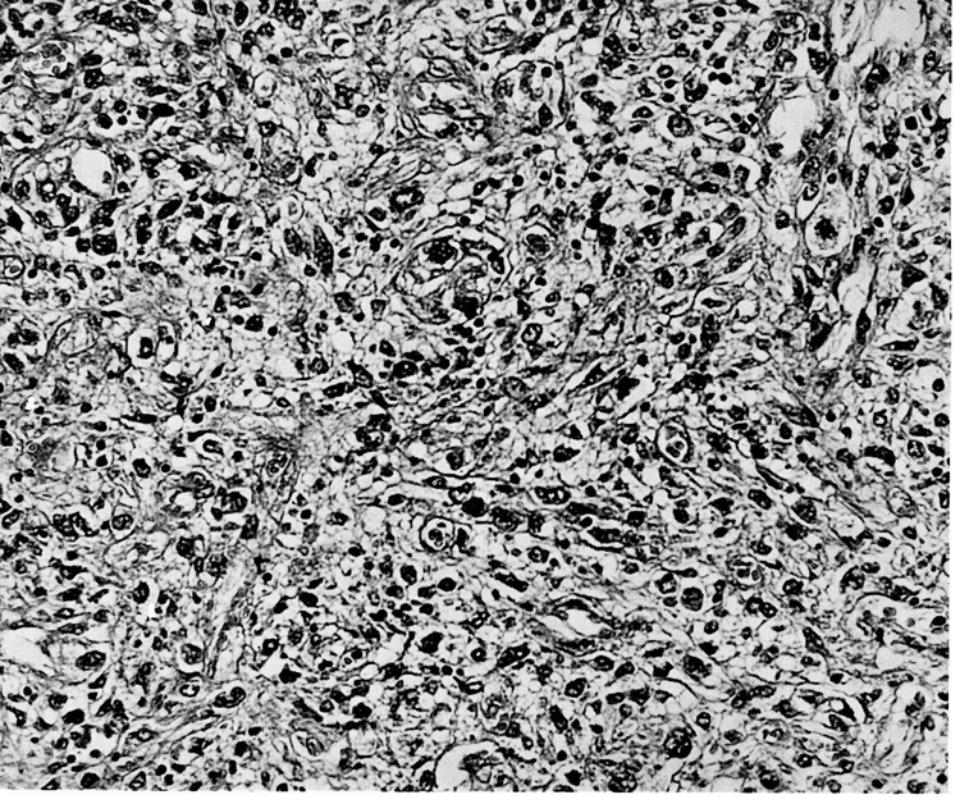

Fig. 3-Rhabdomyosarcoma of heart: Groups of irregular elongated and rounded cells with vacuolated cytoplasm. Some of the cells are in mitosis (X 200).

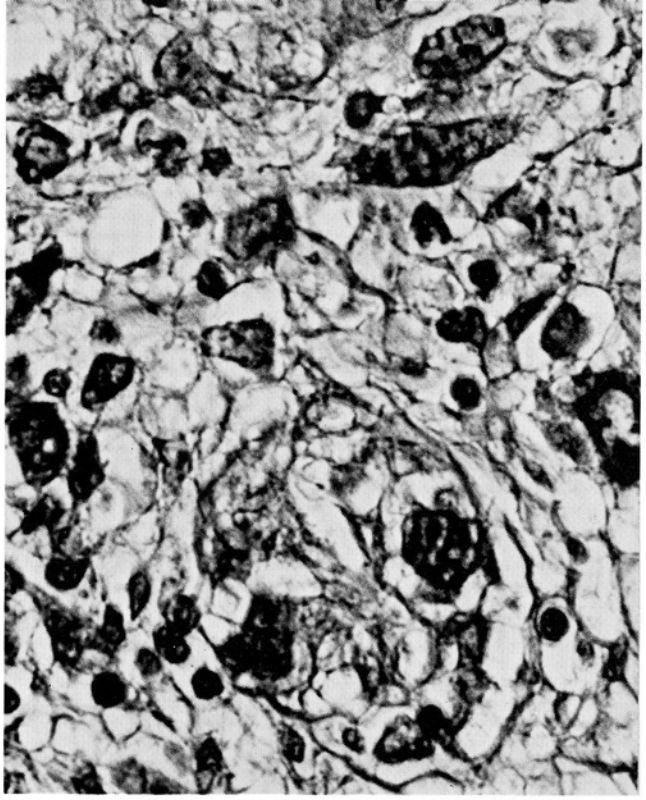

Fig. 4—Detail of Fig. 3. Nuclei display multiple prominent chromatin knots and nucleoli (X 750).

Histopathologic Diagnoses Submitted by Mail

Liposarcoma	53
Hodgkin's	9
Thymic tumor	10
Rhabdomyosarcoma	6
Xanthofibrosarcoma	11
Other sarcomas	10
Others	27

Dr. Liebow: The significance of the glycogen mentioned as a point against liposarcoma, applies also to "xanthofibrosarcoma". Thymomas also do not contain glycogen. I am very glad to see the diagnosis of rhabdomyosarcoma made. The thymus intrudes into almost all of these cases in some form or other.

Dr. Regato: Dr. L. Lowbeer, of Tulsa, also made a diagnosis of rhabdomyosarcoma. Dr. B. Castleman, of Boston, offered myxoid liposarcoma. Dr. R. Lattes, of New York, preferred undifferentiated malignant epithelial tumor which, if primary in the mediastinum, could be of teratomatous origin. Dr. F. Foote, of New York, made a diagnosis of thymic tumor. Dr. M.R. Abell, of Ann Arbor, offered xanthofibrosarcoma, Dr. T.H. McConnell, of Dallas, Hodgkin's disease, and Dr. M. Berthrong, of Colorado Springs, leiomyosarcoma.

This case was submitted to the AFIP (Accession 1259087); their report prepared by Dr. Wm. C. Manion reads: "This is a most intriguing tumor and we have enjoyed examining it . . . The presence of glycogen as demonstrated by P.A.S. stains fairly rules out the possibility of thymoma. The possibility of an angiosarcoma was considered, however, the blood vessels appeared very unimpressive in regard to their structure. The mucicarmin stain was negative yet it was felt by some observers that carcinoma of the lung could not be completely ruled out. The possibility of malignant mesothelioma seemed supported by the nature (sic) of the tumor cell and the presence of glycogen in the cleft-like spaces."

Subsequent history: Following operation the patient had serum hepatitis. She had a course of post-operative radiotherapy lasting 45 days. In September, 1968, she was seen in good health. There is no evidence of recurrence. The roentgenograms of the chest and the esophagogram revealed no abnormality.

Dr. Pool: In tumors that appear to involve the heart, the clinician is faced with the problem of whether or not there is a pericardial effusion. Mesothelial tumors of the pericardium will be accompanied by a bloody effusion and apparently these rare tumors of muscle origin, if that is what this is, are not so accompanied. As far as I know this is one of the few long-term survivors measured in months probably due to that preoperative irradiation. May I ask Dr. Viamonte a question? In the last two cases, I noted he included bronchogenic carcinoma in his differential diagnosis. I was impressed in both cases with the sharp definition of the lateral border of the mediastinum which seemed to go around the tumors.

Dr. Viamonte: The so-called mediastinal form of bronchial carcinoma, frequently seen with undifferentiated carcinomas, sometimes present radiographically as a mediastinal tumor. Very often we see no involvement of the lung and it is difficult to recognize the primary. We often do esophagrams to look for notchings or indentations in an effort to establish the extent of the involvement of the mediastinum. It is possible not to see any abnormal opacity in the lungs and to have a bronchial carcinoma presenting either like a widened superior mediastinum or simulating cardiomegaly.

Dr. Regato: Mention of the radiosensitivity of rhabdomyosarcomas might appear strange to some, but actually rhabdomyosarcomas very often prove to be very radiosensitive; they are not often curable due to the aggressive character of the disease and dissemination.

D.R. Dickson, M.D., Santa Barbara, Calif.: The lady was our family babysitter for a number of years; she is quite disappointed that we have not been able to give

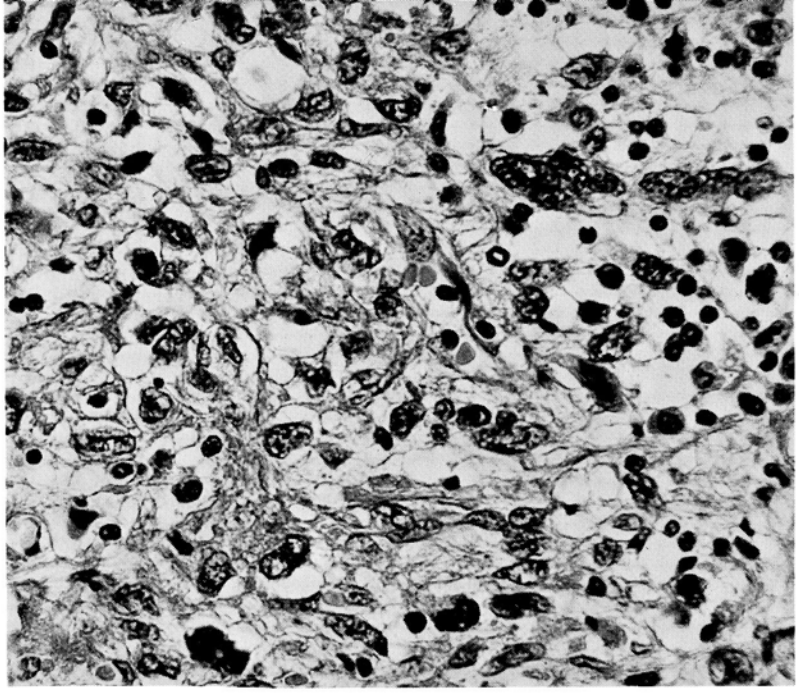

Fig. 5—Strap-shaped cells with abundant fibrillar and vacuolated acidophilic cytoplasm. Some are multinucleated (X 400).

her a diagnosis and that the pathologists in the country have not come up with anything really definitive. We are impressed by the tremendous tubular arrangement of the reticulin about these neoplastic cells. The Armed Forces Institute of Pathology was not impressed with this. Sometime after the AFIP report was received, we sent the slide to the California Tumor Registry and they felt that they did not want to give a diagnosis, but they sent it to the AFIP and six months later the Tumor Tissue Registry forwarded me the letter from the AFIP; I thought we might have some fresh light on it but they recognized the tissue and sent the identical letter that I had received. She is quite well now except for some dysphagia which she attributes to radiation therapy.

Dr. Liebow: Was there a kidney workup in this case and did this tumor have any fat in it?

Dr. Dickson: I think we got it from all sides and if there was some fat there I think I would remember it. The renal workup was not performed.

Dr. Regato: Radiotherapy has proven to be efficacious also in reducing the proportion of recurrences from liposarcomas following operation.

Dr. Viamonte: One of the fellows in our department has found that the most common tumor of the kidney is metastatic carcinoma and most of these are from the lung. We have dealt on three occasions with avascular kidney masses thought to represent cysts, only to find later that they were metastatic from bronchial carcinoma.

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7. *Large-Cell Carcinoma of the Lung*

Contributed by **Ray E. Stanford, M.D.**, Denver, Colorado

THE PATIENT was a 77-year old man in March, 1966, when he gave a history of progressive cough, dyspnea and 30 pounds weight loss over a period of several months; he had been a heavy inhaler of cigarettes. Examination revealed dullness and increased breath sounds over the upper right lung area and an enlarged prostate. There were 12,000 WBC per mm3 with a normal differential; the urine showed Gram-negative organisms.

Dr. Viamonte: Frontal view of the chest reveals a right hydropneumothorax, excavated pulmonary mass with several fluid levels, and a large paratracheal mass. The right visceral pleura is 2.5 cm from the chest wall; irregular thickening of the parietal pleura is noted. The left hilum appears slightly prominent. A 90 minute film of an intravenous pyelogram reveals bilateral hydronephrosis and a deformed bladder secondary to an enlarged prostate. A small bladder diverticulum is observed; no bony metastases are depicted.

Cavitating pulmonary lesions which perforate into the pleural cavity and involve draining nodes can be inflammatory or malignanat. Among the latter are primary (usually squamous cell carcinoma) and metastatic lung neoplasms (adenocarcinomas, squamous cell carcinomas, sarcoma, and lymphomas).

The history of an elderly, heavy smoker, without fever and with rapid weight loss are in favor of an excavating primary lung neoplasm, with secondary excavation, perforation, and metastasis to mediastinal nodes.

Cavitation in neoplastic disease of the lung is fundamentally of two types. There may be obstruction of the bronchus from neoplasm with atelectasis and infection in otherwise normal lung beyond the obstruction, and consequent break-down of previously normal lung tissue, or there may be necrosis, excavation, of the malignant mass itself, so called intraneoplastic necrosis. The differentiation between the two is usually not difficult as the abscess secondary to obstruction will occur in a recognizably atelectatic subsegment, segment or lobe, and the large mass of the obstructing neoplasm is usually visible proximally. By contrast, intraneoplastic cavitation occurs in a well-defined rounded lesion with no surrounding or distal infection or atelectasis of the lung. Exception to this rule occurs if a large excavated peripheral neoplasm secondarily involves the bronchus producing an area of infection or atelectasis. The radiographic criteria for intraneoplastic necrosis is a mass with a centrally located cavity; thick wall which is irregular or nodular in its inner portion; lesion crossing or bulging into another lobe; and no parenchymatous inflammation elsewhere. Peripheral, primary and secondary carcinoma of the bronchus, however, may well present as a thin-walled cyst. Eccentric cavitation in an otherwise solid density has been reported by Bernhard as suggestive of malignant excavation. Another sign is an increasing size of the cavity with constant thickness of the cavity wall. Spontaneous pneumothorax follows extension of the disease to the pleura, rupture of the membrane, or rupture of a bleb.

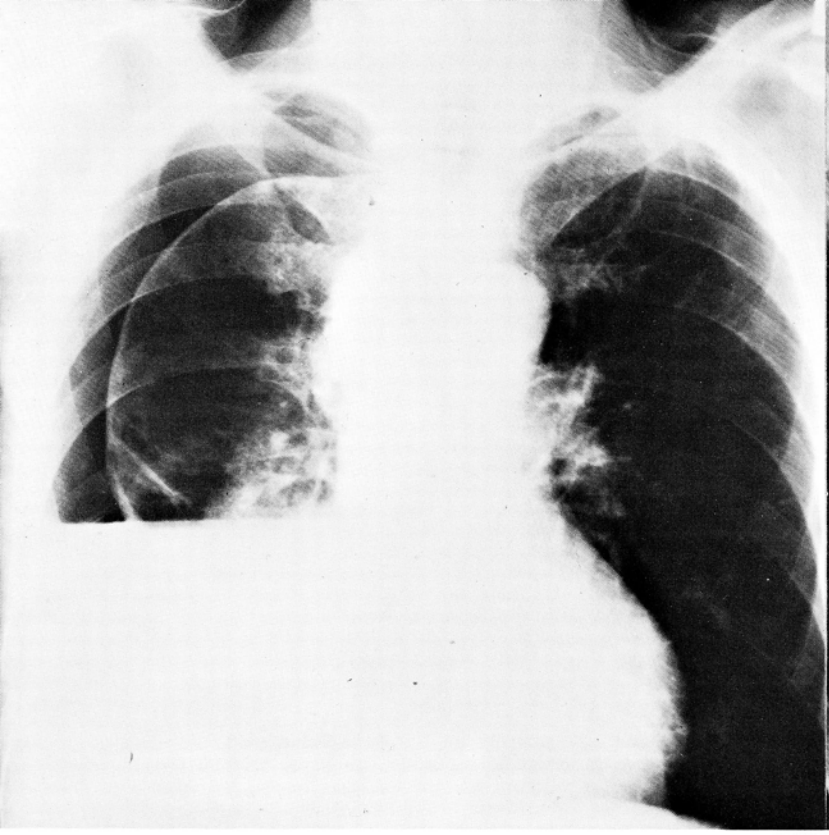


Fig. 1—Right hydropneumothorax and paratracheal mass.

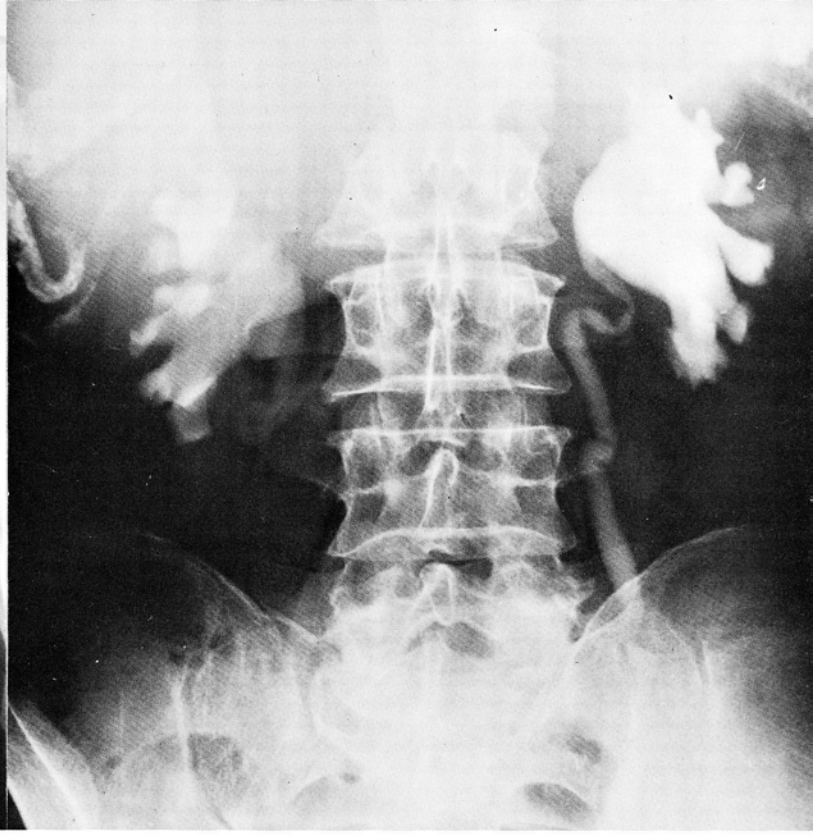


Fig. 2—Bilateral hydronephrosis.

Solitary excavated masses may be due to: 1) excavating granuloma associated with bacterial, fungus or yeast infection, including brucelosis; 2) parasitic disease such as amebiasis, hydatidosis and paragonimiasis; 3) infection or hemorrhage into a pre-existing cyst; 4) necrotic solitary pulmonary infarct; 5) excavating pulmonary hematoma, and 6) lymphomatous deposits, particularly Hodgkin's disease. Multiple excavating lesions may be predominently solid or predominently excavated and the combination of scattered solid and excavated lesions, particularly when they all tend to be of approximately the same size is suggestive of metastatic disease. When the lesions are small, the possibilities include: 1) embolic abscesses; 2) varicella pneumonia; 3) tuberculosis; 4) fungus infection; 5) rheumatoid arthritis; and 6) Wegener's granulomatosis. Theories explaining the mechanism of excavation are: 1) Avascular necrosis (rapid tumor growth outstripping available blood supply: tumor thrombosis or embolism of neighboring vessels and lack of production of new vessels by tumor). When communication with a bronchus ensues necrotic material is discharged leaving a cavity. 2) Ingrowth of malignant cells in a pre-existing cavity which may be congenital or the result of bronchial obstruction with distended air spaces distally. 3) Cystic liquifascient necrosis. According to Liebow, 20% of epidermoid tumors of the lung have broken down by the time the patient comes to autopsy. The most common tumors which metastasize to the lung are: carcinoma of the stomach, breast, lung, prostate, colon, thyroid, pancreas, liver, adrenal, kidney and gonadal tumors.

Dr. Viamonte's impression: MALIGNANT PULMONARY TUMOR

Roentgenologic Impressions Submitted by Mail

Bronchial carcinoma	38
Mesothelioma	27
Metastatic carcinoma	12
Carcinosarcoma	8
"Lymphoma" (sic)	6
Others	5

Dr. Viamonte: A bronchial carcinoma was certainly a likely possibility. It bothered me that there was a mass in the lung that was excavated, unless it was a loculated effusion in the pleural cavity; in that case a mesothelioma certainly should be considered. However, mesotheliomas, when they spread into the mediastinum usually spread in surface and I thought that the PA view of the chest revealed a distinct mass in the right hilar region suggesting metastatic nodes which is not usual radiographically. Metastatic carcinoma and carcinosarcomas, we mentioned as a possibility; I could not relate the abnormalities in the intravenous urogram with the lungs; I think that this additional IVP study was a red herring.

Dr. Regato: Dr. M. Daves, of Denver, Dr. J.F. Wilson, of Colorado Springs, and Dr. P.J. Hodes, of Philadelphia, all offered an impression of carcinoma of the bronchus.

Subsequent history: The patient underwent an orchectomy on April 8th and a transurethral resection on June 17th; he expired on July 27, 1966. The autopsy revealed residual adenocarcinoma of the prostate. An extensive, poorly demarcated neoplastic process filled the mediastinum, the pericardium and the right pleural cavity. Most of the tumor was firm and gray-white in color; there was a 4 x 4 x 4 cm portion occupying the apex of the right lung. The left adrenal gland was the site of a metastasis.

Dr. Liebow: Both the body wall and the lung are involved. The tumor is composed in part of masses of spindle-shaped cells, and in part of tissue with the appearance of epithelium. For these reasons the major problem in differential diagnosis lies between primary carcinoma of the lung and pleural mesothelioma. Primary mesothelial tumors that are even in part epithelial like, almost always tend to involve the pleura diffusely. Thus the absence of such involvement would greatly tend to favor a diagnosis other than mesothelioma. Asbestosis bodies are not found. These are more likely to be associated with mesothelioma than with cancer of the

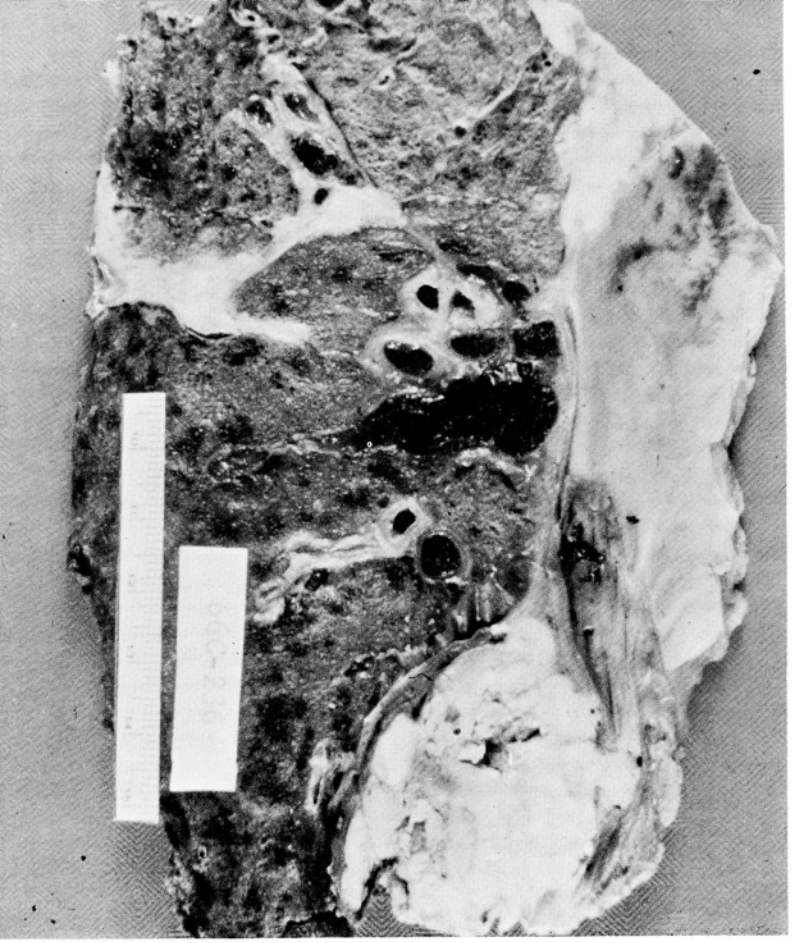


Fig. 3—Gross appearance of the mediastinal tumor at autopsy.

lung. Peripheral large cell tumors or adenocarcinomas of the lung, in contrast with well differentiated epidermoid tumors, will ordinarily have metastasized by the time the chest wall is invaded. This in itself does not necessarily rule out a primary lung tumor.

In the present case transitions are found from what are clearly epithelial cells to elements that resemble sarcoma. Thus there appears to be no merit in calling this tumor a carcinosarcoma. The former occur in masses many cells deep that seem to lie in spaces, but these may be remnants of alveoli rather than true acinar structures.

Fig. 4—Large cell carcinoma of the lung: Cell masses directly line alveoli, the lumina of which are consequently reduced (X 400).

The PAS stain is negative. It therefore appears most reasonable to conclude that this is a large cell undifferentiated tumor, probably primary in the lung.

Dr. Liebow's diagnosis: LARGE-CELL CARCINOMA OF THE LUNG

Histopathologic Diagnoses Submitted by Mail	
Mesothelioma	36
malignant	15
Carcinoma of the lung	27
Undifferentiated carcinoma	16
Rhabdomyosarcoma	15
Melanoma	11
Fibrosarcoma	8
Others	22

Dr. Liebow: Considerable numbers thought that this was carcinoma of the lung but a rather surprisingly large number thought that this was a mesothelioma. The main argument against that is twofold: there is not diffuse invasion of the pleura in the beginning and the careful search of that portion of lung which was available revealed no asbestosis bodies. A careful search will reveal the presence of asbestosis in a considerable proportion of patients with mesothelioma of the lung, not in the tumor, but more commonly in the lung itself. No such things were found in this case. Rhabdomyosarcoma, melanoma, and fibrosarcoma do not grow along alveoli in the acinar-like pattern of the present tumor. The absence of PAS-positive material is against rhabdomyosarcoma.

Dr. Regato: Dr. D. Dawson, of Colorado Springs, also made a diagnosis of carcinoma of the lung, giant-cell type. Dr. J.B. Frerichs, of El Paso, offered sarcoma, "mostly fibro, but somewhat like rhabdos." Dr. W.J. Holoday, of Columbus, Ohio, suggested malignant melanoma and Dr. J.M. Woodruff, of Denver, malignant mesothelioma.

Dr. Viamonte: I would like to ask if this is a truly excavating tumor when first seen and what was the pathogenesis of the pneumothorax.

Fig. 5—General view of the epithelial component of the tumor bordering upon lung tissue peripherally (X 25).

Fig. 6—Reticulum stain to demonstrate altered residual walls of alveoli. The reticulum fibers do not penetrate among the epithelial cells (X 300).

Fig. 4

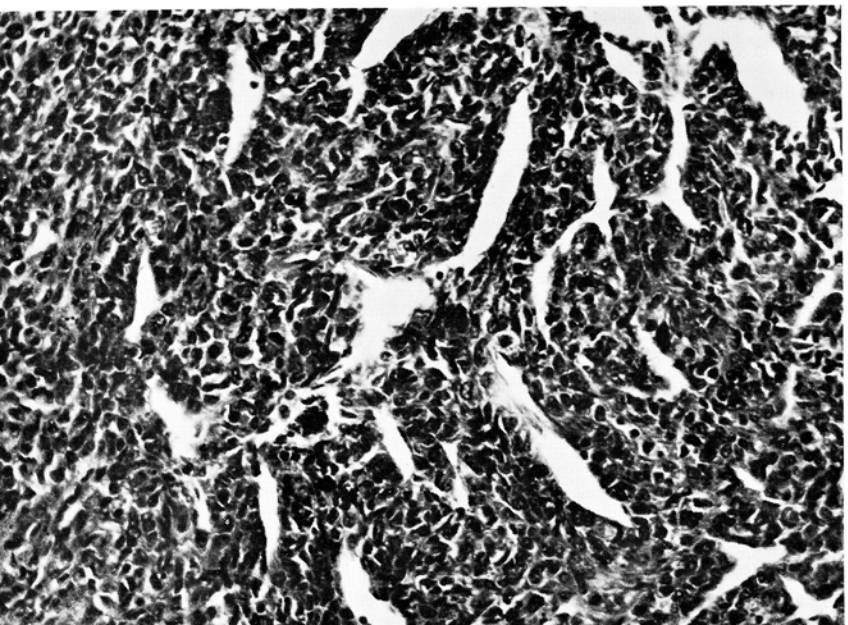


Fig. 5

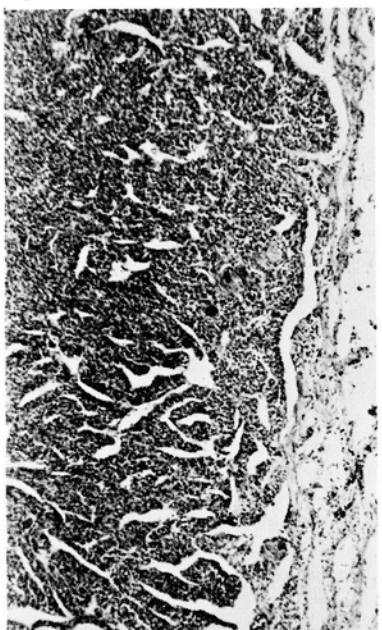
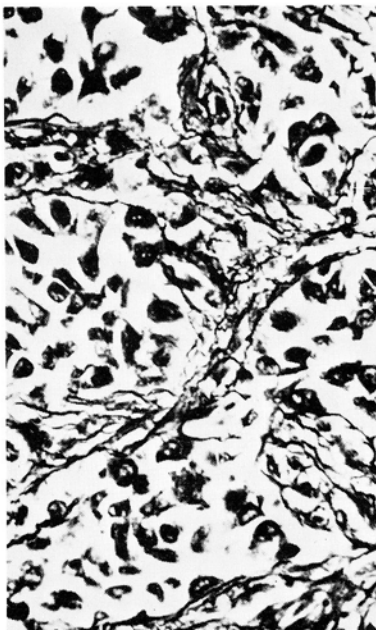


Fig. 6



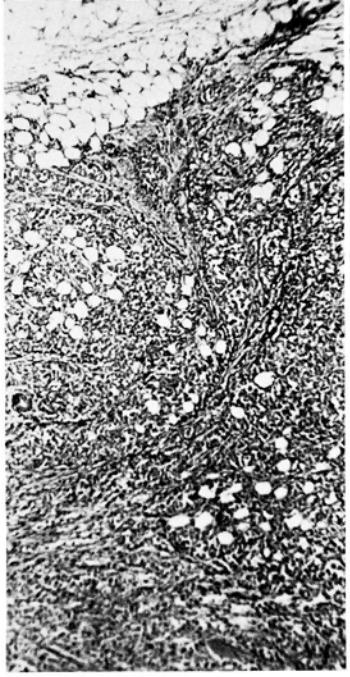


Fig. 7

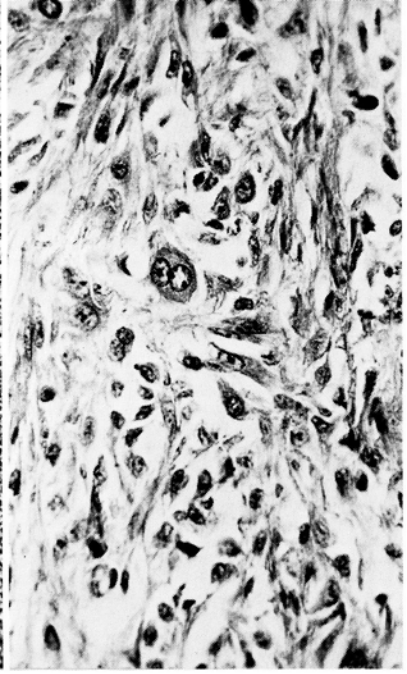


Fig. 8

Fig. 7—Invasion of chest wall by rounded and spindle-shaped cells (X 25).

Fig. 8—Spindle-celled component of the tumor. The cells resemble those of a sarcoma. One large element is binucleated (X 300).

R. Stanford, M.D., Denver, Colo.: At autopsy there were two types of tissue grossly involved in this lesion; the white tissue which involved the pleura along the medial surface of the right lung and then the large nodule, which in the fresh was yellow. These tissue types were very different and gave rise to some speculation as to whether this was indeed a single type of tumor or whether there were two components. I presume that the cavitation was due to marked necrosis in the center of one large nodule in the upper right. There was no evidence of asbestos bodies or granulomas in any of the sections examined. Another interesting feature of this case is the present of well differentiated adenocarcinoma of and limited to the prostate; so we have a case of two or three malignant neoplasms in a man who died, not of any of them, but of coronary thrombosis.

Dr. Pool: I have never seen pneumothorax, other than iatrogenic, in mesotheliomas. As far as I know, carcinoma of the lung is much more likely to be associated with other primary carcinomas; perhaps ten percent of all cases of lung cancer will be found to have another primary elsewhere. I was not aware of the association being this high except among older men; prostatic carcinoma one would expect to find at least in perhaps fifteen to twenty percent of patients who are 77 years old.

Dr. Regato: In other words, if a man lives long enough and he smokes long enough he can have both.

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8. *Neuroblastoma*

Contributed by R.D. Schultz, M.D., K.H. Wegner, M.D., R.T. Weaver, M.D., J.F. Barlow, M.D., D.M. Lang, M.D., and B.T. Pitt-Hart, M.D., Sioux Falls, South Dakota

THE PATIENT was an 11-year old girl in August, 1966, when she complained of anorexia and of a recurrent painful swelling of the left side of the chest wall, posteriorly. Examination revealed a wide-based watchglass-like tumefaction, raised 2 cm over the surface of the posterior chest wall at about the level of the 8th rib; there was dullness to percussion of the left pulmonary base. There were 13,300 WBC per mm^3 with 72% polymorphonuclears; the sedimentation rate was 45 mm per hour.

Dr. Viamonte: Frontal chest roentgenogram reveals a large left pleural effusion and no signs of lung or cardiovascular involvement. The left ribs, left scapula and thoracic spine cannot be evaluated adequately because of lack of bone detail.

Pleural effusion in an 11 year old patient with a soft tissue mass in the chest wall may suggest an inflammatory process such as actinomycosis. However, the lack of fever and of a fistulous tract and rarity of this disease in children would persuade me to depart from this diagnosis. The 13,300 WBC per mm^3 with 72% polymorphonuclears and a sedimentation rate of 45 mm per hour might suggest an inflammatory process. Malignant tumors, however, may present with this same picture. Round cell sarcomas, among the primary malignant bone tumors (Ewing's sarcoma being the most frequent one which often simulates an infection), neurogenic tumors (particularly neuroblastoma), lymphoma, and primary malignant pleural tumors are possibilities to be considered in this case. Other possibilities: A) Thoracic Wall Lesions: (Malignant melanoma, chondroma, fibrous dysplasia, hemangioma, osteomyelitis, eosinophilic granuloma, metastasis from neuroblastoma or osteosarcoma). B) Pleural lesions: (Hemangio-endothelioma, pleurisy, chylothorax, empyema, trauma).

Dr. Viamonte's impression: 1) ROUNDED-CELL SARCOMA, 2) NEUROBLASTOMA, 3) ACTINOMYCOSIS

Roentgenologic Impressions Submitted by Mail

Ewing's sarcoma	28
Soft tissue sarcoma	12
Mesothelioma	11
Actinomycosis	10
Neuroblastoma	6
"Lymphoma" (sic)	5
Leukemia	4
Others	18

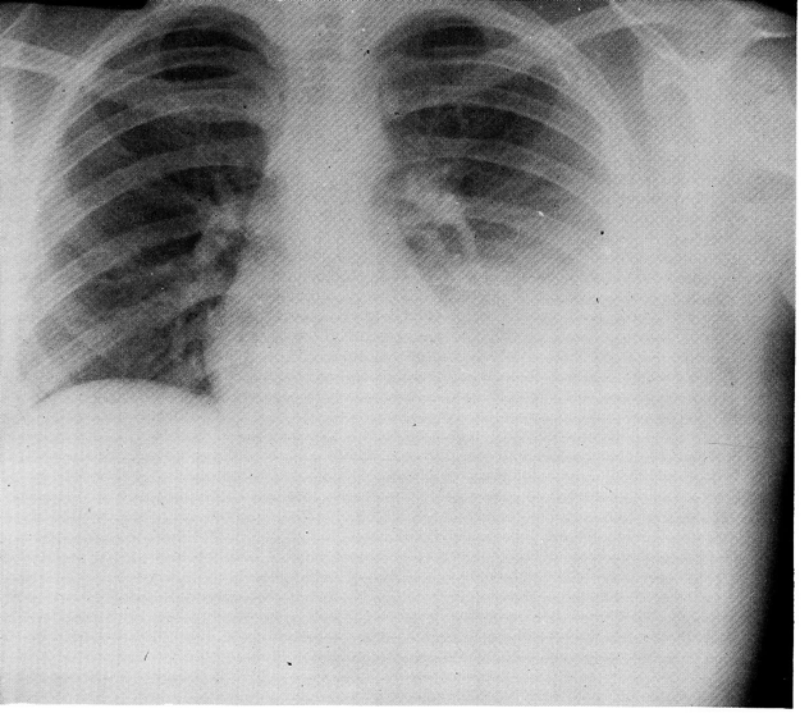


Fig. 1—Large left pleural effusion with no signs of lung involvement.

Dr. Viamonte: A Ewing's sarcoma certainly is the first bet of a round cell sarcoma, generally speaking. Mesothelioma is unlikely; I am not aware of a mesothelioma budding through the chest wall and accounting for a soft mass on the chest wall. We ruled that out on the basis of lack of fever. Neuroblastoma is also considered a round cell sarcoma; at the AFIP, round cell sarcoma is a basket where several histologic diagnoses fall into: Ewing's sarcoma, neuroblastomas, reticulum cell sarcomas and multiple myeloma.

Dr. Regato: Dr. B.L. Pear, of Denver, offered an impression of neuroblastoma. Dr. D. McFarland, of San Antonio, suggested actinomycosis.

Operative findings: On October 6, 1966, a left sided thoracotomy was done with removal of the sixth rib. Marked pleural adhesions were encountered; erosion of two lower ribs was noted. A lower lobectomy was attempted; the upper lobe bronchus was injured and anastomosis was unsuccessful: a total pneumonectomy was carried out. The left lung contained gray-white nodules protruding through the pleural surface; on section there was little normal lung remaining, most of it being occupied by tumor, necrosis or hemorrhage.

Dr. Liebow: Differential diagnosis in the present case lies between Ewing's tumor and neuroblastoma. That the differentiation may be difficult to make is suggested by the opinion of some of such high authority as Willis, who state that the lesions are identical. There are, however, tumors composed of plump or elongated spindle cells that involve bone with peculiar onionskin ossified elevations of periosteum, without evidence of origin in the adrenal medulla or of the sympathetic chain, that fit Ewing's original description. At least for the present it is well to maintain the concept that these represent a distinct entity. In children some of these involve ribs and the chest wall and extend into the lung. On occasion these can be removed surgically en masse with good clinical result (Lindskog).

In the present instance only "erosion" of the ribs is mentioned without the changes characteristic of Ewing's tumor in the periosteum. Histologically the arrangement and plumpness of the cells, as well as the lacy, indistinctly defined characteristics of the cytoplasm and the multiple foci of necrosis, are quite typical of neuroblastoma. The age of the patient is compatible with either diagnosis.

Dr. Liebow's diagnosis: NEUROBLASTOMA

Histopathologic Diagnoses Submitted by Mail

Neuroblastoma	63
Ewing's sarcoma	44
Sympathicoblastoma	9
Rhabdomyosarcoma	6
Others	12

Dr. Liebow: Neuroblastoma and Ewing's sarcoma, two conditions that are difficult to tell apart, represent the predominant opinion. Considering rhabdomyosarcoma, it is a great comfort to find striations but the diagnosis is always in doubt unless we do. These cells are larger and less well differentiated and have more vacuolated cytoplasm than rhabdomyoblasts.

Dr. Regato: Sister Joseph Ignatius, of Cincinnati, also made a diagnosis of neuroblastoma. Dr. M. Wheelock, of Miami, preferred sympathicoblastoma, Dr. W.J. Frable, of Richmond, Virginia, Ewing's sarcoma, and Dr. M. Berthrong, of Colorado Springs, embryonal rhabdomyosarcoma. This case was submitted to the AFIP (Accession 1229766). The report, prepared by Dr. S.H. Rosen, concluded to an undifferentiated malignant neoplasm, possibly a metastatic neuroblastoma.

Subsequent history: A mild course of post-operative radiotherapy was administered. Chest pains increased

Fig. 2—Neuroblastoma: Cell masses in radiating arrangement about focus of necrosis at the center. Septum of connective tissue at the periphery (X 200).

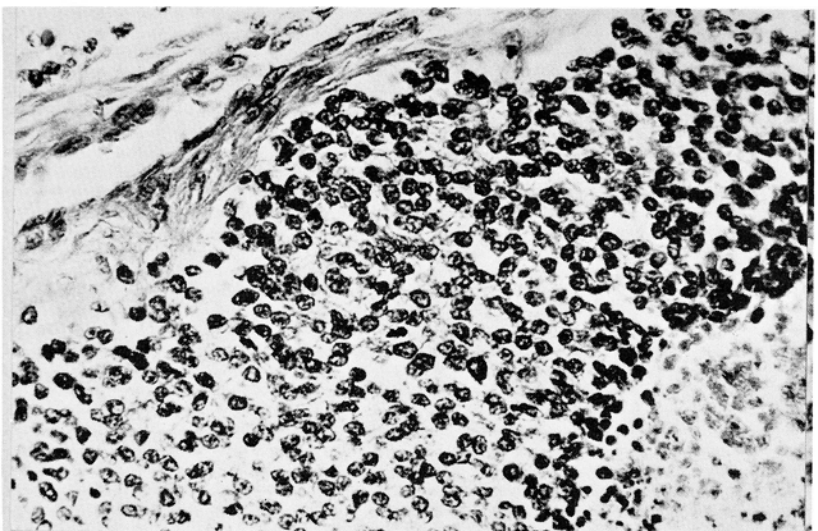
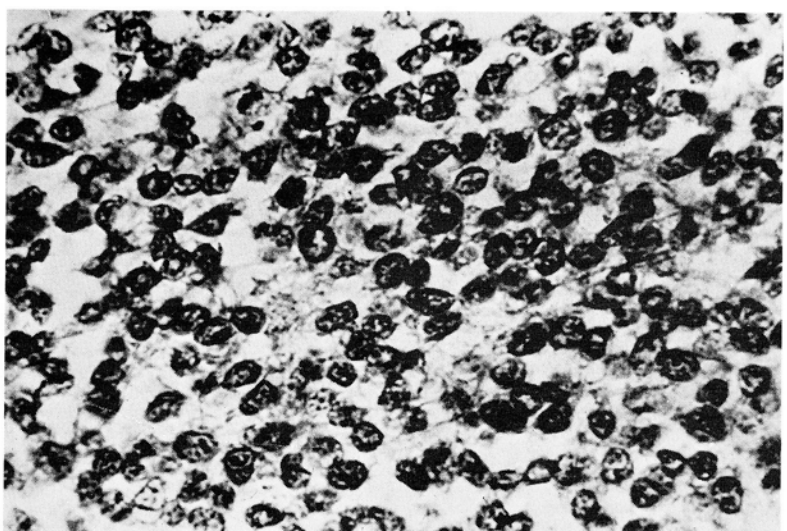


Fig. 3—Detail of typical rounded cells, some of which are in mitosis (X 400).



followed by vomiting and paraplegia. The patient expired on April 4, 1967. At autopsy the tumor was found in the mediastinum, right lung, left adrenal gland, para-aortic nodes and bone marrow.

Dr. Pool: This case emphasizes for the clinician the value of biopsy in planning treatment. Knowing as we now do the total course of the illness, maybe a thoracentesis or an incisional biopsy of the presenting chest wall mass would have established a diagnosis. I do not know whether the surgery provided as much palliation as combinations of chemotherapy and radiation therapy might have.

M. Wheelock, M.D., Miami, Fla.: Dr. Liebow, the implication is that a neuroblastoma arising in the sympathetic chain is against the adrenal? Is that the idea?

Dr. Liebow: I do not know how to distinguish these two tumors. I think the cells are of the same fundamental type. I do not know that there is any point in making any such distinction.

Question: Was a VMA done?

R. Schultz, M.D., Sioux Falls, S.D.: I do not believe VMA determinations were done. At the time, catecholemines were done several days after surgery and these were within normal limits. At the time of autopsy, the mediastinum was filled with tumor. The tumor in the left adrenal gland was a small focus of metastasis and not a primary. We feel it probably arose within the lung itself or maybe more likely within the mediastinum, with secondary lung involvement.

L.M. Lowbeer, M.D., Tulsa, Okla.: A diagnosis of neuroblastoma can sometimes be made from the bone marrow; cells are found which may resemble those of a lymphoblastoma but which often have arrangements characteristic of neuroblastoma.

F. Buschke, M.D., San Francisco, Calif.: The differential diagnosis between a neuroblastoma and a Ewing's sarcoma, from the clinician's point of view, is extremely important. Sometimes we can help the pathologist with adequate radiographic data; this was, of course, insufficient for interpretation radiographically. If the patient shows extensive disease and has Ewing's sarcoma, the prognosis is, of course, hopeless. This patient was hopeless anyway, apparently. But we have seen patients with neuroblastoma who had metastatic disease in bone, liver and other organs and still made a spontaneous recovery; this happens more often than it is suspected. One of my associates has reported a group of thirty patients; 25% that had advanced disease spread in bones or liver and had apparently spontaneously recovered. I have two patients who seemed to be inactive for ten years; one of them had a demonstrable ganglioneuroma which became active again after twelve years and finally the patient died. I think it is important to realize that some of these can spontaneously regress to a point of cure. In patients with advanced neuroblastoma we treat only the critical foci, for instance, and then leave the patient alone hoping that nature would take care of the rest.

Dr. Regato: It all depends upon how deadly the treatment is. If the patient receives too much of that aggressive chemotherapeutics, he may not make it.

Dr. Liebow: The distribution of the lesion found at necropsy, especially the involvement of one adrenal, favors the diagnosis of neuroblastoma. In regard to spontaneous recovery of neuroblastoma a surgeon named Harvey Cushing and a pathologist, Bert Wolbach, reported in the middle 1920's a case in which on subsequent biopsy, neuroblastoma gradually transformed itself into a ganglioneuroma apparently maturing with the patient with a recovery.

Dr. Regato: There have been others reported in the literature and for that matter, neuroblastomas which had metastasized to the liver have also been controlled by radiotherapy.

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9. *Wegener's Angiitis and Granulomatosis*

Contributed by A.W. Gottmann, M.D. and J.C. Maisel, M.D., Denver, Colorado

THE PATIENT was a 44-year old woman in January, 1968, when she complained of cough, malaise and weight loss. Examination revealed some flatness to percussion of the mid right lung field and râles in the right base; there was no significant adenopathy, no hepatomegaly or splenomegaly; the temperature was 103 degrees F., at night. There were 5,000 WBC per mm 3 with a normal differential; the sedimentation rate was 2mm per hour. Bronchosocopy uncovered no abnormalities; the bone marrow was normal.

Dr. Viamonte: Frontal and lateral views of the chest reveal multisegmental infiltrates involving particularly the anterior segment of the right upper lobe, right middle lobe, and posterior segment of the right lower lobe with a distinct air bronchogram. An azygos lobe is an incidental finding. No abnormalities are observed in the remainder of the chest.

The typical alveolar pattern (disseminated pulmonary infiltrates with ill-defined margins, coalescence, and air bronchogram) seen on the roentgenogram and the patency of the bronchial tree corroborated by the negative bronchoscopic examination indicates that we are dealing with a multisegmental disease process involving the peripheral portion of the airways. The possibilities are: 1) Malignant process: broncho-alveolar carcinoma and lymphoma. 2) Benign process: pneumonitides, granulomatous diseases, histiocytosis, alveolar proteinosis, hyaline membrane disease, alveolar microlithiasis, and conditions which cause hemorrhage, edema, infiltration, focal atelectasis, fibrosis or combination of these.

The presence of fever; of a low total white blood cell count; normal differential, sedimentation rate, and bone marrow, aspiration studies should rule out bacterial and mycotic infections, and malignant tumors. The fact that

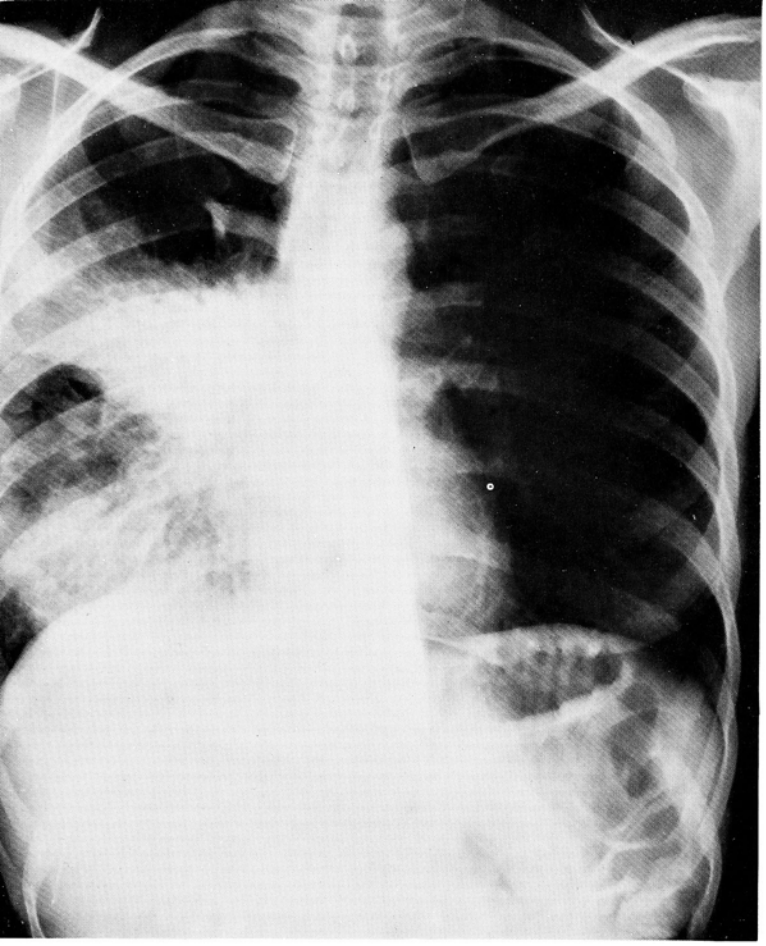

Fig. 1—Infiltrates of the three right pulmonary lobes.

Dr. Liebow is the arbitrating pathologist makes me favor a non-malignant process such as one of the interstitial pneumonias. Interstitial pneumonias may be acute or chronic, and focal or diffuse. They are classified into five types: 1) Usual or classical (UIP). 2) Bronchiolitis obliterans with diffuse alveolar damage (BIP). 3) Desquamative (DIP). 4) Lymphoid (LIP), and 5) Giant cell (GIP). Of these, multilobar pneumonitides with patent bronchial tree, and with unassociated pleural effusion, cavitation, and cardiovascular involvement, and presenting a wedge-shaped density, the desquamative interstitial pneumonia is a very likely possibility.

Dr. Viamonte's impression: 1) INTERSTITIAL PNEUMONITIS, 2) ALVEOLAR PROTEINOSIS, 3) ALVEOLAR LYMPHOMA

Roentgenologic Impressions Submitted by Mail

Alveolar carcinoma	35
Bronchial Carcinoma	28
Pneumonia	12
"Lymphoma" (sic)	5
Others	13

Dr. Viamonte: Bronchial carcinoma I would not consider. I would consider bronchio-alveolar carcinoma which is a peripheral type of bronchial neoplasm. This could not be a lobar pneumonia; it would have to be a peripheral type of pneumonia where the central airways are patent. Alveolar lymphoma is a distinct possibility.

Dr. Regato: Dr. E. Salzman, of Denver, offered bronchiolar-cell carcinoma; Dr. J.F. Wilson, of Colorado Springs, preferred alveolar-cell carcinoma. Dr. P.J. Hodes, of Philadelphia, suggested Rickettsial pneumonia.

Operative findings: On January 11, 1968, a thoracotomy was done: portions of the anterior segment of the right upper lobe and of the superior segment of the lower lobe presented a blue-gray discoloration and appeared firm but not nodular. Surgical specimens were removed for biopsy.

Dr. Liebow: The significant changes are those of angiitis associated with focal necrosis of the lung, but often also without involvement in the necrosis but rather related to an infiltrative process predominantly of mononuclear cells. The latter often are bizarre.

The angiitis is best brought out in elastic stains. Both arteries and veins are involved, but the changes predominate in the latter. In the elastic stains it is evident that at the sites of involvement the continuity of the membranes has been focally, and in some instances subtotally, interrupted. The lumina of many of these vessels are restricted by accumulations of the same types of cells as infiltrate the pulmonary parenchyma. This process may be extensive without thrombotic occlusion of the vessels but with a lifting of the endothelium. In the elastic stains especially it is clear, however, that many vessels have been totally occluded by progression of this infiltrative process. The outlines of these vessels can only vaguely be discerned in other than the elastic tissue stains. There is evidence also of infiltration of the walls of bronchi and bronchioles, with focal loss of epithelium, and these structures also are involved in the necrotizing process.

The cells that infiltrate the vessels, bronchi and inter-alveolar septa, and which in many places also fill the alveoli, in large part consist of "plasmacytoid" elements. Some of these are typical plasma cells, but others are intermediate between plasma cells and larger reticulo-endothelial elements. Still others are rather bizarre and contain irregular nuclei and in some instances prominent nucleoli. Occasional mitoses are found. In addition there are various types of large mononuclear cells, some of which may represent proliferated alveolar lining cells, but others of which may be phagocytic pneumocytes or reticulo-endothelial ancestral forms. The appearance begins to approach that of lymphoma or neoplasm of reticulo-endothelial tissue.

Foci of necrosis are associated with only minor degrees of hemorrhage, if any. In many instances occluded vessels with subtotally necrotic walls can be found within or in relation to these foci of necrosis which thus have the appearance either of granulomas or of "white infarcts". Despite the necrosis, however, polymorphonuclear leucocytes are only rarely associated with these lesions. Eosinophils are exceedingly rare.

These lesions are similar, if not identical, with those of Wegener's granulomatosis of the lung. Since these have not been associated with involvement of the upper respiratory tract, nor with focal glomerulonephritis, we have referred to such cases as "Limited Forms of Angiitis and Granulomatosis of Wegener's Type" (Am. J. Med. 41: 497-527, 1966). We have seen tissue from approximately fifty patients with this condition. In addition we have observed material from an additional fifteen patients with an in many ways similar condition but with such atypical cells that distinction from reticulo-endothelial neoplasm has been problematical. Only in one of these has the disease progressed with involvement of lymph nodes, as in reticulum cell sarcoma.

In the "limited" form of Wegener's granulomatosis, the process can be confined to the lung but can also involve the kidney in a focal manner identical to that of the lung and without glomerulonephritis. In the

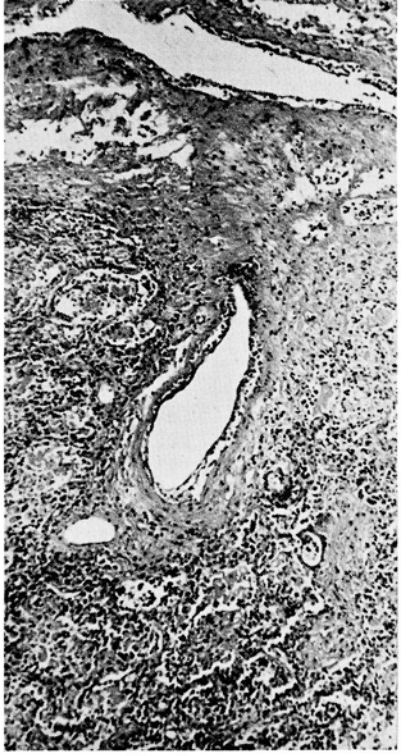

Fig. 2

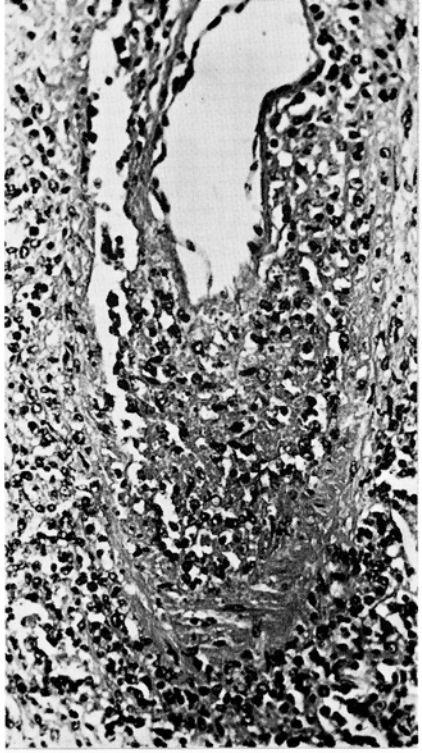

Fig. 3

Fig. 2—"Lymphomatoid" variant of Wegener's granulomatosis: There is a mass of necrotic tissue infiltrated with atypical lymphoid and plasmacytoid cells surrounding a small artery. The endothelium of the latter also is elevated by similar cells. A vein at the right of the photograph is similarly involved (X 25).

Fig. 3—Atypical plasmacytoid cells surround and infiltrate a largely necrotic artery. These cells lie within a granular acidophilic material between the endothelium and the media (X 250).

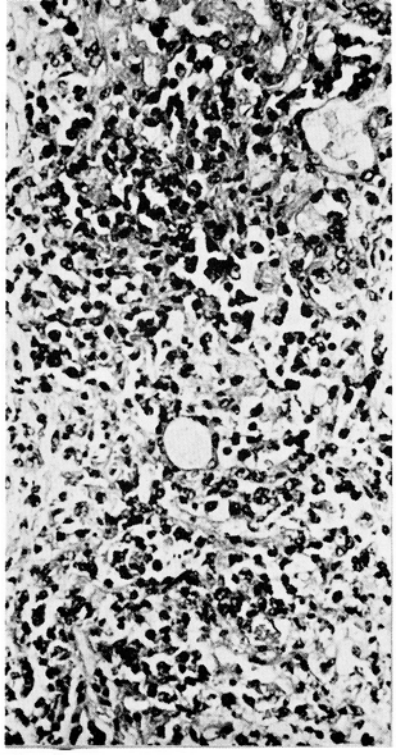

Fig. 4

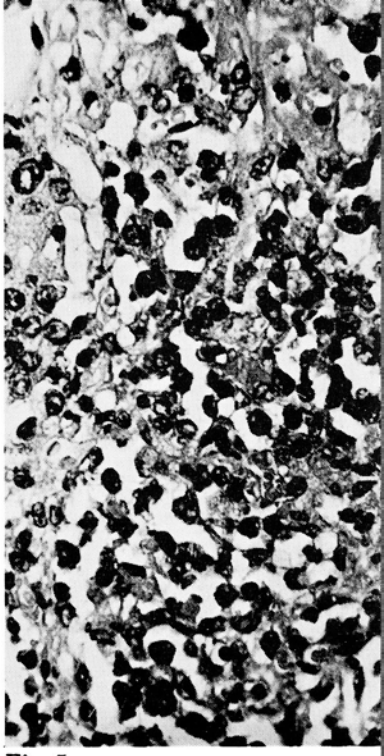

Fig. 5

Fig. 4—Necrotic tissue with lymphomatoid infiltrate (X 250).

Fig. 5—Detail of lymphomatoid infiltrate. Some of the cells are atypical reticuloendothelial elements. Others are sm aller and have plasmacytoid characteristics, i.e. eccentric nuclei with coarse, radially arranged chromatin segments, and vacuolated basophilic cytoplasm (X 400).

"lymphomatoid variant" the kidney also may contain infiltrates of bizarre cells with hyperchromatic nuclei and predominantly basophilic cytoplasm in active proliferation.

In our series the patients have been of either sex and most of them have been middle aged. The disease may pursue a fulminant course, but in some patients appears to have responded to adrenal corticosteroid or azothiaprine therapy, with remission for as long as 13 years, or possibly cure.

It is now evident that the limited form is much more common than the classical form of Wegener's granulomatosis, and that indeed the former is not rare. It is noteworthy that the condition may be entirely asymptomatic, despite the presence of massive necrosis as seen in biopsy material. In such patients lesions are discovered in roentgenograms, where they usually appear as multiple, rounded masses involving predominantly the lower portions of the lung. They resemble metastases, but are less sharply circumscribed.

As to etiology, nothing is known at present. In most instances there is no evidence of dysproteinemia, a finding somewhat against an allergic pathogenesis for the condition. All efforts to demonstrate bacteria and fungi have failed. It is entirely possible, however, that the disease may be of viral etiology. Such an etiology may bring it into line with such conditions as "Burkitt's lymphoma", where an apparently neoplastic process has been shown to contain a herpes-like virus. It is fair to state, however, that the causative relationship of such viruses has been questioned.

Dr. Liebow's diagnosis: WEGENER'S ANGIITIS AND GRANULOMATOSIS (limited lymphomatoid variant)

Histopathologic Diagnoses Submitted by Mail

Desquamative interstitial pneumonitis	33
Pneumocystic carinii pneumonitis	14
Chronic organizing penumonia	7
Cholesterol (lipoid) pneumonia	14
Plasma-cell pneumonia	5
Hair spray inhalation!	1
Carcinoma	31
Others	21

Dr. Liebow: The variety of diagnoses submitted reflects the handicap of not having elastic stains in hand. The usefulness of this procedure cannot be overestimated in depicting both the location of vessels and the degree of damage to their walls. Among the diagnoses submitted I think that desquamative pneumonia can be ruled out in this case of very heterogeneous infiltrate with such radiographic findings. The polymorphous cellular population and the necrosis should at once rule out DIP. The presence of a cholesterol pneumonitis is to be expected whenever there is obstructive bronchial disease; it is not specific at all. One can get this kind of obstruction from infections or sometimes from non-infectious causes, even tumor. Enlargement of tumor cells accumulate behind the obstructed bronchioles. Certainly, bronchi are involved and, therefore, it is not surprising to find considerable numbers of fat-filled phagocytes. This is simply symptomatic of bronchitis and nothing else. It is of interest that some pathologists diagnosed "plasma cell pneumonia", or *Pneumocystis carinii* pneumonia, surely not on the demonstration of organisms, but rather on the presence of plasmacytoid elements.

Bronchial obstruction consequent to infiltration or necrosis with subsequent partial healing accounts for focal accumulations of fat-filled phagocytes, which some have called "cholesterol (lipid) pneumonia". Lipoid and cholesterol pneumonia should be considered the same if they are endogenous. In those cases that have been previously reported as cholesterol pneumonitis, careful examination always shows a bronchial obliteration probably resulting from bacterial superinfection of an original viral disease in the lung. To my knowledge no proof exists of permanent damage to lung by ordinary hair sprays. The basis for the diagnosis of carcinoma is unclear. The degree of atypical epithelial proliferation seen in this patient is to be expected where there has been so much damage and repair to the lung.

Dr. Regato: Dr. F.P. Bornstein, of El Paso, made a diagnosis of malignant reticuloendotheliosis plus lipoid pneumonia. Dr. B. Castleman, of Boston, offered chronic pneumonitis with lipid changes. Dr. R.D. Schultz, of Sioux Falls, preferred desquamative interstitial pneumonitis. Dr. R. Lattes, of New York, suggested a diagnosis in a single word: *ameba!*

In February, 1968, Dr. Robert A. Vogel, of Denver, submitted this case to Dr. A. Liebow. The following is a paraphrase of Dr. Liebow's letter: 1. The appearance is not one of *desquamative interstitial pneumonia*; in DIP the alveoli are filled with massive numbers of predominantly granular pneumocytes but the cells do not become vacuolated to the extent and the blood vessels do not contain large mononuclear cells, as observed in this case. 2. There is no clearly evident *bronchiolar obstruction* by large cells containing fat, although that seems to be part of the mechanism here. 3. A *diffusively invasive epithelial neoplasm* could produce an extensive interstitial reaction with increase in the height of the cells that line the alveoli, but the foamy material in the large cells does not contain mucin; we must conclude that it represents lipid. There remains to be prominently considered 4. *lymphoma*, 5, *lymphomatoid allergic pneumonitis* and 6. *vasculitis*. Both in the lung and in the lymph nodes there is striking proliferation of what appear to be somewhat atypical mononuclear cells, which often resemble plasma cells, with numerous mitoses present. It is these cells that infiltrate the vessels and often fill their lumina, a process made clearly evident in elastic stains. I think lymphoma is not likely in the absence of mediastinal lymph node involvement and splenomegaly. The diffuse form of pseudolymphoma which we have called "lymphoid interstitial pneumonia" is not present here. A reasonable interpretation is that the atypical reticuloendothelial response, the angiitis and the granulomatosis, when they exist, represent components of an allergic response which may be found together or separately.

Subsequent history: Following the operation the patient improved markedly on steroid therapy. On January 21st she had a gastric hemorrhage, the steroids were decreased, the fever returned. She developed mediastinal emphysema causing dysphagia and on February 2, 1968, she expired.

At autopsy the right lung was found to be firm; its alveolar septa were uniformly thickened by a dense infiltrative and proliferative reaction with obliteration of the alveoli by large granular macrophages and fibrinoid material. The lining of the thinned-out bronchioles was preserved. Large clumps of bacteria were occasionally found among the cells. The material in the cells was sudanophilic, stained negative for iron and was P.A.S. positive. Giemsa stains revealed cocci and rod bacteria in both lungs. There were raised nodules on the surface of the kidneys. On microscopic examination these nodules were found to be composed of sheets and cords of infiltrating bizarre, multiform cells with eosinophilic nucleoli and occasional mitoses, surrounding areas of necrosis. The same cells were found in the thickened wall of the terminal ileum and in the mesentery. The cellular elements of the bone marrow were for the most part replaced by loose connective tissue; the overall cell-fat ratio was less than 1 to 9.

Dr. Pool: Cytologic studies will often give you the diagnosis if you are dealing with exogenous lipoid or with alveolar cell or terminal bronchial lung cancer. The radiologist does not seem to be able to help much any more. I would like to propose to the pathologist that the surgeon at one sitting proceed in an orderly way with diagnostic procedures until appropriate pathology is arrived at: first, a scalene fat pad biopsy; if no pathology is encountered, a mediastinal biopsy, either the scope or through a small anterior incision; if a diagnosis is still not achieved, with the patient still under anethesia, a biopsy of the lung should be dome so that the surgeon, in teamwork with the pathologist, does not leave the operating room until tissue diagnosis is achieved. It is also very important that another ally, the microbiologist, be brought into the picture because to take out a piece of lung and not to culture it is indeed sinful.

P.J. Hodes, M.D., Philadelphia, Pa.: Actually, I am a little amused by John Pool, who said he got no help from the radiologist. Dr. Viamonte told him exactly what it was and he told him what it was not. The only thing that Dr. Viamonte could not tell him was that there were amoeba or Rickettsia there. Dr. Liebow comes along and talks about angiitis. Of course, I can visualize the angiitis being the result of some organism somewhere and until the microbiologist has really gotten into this I really do not know where we are. As far as the alveolar proteinosis, in my experience, it has been more often bilateral.

J. Maisel, M.D., Denver, Colo.: The autopsy findings which followed the last clinical detail by about one week were submitted to Dr. Liebow. With our finding of the nodules in the ileum and kidney we felt we had come upon a lymphosarcoma arising in the ileum and involving the lungs only secondarily. The pertinent findings were very heavy lungs which had been destroyed in part by a bacterial process superimposed and very little additional information.

Dr. Regato: But your diagnosis was a malignant lymphoma of the terminal ileum with metastasis. Is that right?

Dr. Maisel: Correct.

Dr. Liebow: It is of interest that some of these patients who have had the limited form of Wegener's have carried the diagnosis of lymphoma for as long as thirteen years. By limited, it is meant that the lesions are not those of the classical kind; some of these patients, both of the limited form and of the lymphomatoid variant have had lesions in the skin as the primary manifestation of the disease with very little evidence of involvement of the lung. One of our patients carried the diagnosis of lymphoma for a very long time and did have involvement also of the intestine focally; the process is very similar to what is seen in the lung, not only this peculiar infiltrate that some diagnoses as lymphosarcoma and others as a kind of tissue response. The debatable character of the pathology in this case is well brought out in

the lesions found at necropsy, which are indeed similar to those in some other patients. Here the bizarre, but still plasmacytoid, characteristics of the reticulo-endothelial cells in the lesions of the kidney, ileum and mesentery could well suggest neoplasia. In other instances, with a smiliar distribution of the lesions, the cells have been less bizarre and more like those of ordinary plasma cell infiltrates as seen in the classical forms of Wegener's granulomatosis. The query may be raised of whether the process represents "lymphomatoid Wegener's granulomatosis", or "lymphoma with angiitis and granulomatosis". Of the greatest theoretical interest is the question of whether an immunological disturbance, or possibly a viral infection, could express itself on the one hand in an angiitis and associated necrotizing lesions, and on the other in atypical proliferation, or even "neoplasia" of cells of the reticulo-endothelial system.

M. Berthrong, M.D., Colorado Springs, Colo.: Dr. Liebow, with all of the plasmacytoid and plasma cells seen in variants of Wegener's, are there immunoglobulin derangements in the circulating blood?

Dr. Liebow: We have seen a considerable number of these patients and none have been found. This is rather disturbing, if one considers this an immune response of some kind, but those are the facts in cases that have been studied so far.

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10. *Mestastatic (?) Fibromyxoma*

Contributed by J. L. Kovarik, M.D., and E. P. Barlock, M.D. Denver, Colorado

THE PATIENT was a 46-year old woman in October, 1966, when she complained of dyspnea and metrorrhagia; one leg had been amputated at age 16 for "osteomyelitis."

Dr. Viamonte: The single frontal chest roetgenogram reveals partial collapse of the right lung to 1.5 cm from the chest wall. A small amount of fluid in the right costophrenic angle, and at least five spherical nodules which average 1.4 cm in diameter. These nodules are seen some in the lung and some implanted in the pleura and projecting into the pleural cavity. The latter are best observed in the lateral view of the chest. A large right retrohilar mass is seen in both projections. Two of these nodules have a rim of calcium and one appears denser in its central portion. If all the lesions were in the lung one would have to consider the possibility of nonmalignant lesions such as granulomas and metastatic disease. Because some appear attached to the pleura, metastatic disease is the most probable diagnosis. The pattern of calcification suggests metastases from an osteosarcoma. Unilateral lung involvement in osteosarcomas is not uncommon (Jaffe). Late metastases have been reported although they are most unusual. The diagnosis of "osteomyelitis" at age 16 was probably wrong.

Dr. Viamonte's impression: MESTASTATIC OSTEOSARCOMA

Roentgenologic Impressions Submitted by Mail

Mesothelioma	25
Mesenchymoma	23
Metastatic carcinoma	10
Metastatic osteosarcoma	8
Others	22

Dr. Viamonte: It would be unusual for a mesothelioma to be present in the form of pulmonary nodules. In the radiographs sent to me there was a label of diagnostic pneumothorax; this is usually done in order to determine if the parietal pleura and the visceral pleura have metastatic nodules. I would not consider mesenchymoma because multiple nodular lesions in the lung, if anything, should make one suspect metastatic disease. Rare cases of sarcoidosis and Wegener's and some granulomatous disorders may appear as nodules but I would not consider mesenchymoma. Metastatic carcinoma is a possibility, however, two of these nodules had calcium and I want to insist on that. There is no question that they were denser in the center and had a rim of dense calcification; thus, I would not consider metastatic carcinoma; the only diagnosis for me is metastatic osteosarcoma.

Dr. Regato: Dr. L. O. Martinez, of Miami, suggested endometriosis of the lung. Dr. I. Friendlich, of Philadelphia, offered metastatic choriocarcinoma.

Operative findings: On November 28 and 29th, 1966, two consecutive thoracocenthesis brought 3000 cc of amber fluid. On December 2, 1966, a right thoracotomy was done: the right lung was occupied by several masses which were only partially excised. The removed fragments consisted of rounded masses of tissue, about 3 cm in diameter, with smooth cut surfaces and homogeneous pink color.

Dr. Liebow: This tumor has the structure largely of fibromyoma but there are within it also large masses of hyaline connective tissue. In places hyaline acidophilic material embeds rounded rather than stellate cells giving the appearance of osteoid tissue. Mitoses are few.

Mesothelioma is to be considered in the differential diagnosis, since such tumors may in part have a myxomatous or even chondroid structure. In the present case, however, multiple nodules are evident radiographically and it is probable that some of these are intraparenchymal. This would not be typical of mesothelioma.

It is entirely possible that the lesion for which the patient's leg was amputated thirty years ago was in fact not osteomyelitis, but rather a sarcoma of cartilage or bone. In that instance, despite the benign histological characteristics, the pulmonary lesion could represent metastases. An analogue is the so-called benign "metastasizing fibroleiomyoma" (Steiner). We have encountered

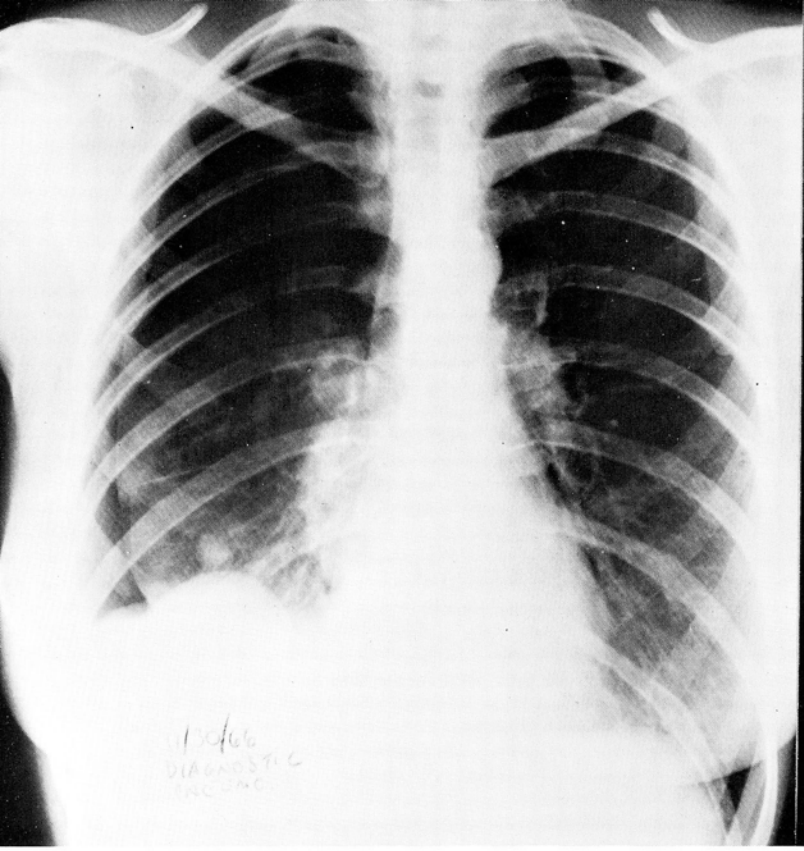


Fig. 1—Rounded nodules of the right lung with partial pulmonary collapse and pleural fluid.

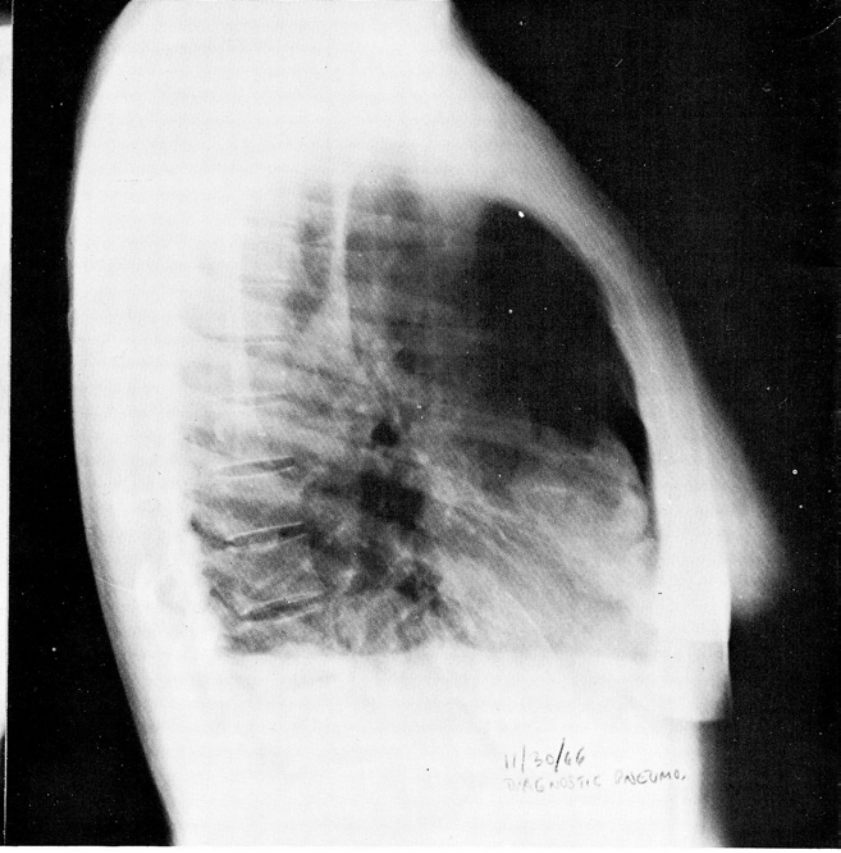


Fig. 2—Lateral view of the pulmonary nodules.

eight examples of this condition with bilateral slowly growing metastases. In all instances the patient either still had leiomyomata of the uterus or had had a hysterectomy for such tumors, in some instances many years previously. Remarkably the metastatic tumors had a benign appearance. Other examples of very late appearance of intrapulmonary metastases exist, as in melanoma, or even in rare instances in chorionepithelioma where the lesion may appear within the lung in the late fifties, long after the menopause.

While such late metastases are uncommon in malignant bone tumors, this appears to be the most reasonable possibility in the present case.

Dr. Liebow's diagnosis: METASTATIC(?) FIBROMYXOMA

Histopathologic Diagnoses Submitted by Mail

Osteosarcoma	38
Fibrosarcoma	14
other sarcomas	15
Neurileomoma	22
Fibrous mesthelioma	16
Malignant mesenchymoma	9
Fibromatosis	3
Others	20

Dr. Liebow: There is a preponderance of those who thought that this was osteosarcoma or fibrosarcoma; I presume the implication is that the lesion was metastatic from the bone. I do not think this lesion has many of the characteristics of neurilemoma. Fibrous mesothelioma is of interest because of the fact that there can be such foci in a true mesothelioma but the interparenchymal position is strongly against it. Fibromatosis, the state of proliferation of fibrous tissue which can involve many different organs, is another consideration in this case. The multinodular characteristic of this lesion is difficult to explain on any basis other than metastasis, except as "fibromatosis" or a form of "sarcomatosis". The myxomatous and osteoid appearance of the lesion, however, is less compatible with the former diagnosis than with late metastases from a bone tumor. A sarcomatosis can indeed have the structure of myxosarcoma.

Dr. Regato: Dr. J. H. Coffey, of Fargo, made a diagnosis of osteosarcoma. Dr. P. B. Visconti, of Denver, preferred fibrosarcoma or myxosarcoma. Dr. P. C. Dyke, of Denver, offered liposarcoma. Dr. R. R. Holloman, of Denver, saw it as a chondromyxosarcoma. Dr. M. Wheelock, of Miami, offered xanthofibroma. Dr. S. H. Choy, of San Francisco, neurilemoma. Dr. T. H. McConnell, of Dallas, offered mesothelioma as the correct diagnosis and Dr. R. E. Stanford, of Denver, simply fibrosis.

Subsequent history: Following the surgical intervention periodic roentgenograms revealed progressive increase of the residual tumor. On October 3, 1967, there was extensive involvement of the right hemithorax diaphragm and mediastinum. From October to December, 1967, she was irradiated with resulting diminution but no complete disappearance of the tumor. In August, 1968, the patient was in relative good health, performing her regular duties and maintaining her weight in spite of recurrences.

Dr. Pool: I would like to point out that we do not really have a clue as to the rate of the growth of this tumor. We had a case of solitary metastatic chondrosarcoma in a lung that, on serial films, had been growing for nine years before resection. In the next six years no others appeared.

J. Kovarik, M.D., Denver, Colo.: We could not get any more pertinent data on this history of osteomyelitis

Fig. 3—Gross appearance of one of the nodules at thoracotomy.

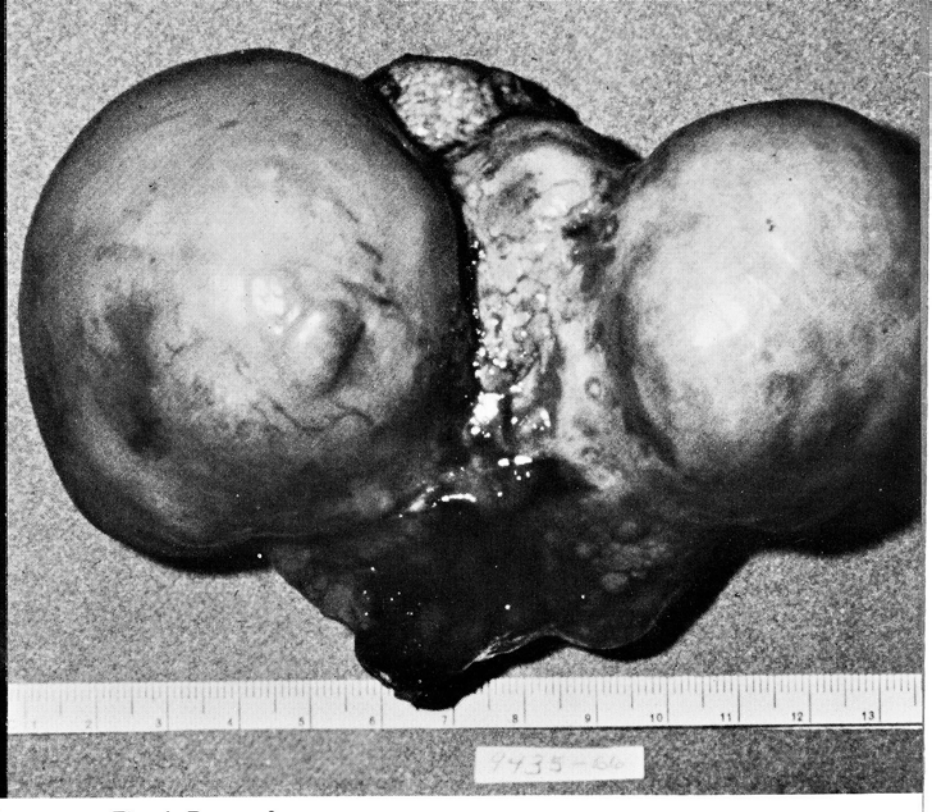


Fig. 4—Removed masses.

thirty years prior. However, there was a definite history of injury followed by chronic draining sinus and subsequent amputation. Prior to thoracotomy this patient had IVP's, barium enema and bilateral mammograms, all of which were interpreted as being normal. Likewise when she had the thoracentesis, the pleural cytology was negative; LDH was 450 units. The largest tumor, measuring 15 cm in diameter, was firmly attached and was excised from the diaphragm itself; grossly there was no evidence of intrapulmonary tumor. These were easily removed from the visceral and from the parietal pleura mostly in the lower half of the hemithorax. We like to get a chest film following thoracentesis. If this shows a pneumothorax and if the thoracentesis has been performed by one of our residents we criticize his technique. If I personally have done the thoracentesis, this is a "diagnostic pneumothorax". Since the last report, this patient has received another course of radiation therapy because of recurrence and some pleural effusion. She is now on Methotrexate. Her general condition is good but deteriorating; she is gradually loosing weight and has considerable pain.

L. Lowbeer, M.D., Tulsa, Oklahoma: Lichtenstein and Bernstein reported three cases of a tumor which, for lack of a better term, they call mesenchymous chondro-

Fig. 5—Metastatic osteochondrosarcoma of bone in lung: Atypical osteoid and chondroid tissue. Some of the vessels are stellate and lie within a myxomatous matrix (X 200).

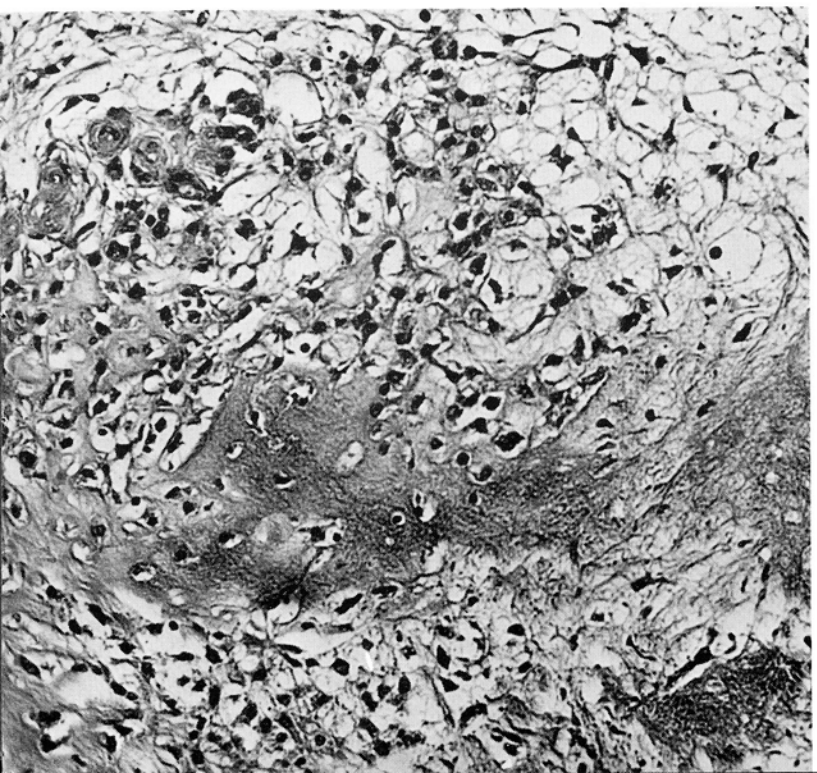
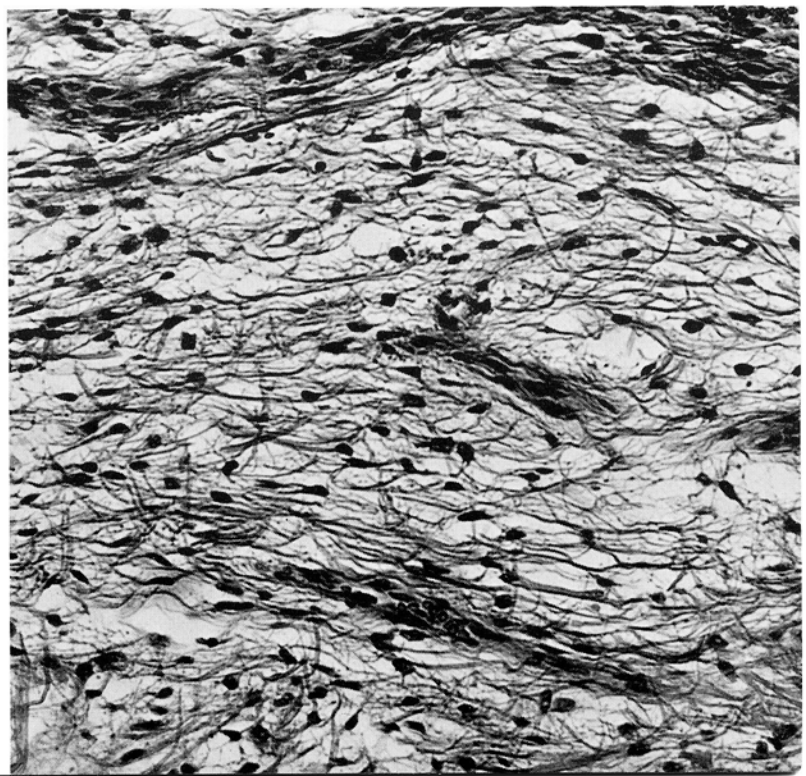


Fig. 6—Spindle celled myxomatous component of the tumor (X 400).



sarcoma. The structure was very similar to what we have seen here and they were characterized by the occurrence of a tumor in the bone and then 15, 20 or 25 years later by the occurrence of a similar tumor in another bone. The question here being whether that was a metastasis from the first tumor, or a primary, multicentric, chondrosarcoma. There is no question that some of these areas must have shown some calcification as the radiologists saw it. Regardless of what kind of origin this tumor has, it seems to belong to that same group and the characteristics are of very long intervals. Conceivably, this tumor could originate perhaps from a bronchus or from a cartilage of a rib if there is any local connection between.

Editor's note: This patient expired on January 11, 1969. No autopsy was obtained.

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11. *Pseudolymphoma (giant lymph node hyperplasia) of the Mediastinum*

Contributed by M. R. Abell, M.D., P. Scholtens, M.D.
and W. Martel, M.D., Ann Arbor, Michigan

THE PATIENT was a 24-year old woman in February, 1967, when she complained of dyspnea and chest pains of six months duration. Six years previously a "mediastinal tumor" had been diagnosed on a routine roentgenogram but she had refused surgery. On examination no abnormalities were found; laboratory procedures were non-contributory.

Dr. Viamonte: Frontal chest roentgenogram and frontal tomogram 8 cm from the posterior chest wall reveal a 4.5 x 5.5 cm non-calcified right paratracheal mass displacing the trachea to the left. No other abnormalities are observed.

Masses in this location may be due to intrathoracic goiter, thymoma, adenopathy, (benign or malignant), bronchogenic cyst, and mesenchymal mediastinal tumor. The history of a "mediastinal tumor" diagnosed on a routine chest roentgenogram at age 18 (six years before) should suggest a benign process. However, the complaints of dyspnea and chest pains of six months duration might indicate the malignant transformation of a benign tumor, the slow growth of a malignant mediastinal tumor, or the further enlargement of a benign process. We have seen an identical radiographic abnormality in two cases which prove to have unilateral, giant lymph node hyperplasia simulating a thymoma clinically, radiographically, and pathologically. They have been reported in the anterior, middle, and posterior mediastinum. Most cases reported have been on patients between 20 and 45 years of age, the masses have been unilateral and more than 3.5 cm in diameter.

Dr. Viamonte's impression: 1) GIANT LYMPH NODE HYPERPLASIA, 2) THYMOMA, 3) GOITER

Roentgenologic Impressions Submitted by Mail

Thymoma	37
Goiter	12
"Lymphoma" (sic)	8
Lymphoid hyperplasia	2
Others	24

Fig. 1—Paratracheal mass.

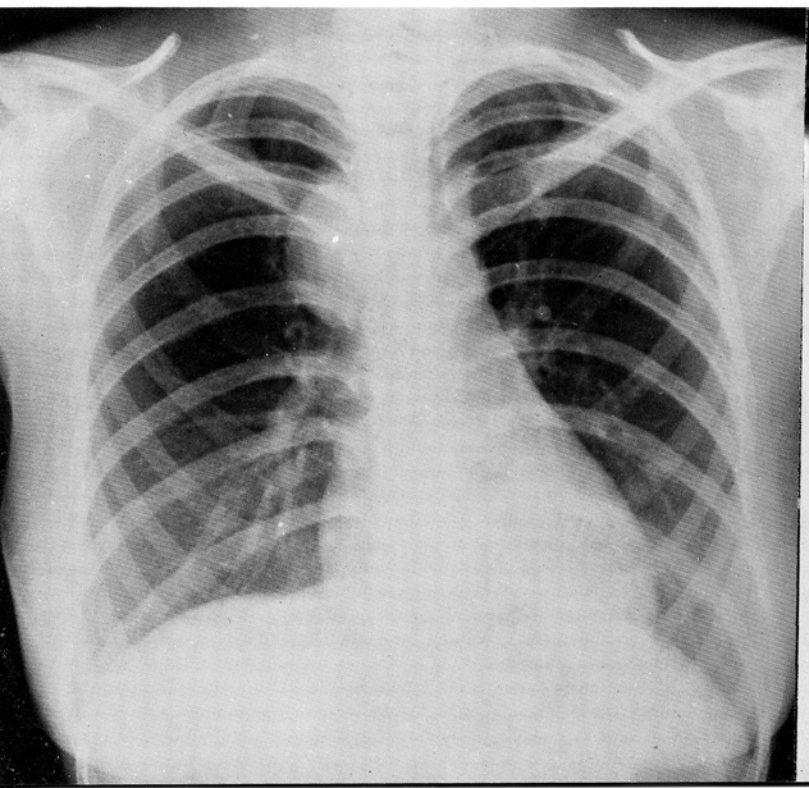
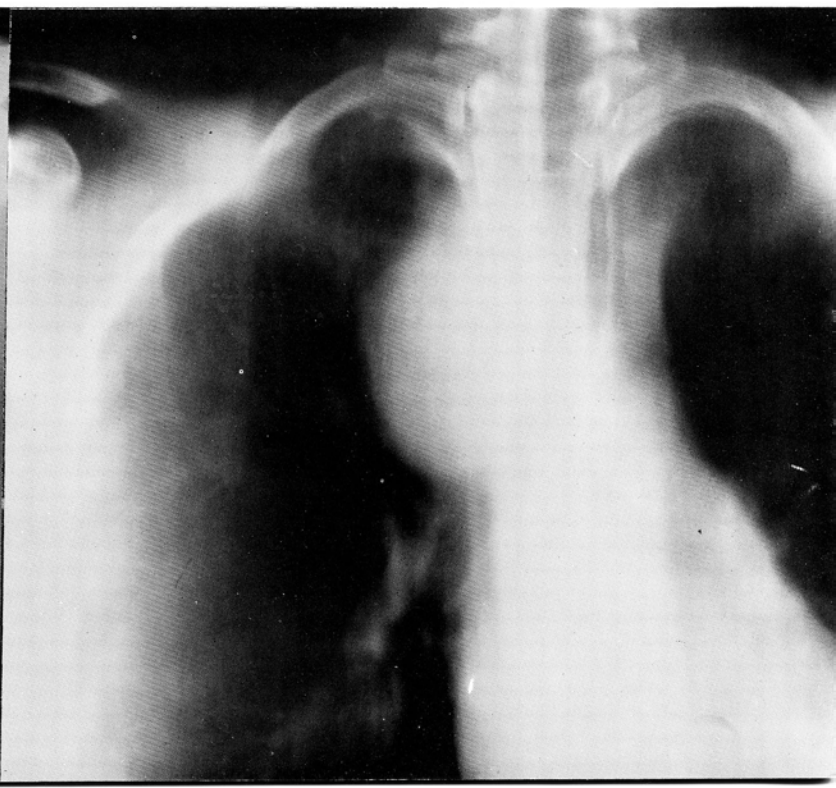


Fig. 2—Displacement of trachea to the left.



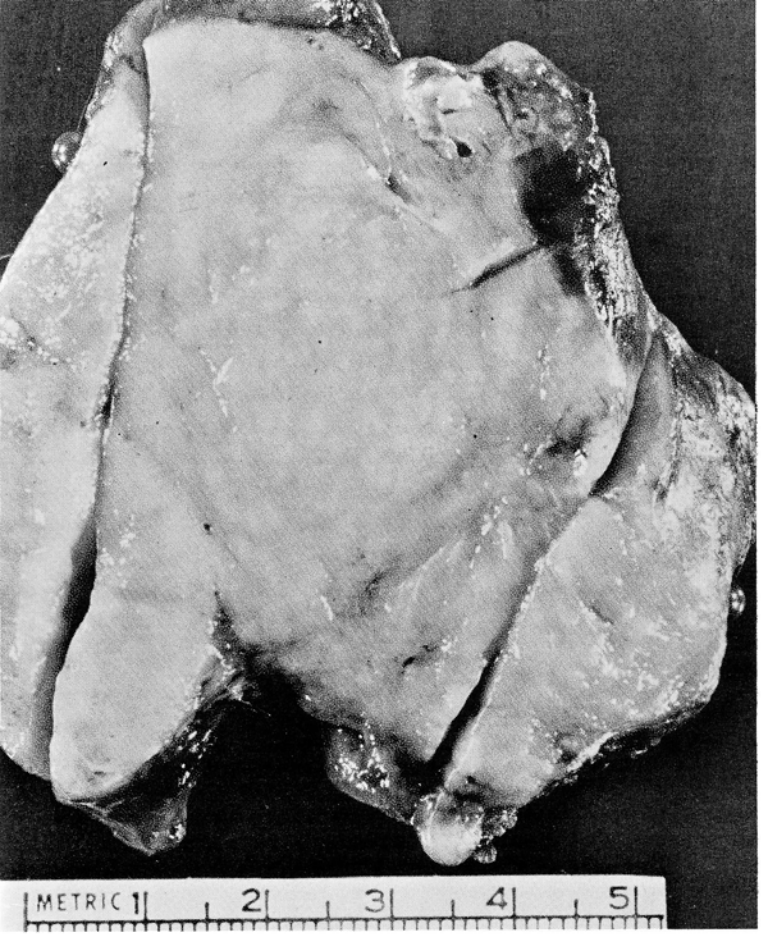


Fig. 3—Gross appearance of the excised mass in cross section.

Dr. Viamonte: Thymoma is an excellent possibility. Goiter is much more common than lymph node hyperplasia. However, this eight year history and the age of the patient would make me consider that this is lymphoid hyperplasia. Lymphoma is certainly a possibility, however, a lymphoma which would present as a self-confined mass would be most unlikely with eight years duration.

Dr. Regato: Dr. D. McFarland, of San Antonio, also suggested a goiter. Dr. C.H. Taggart, of Colorado Springs, offered a thymic tumor.

Operative findings: On February 13, 1967, a left postero-lateral thoracotomy was done. A large multilobated mediastinal mass was encountered, extending from the subclavian to the azygos veins and from the vena cava, anteriorly, to the esophagus, posteriorly. There were no adhesions. The vascular pedicles were divided and the mass removed.

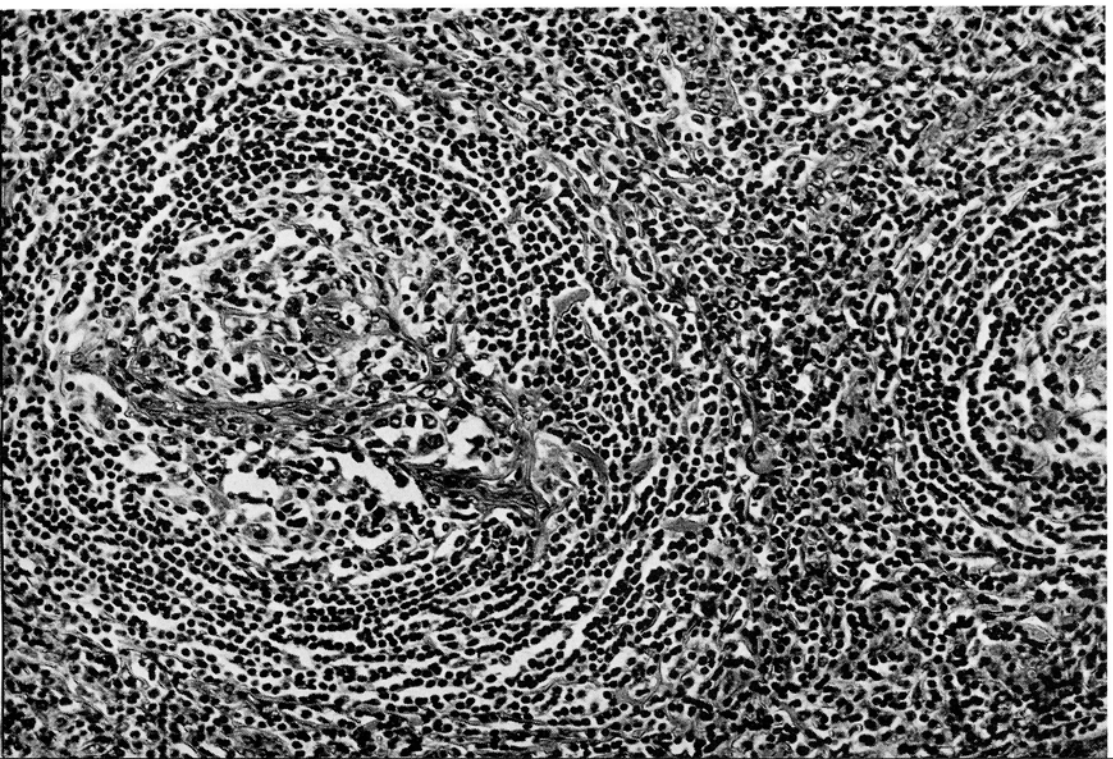
Dr. Liebow: Despite the large size of this mediastinal mass, the histological features indicate not a lymphosarcoma, but rather a benign form of hyperplasia of lymphoid tissue. This has been called "giant lymph node hyperplasia" by some (Castleman, Inada), but the term "pseudolymphoma" may be better, since it suggests a similarity to certain intraparenchymal pulmonary lesions so designated by Saltzstein.

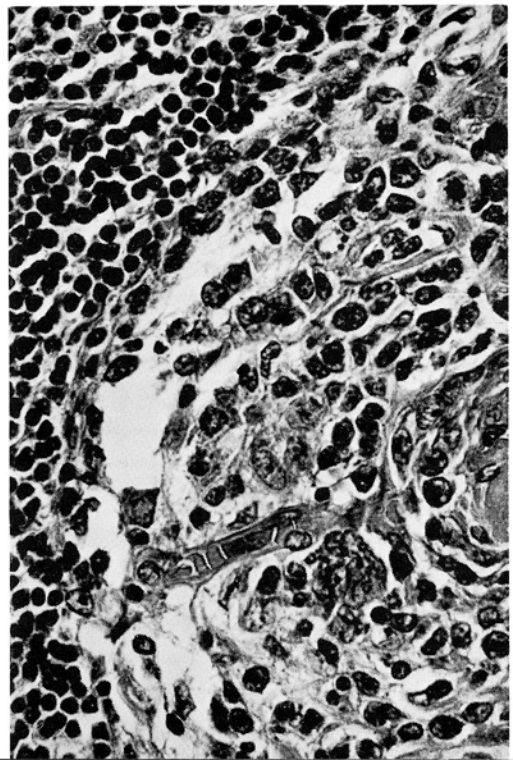
"Germinal centers" are prominent but are often small, partly hyalinized and penetrated by prominent vessels. The component cells have a whorled arrangement. Large and somewhat bizarre elements presumed to be reticuloendothelial cells are prominent among them. These are surrounded by only a narrow band of regularly arranged, closely packed lymphocytes and are widely separated by a mixed population of small mononuclear cells among which plasma cells are numerous. The prognosis of these lesions after surgical removal is good.

The fundamental nature of this type of tissue response is, like that of pseudolymphoma, obscure. Very recently a pulmonary lesion like that of pseudolymphoma but so diffuse as to result in pulmonary insufficiency has been described. This has been called "lymphoid interstitial pneumonia". The cellular composition of the lesion might suggest an immune mechanism. However, most of these patients do not have a dysproteinemia of other clue to suggest such a process.

Fig. 4—Pseudolymphoma ("giant lymph node hyperplasia") of mediastinum: Lymphocytes concentrically arranged about a reaction center". In the tissue separating these follicular structures there is a mixed infiltrate of lym phocytes, plasma cells and large mononuclear elements (X 200).

Fig. 5—Detail of reaction center. Hyalinized rounded nodule at right is surrounded by variable larger reticuloendothelial cells, some of which are multinucleated. Prominent vessel enters the reaction center (X 400).





Dr. Liebow's diagnosis: PSEUDOLYMPHOMA

Histopathologic Diagnoses Submitted by Mail

Lymph node hyperplasia	60
Lymphoid hamartoma	21
Thymoma	28
Hodgkin's	8
Others	9

Dr. Liebow: For the most part the participants stress lymphoid hyperplasia, or a term that has also been applied to the same condition, lymphoid hamartoma. This term, hamartoma, is an undersirable one but the implication is still the same as that for lymph node hyperplasia. The resemblance to thymoma is only vague. Germinal centers are not characteristic of thymoma. The whorled reticulo-endothelial cell masses have only a faint resemblance to Hassall's corpuscles and are clearly not of squamous epithelial origin. Hodgkin's disease is surely not supported by the general absence of Reed-Sternberg cells, outside of what appear to be true germinal centers.

Dr. Regato: Following a variety of adjectives: giant, hamartomatous, benign, hyperplastic, mediastinal, etc., betraying a gift for semantic confusion, most experts concurred in the diagnosis. Dr. L. Lowbeer, of Tulsa, saw granulomatous Hodgkin's in the lymphadenitis. Dr. D. Mulkey, of Denver, offered a diagnosis of thymic granulomatosis.

Dr. Pool: When I studied this film, it seemed to me that a bronchogenic cyst in this young woman was very much in the differential diagnosis.

Dr. Viamonte: I had a long list and that is certainly a distinct possibility. I would say that, statistically, a lesion that presents with this appearance would either be a primary tumor or intrathoracic goiter; among the submitted impressions, these were the two favorite diagnoses.

M. Abell, M.D., Ann Arbor, Michigan: We prefer the term lymphoid hamartoma rather than hyperplasia for several reasons. These lesions are solitary, they do not involve more than one lymph node and commonly they only involve a part of a lymph node; at one pole you will find the remnant of atrophic nodal tissue, so this is a tumor mass within a lymph node. They commonly are found in ectopic locations, they may reach sizes up to 15 cm in diameter and so we cannot consider this as a hyperplasia in the usual sense; we think there is some other malformation or failure in development of the node, with a hyperplasia that should be separated from the usual forms of lymph nodal hyperplasia. This one has many more plasma cells than we usually see and of fourteen of these that we have collected two were loaded with plasma cells. Recently I have heard of two of these lesions that were associated with dysproteinemia; the ones that have massive plasma cells and proliferation may have other manifestations. The last one of these that we have seen is in the inner aspect of the thigh. The lesions occur in the pelvis, the retroperitoneum, in the mesentery. They are not restricted to mediastinum or neck; we think that this is different than the pseudolymphoma of lung. In this patient there is no additional information; we have follow-up information on four others over ten years and no other lesions have developed.

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12. *Sclerosing Mediastinitis*

Contributed by Mark E. Williamson, M.D., Colorado Springs, Colorado

THE PATIENT was a 35-year old man in October, 1967, when he was seen because of hemoptysis. Two years previously a routine roentgenogram had uncovered a mediastinal mass which was removed and diagnosed as a "thymic tumor"; the patient declared to have gained 35 pounds in weight in the last six months. On physical examination there were no significant abnormalities; laboratory procedures were within normal limits; on esophagoscopy there were no abnormal findings; bronchoscopy revealed "chronic bronchitis."

Dr. Viamonte: The frontal chest roentgenogram reveals a mediastinal mass obscuring the outline of the aortic knob and of the proximal descending aorta, and slightly displacing the trachea to the right. The ascending aorta and the superior vena cava are not identified probably because of the slightly right anterior obliqued position of the patient or possibly due to extension of the tumor into the anterior mediastinum and to the right of the midline. No other abnormality is observed.

The mediastinal abnormality without clinical history would be compatible with any posterior and middle mediastinal infiltrating tumor (neurogenic tumor, lymphoma, metastatic disease, etc.) as well as could be related to non-malignant processes, such as dissecting hematoma of the aorta, mediastinitis, mediastinal hemorrhage, lipomatosis, etc. The history of a "thymic tumor" removed two years previously would suggest recurrence of a malignant thymoma. Hemoptysis might be related to bronchial invasion or be secondary to the chronic bronchitis demonstrated at bronchoscopy.

Dr. Viamonte's Impression: 1) MALIGNANT THYMOMA, 2) METASTATIC CARCINOMA, 3) LYMPHOMA (sic)

Roentgenologic Impressions Submitted by Mail

Hodgkin's	35
Malignant thymoma	12
"Lymphoma" (sic)	9
Oat-cell carcinoma	7
Others	5

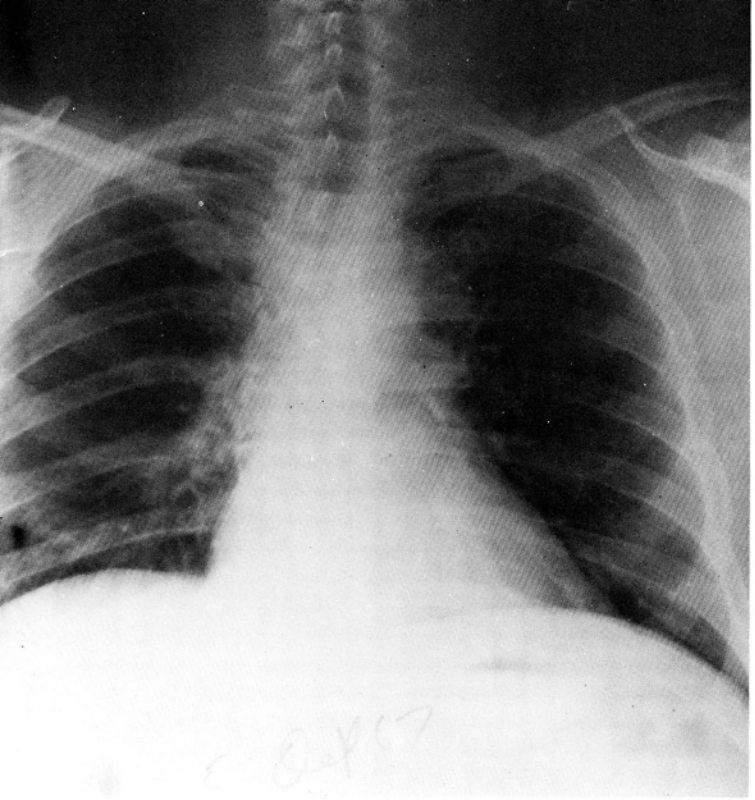


Fig. 1—Mediastinal mass over the aortic knob.

Dr. Regato: Dr. M. Daves, of Denver, suggested thymic "lymphoma"; Dr. B.L. Pear, also of Denver, offered thymic Hodgkin's.

Operative findings: On October 17, 1967, a left thoracotomy was done. The removed specimen measured 6 x 6 x 5 cm and weighed 34 gm; it contained a 4 cm tumor which on cross section appeared yellowish-white in color and presented cystic areas containing a reddish-brown material.

Dr. Liebow: The tissue removed two years previously is available for examination and does indeed have the structure of a thymoma of the "epithelial" type. Here the predominant elements are masses of large cells separated by thin fibrous septa. Near the latter the epithelial cells are cuboidal or columnar, often in palisade arrangement. Diffusely scattered among them are cells with the appearance of lymphocytes. This is one type of thymoma that is relatively commonly associated with evidence of myasthenia, although no manifestations of this are recorded.

A block of tissue obtained at the second operation consists of whorled hyaline material that contains small clefts, either apparently empty or filled with plasma cells and lymphocytes. The hyaline material has the appearance of "paramyloid". In some places cells occur in masses of considerable size, especially in perivascular position. Much of the lesion, however, is almost devoid of blood vessels. Hassall's corpuscles occur in some of the most richly cellular parts of the lesion and within some there is evidence of atypical proliferation, with some cells in mitosis, and some of rather bizarre appearance. The nuclei of the latter are quite prominent. These, however, appear to be of epithelial origin and are not Reed-Sternberg cells. It is difficult to disprove that these may represent residual cells of a tumor, although it appears more likely that they appertain to Hassall's corpuscles. It may be concluded that the lesion best fits the diagnosis of "sclerosing mediastinitis" of non-specific type. This diagnosis implies that there is no evidence of histoplasmosis, tuberculosis, or any other infectious agent.

Dr. Liebow's dignosis: SCLEROSING MEDIASTINITIS

Histopathologic Diagnoses Submitted by Mail

Thymoma	63
Sclerosing mediastinitis	31
Hodgkin's disease	26
Others	17

Dr. Liebow: The differential diagnosis of Hodgkin's disease and of the closely similar, or according to some identical, "granulomatous carcinoma of the thymus" described by Lowenhaupt, has already been considered. While the sclerosing mediastinitis may be a postoperative complication of the earlier resection of the thymoma, its histological structure is quite different from that of the thymoma itself.

Dr. Regato: Dr. R.D. Schultz, of Sioux Falls, made also a diagnosis of sclerosing mediastinitis. Dr. W.J. Holoday, of Columbus, Ohio, and Dr. M.R.Abell, of Ann

Fig. 2—Sclerosing mediastinitis: Hyaline connective tissue with many cleft-like spaces filled with groups and cords of plasma cells (X 200).

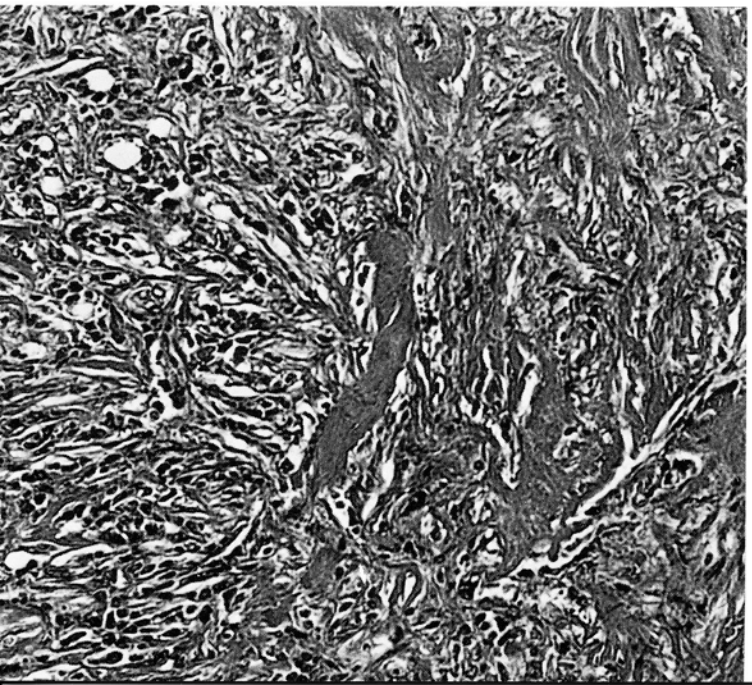
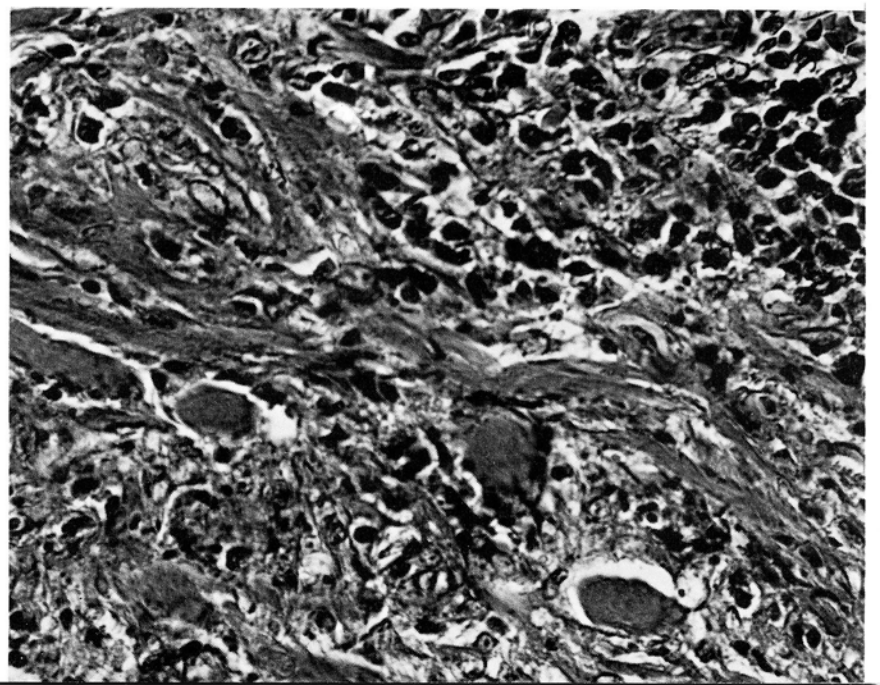


Fig. 3—Detail of Fig. 2 to show masses of plasma cells in cleft-like spaces among sheets of hyalinized tissue.



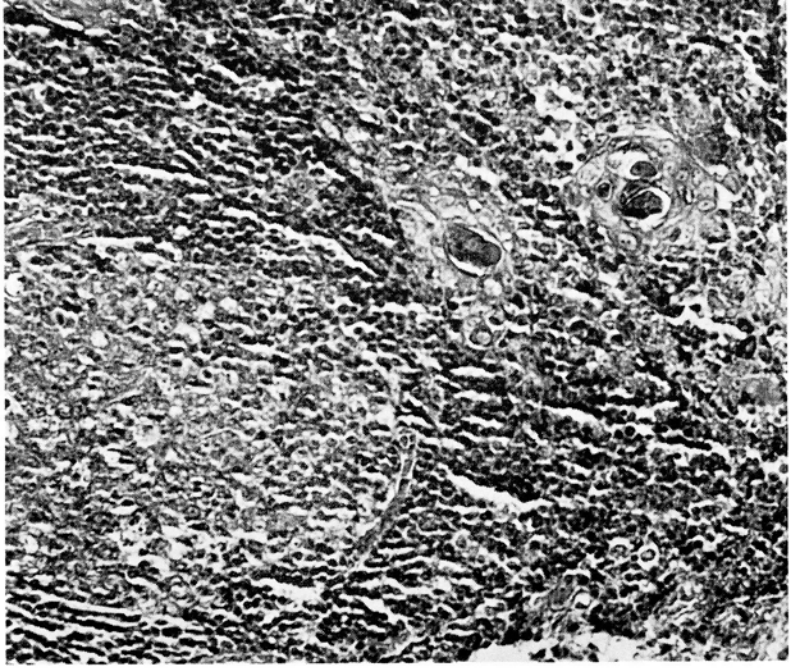


Fig. 4—Remnant of thymic tissue. Two Hassall's corpuscles are seen near the upper right margin of the photograph. Surprisingly, a large germinal center with many cells in mitosis is seen in the left lower corner (X 200).

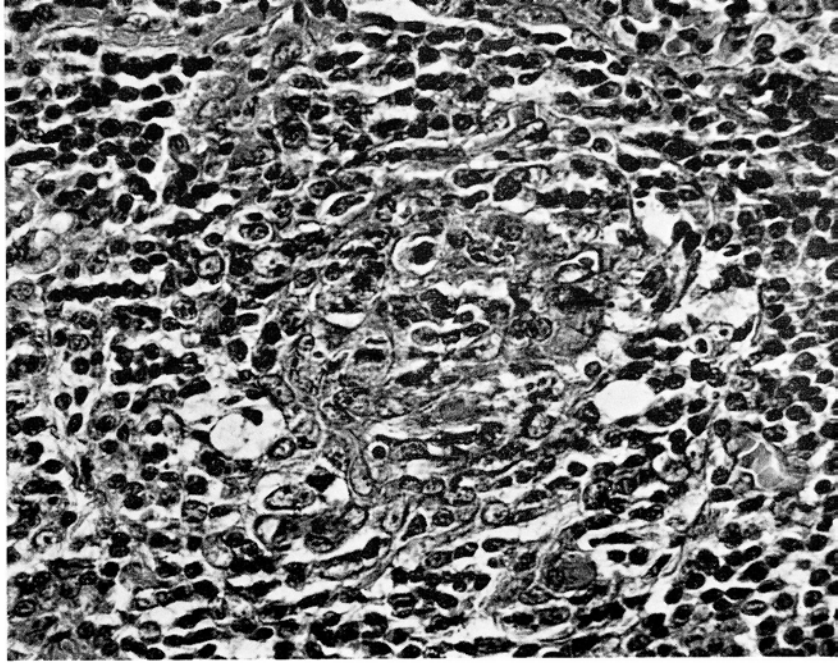


Fig. 5—Remnant of thymic tissue showing large proliferated "reticular epithelial cells" of the thymus. Two of these cells are in mitosis.

Arbor, preferred nodular sclerosing Hodgkin's disease. Dr. W.J. Frable, of Richmond, Virginia, suggested granulomatous thymoma, whereas Dr. J. Rosai, of Saint Louis, saw post-operative residual thymoma and fibrosis.

Subsequent history: The patient is being followed at the Air Force Academy Hospital. He was last seen in September, when he was in good health. The roentgenogram of the chest showed no abnormalities.

Dr. Pool: We have seen recurrences and what might be classified as metastases in axillary nodes and thoracic vertebrae as late as seven years after the initial resection and radiation therapy of malignant thymomas. I should like to ask a question about this mediastinal sclerosis: Does it have any relationship to the type of sclerosing fibrosis that is sometimes seen retroperitoneally, associated with the taking of certain drugs?

Dr. Liebow: I think not in the vast majority of cases, but possibly in some. However, most of the sclerosing mediastinitis is in fact histoplasmosis which appears to escape the nodes and to produce a general mediastinal reaction; it may lead to calicification ultimately with occlusion of pulmonary arteries or veins or both and, sometimes, formation of calcified thrombi in these vessels. That is by far the most common mechanism for sclerosing mediastinitis. Less commonly is the tuberculous process which pursues somewhat the same course but this reaction I have not previously seen in relation to any kind of mediastinal lesion including thymoma.

Dr. R. Lund, Casper, Wyo.: Dr. Regato, could you tell us what the role of radiation therapy is in thymoma. When is it indicated?

Dr. F. Buschke, San Francisco, Calif.: It depends on the thymoma. In the first place there is the granulomatous thymoma of Lowenhaupt with which we are quite familiar because it is the speciality of the house at the University of California. That is a lesion that can be treated effectively with radiation therapy and cured. We have quite a number of cases that I have been watching now that were treated about twenty years ago. As far as Hodgkin's located there, I do not know. Zuppinger calls this anterior mediastinal Hodgkin's non-granulomatous thymoma; he has cured, permanently, eight out of thirty-two cases: that is pretty good for Hodgkin's disease. Epithelial thymic tumors usually do not respond too well. The lymphomas are an object for radiation therapy. In the presence of myesthenia gravis radiotherapy is a very effective treatment; a number of our surgeons request routinely pre-operative radiotherapy for they claim that the risk is considerably reduced. We have a number of cases where this was given as a preoperative treatment and the patient never came to surgery because it was not necessary. It is more effective in those cases of myesthenia where tumor can be demonstrated than those where we cannot radiographically demonstrate it.

Dr. Regato: The success in the treatment of thymic tumors is due to their early discovery. Once the thoracic surgeon has gotten that far, it is usually a simple matter for him to remove the tumor and we learn of its nature after it has been surgically treated. Those that we deal with most of the time are those that either cannot be removed or recur after surgery; the majority of these tumors are only locally malignant and do not metastasize. In our experience they have proven to be radiosensitive, not only the lymphomatous but the epithelial also. They require extensive radiation therapy. Often, they are treated with too narrow fields and they might recur outside of the field; I would advise that it be made sure that the field is wide enough to encompass all of the potential area of involvement. With the help of surgeon, one can have a good idea of the extension; perhaps metal clips can be put around the lesion if the surgeon is not going to contemplate excision. When it is a matter of recurrence, it is more difficult because then you do not know exactly the limits and the best thing to do is to choose a wide field and treat the patient over a long period of time; you are not in need of punching very hard for most of these tumors are radiosensitive; it is only a matter accumulating a sufficient amount of radiations over the entire area of potential involvement. Some of them are sufficiently malignant to recur in spite of adequate irradiation. Those are the exception. One is always left in doubt as to whether the recurrence came because the irradiation was inadequate or because the tumor was not biologically susceptible to control by radiotherapy.

13. *Sclerosing Hemangioma of the Lung*

Contributed by **Lawrence I. Gottlieb, M.D.**, Salt Lake City, Utah

THE PATIENT was a 61-year old woman in May, 1967, when she was operated on for a lump in the left breast and diagnosed as "adenocarcinoma"; one month later a follow-up examination revealed no abnormalities of the surgical scar and no significant adenopathy; the opposite breast was normal; the hemoglobin was 12 gm% and there were 4600 WBC per mm^3.

Dr. Viamonte: A solitary, spherical, 2.3 x 3 cm mass, without evidence of calcium is observed in the lower half of the right lung. The left breast has been removed. No other abnormalities are detected in this single, frontal chest roentgenogram. Solitary, non-calcified, pulmonary nodules can be either benign or malignant. Needle aspiration biopsy under fluoroscopic guidance is the best practical means for ruling out a malignant tumor.

We assume that, following good medical practice, a chest roentgenogram was obtained prior to surgery. If a pulmonary nodule would have been discovered, I expect this would have been mentioned in the history. I am then assuming that this nodule is of recent appearance, and therefore, corresponds to a rapidly growing lesion. It is logical to try to relate the lesion of the breast to the pulmonary nodule. The only rapid growing metastasis from a breast tumor that I am aware of is malignant hemangioendothelioma. However, the breast nodule was diagnosed as "adenocarcinoma". I am unaware that a metastasis from an adenocarcinoma of the breast would attain this size in one month. Also it is unlikely that a malignant hemangioendothelioma would be confused for an adenocarcinoma. Therefore, I will suggest that the breast lesion and the pulmonary nodule are unrelated. I know of no primary pulmonary tumor that will reach this size in one month, (assuming an average cancer cell to be about 25 micra in diameter, a 2 cm nodule would have about 29 doublings and 512 million cells).

In patients under 40 years of age almost all solitary malignant nodules double in size within forty weeks whereas benign nodules double in size in more than seventy weeks. However, rapid doubling time in a solitary pulmonary nodule over the age of forty is more strongly suggestive of an inflammatory lesion than a malignant tumor.

Dr. Viamonte's Impression: 1) VASCULAR HAMARTOMA, 2) WEGENER'S GRANULOMA

Roentgenologic Impressions Submitted by Mail

Metastatic carcinoma	26
Peripheral adenoma	25
"Lymphoma" (sic)	3
Hamartoma	2
Others	12

Dr. Viamonte: I do not believe that this lesion is related to a neoplasia. I would agree with those who mention hamartoma; I would just qualify it as a vascular hamartoma.

Dr. Regato: Dr. E. Salzman, of Denver, offered hamarto-chondroma. Dr. J.D. Cox, of Colorado Springs, offered primary or metastatic adenocarcinoma. Dr. N. Goodman, of Denver, and Dr. I. Friendlich, of Philadelphia, suggested a resolving pulmonary infarction.

Operative findings: On June 6, 1967, a right middle lobe lobectomy was carried out; it contained a well demarcated hard nodule, 2.4 cm in diameter which on cut surface appeared homogeneous gray-white with yellow streaking.

Dr. Liebow: The tumor consists largely of spindle-shaped cells often outlining small channels, some of

Fig. 1—Solitary sperical non-calcified mass of the right lung.

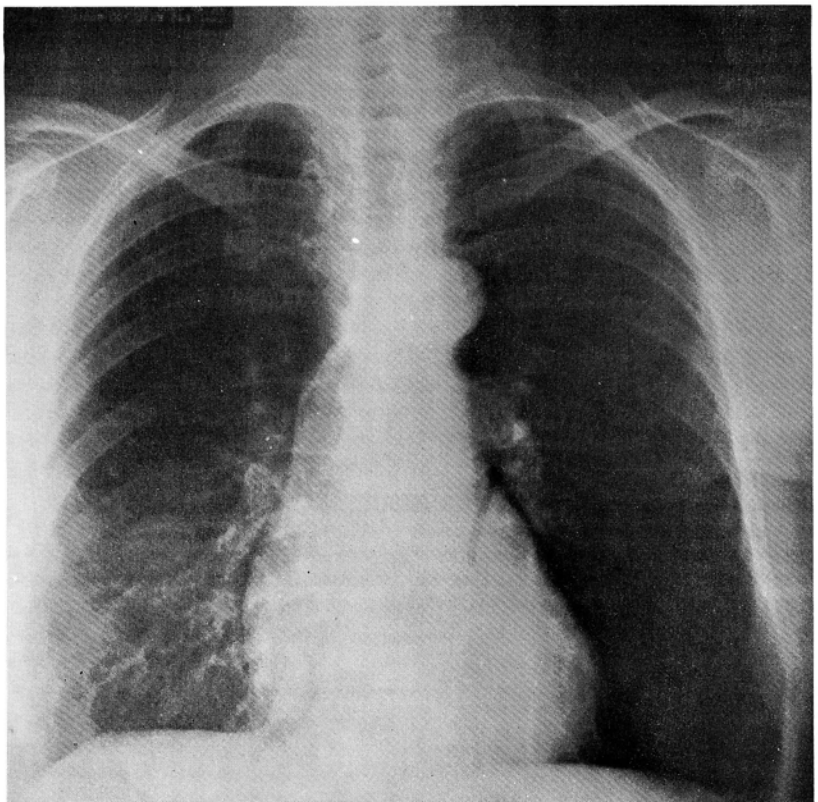
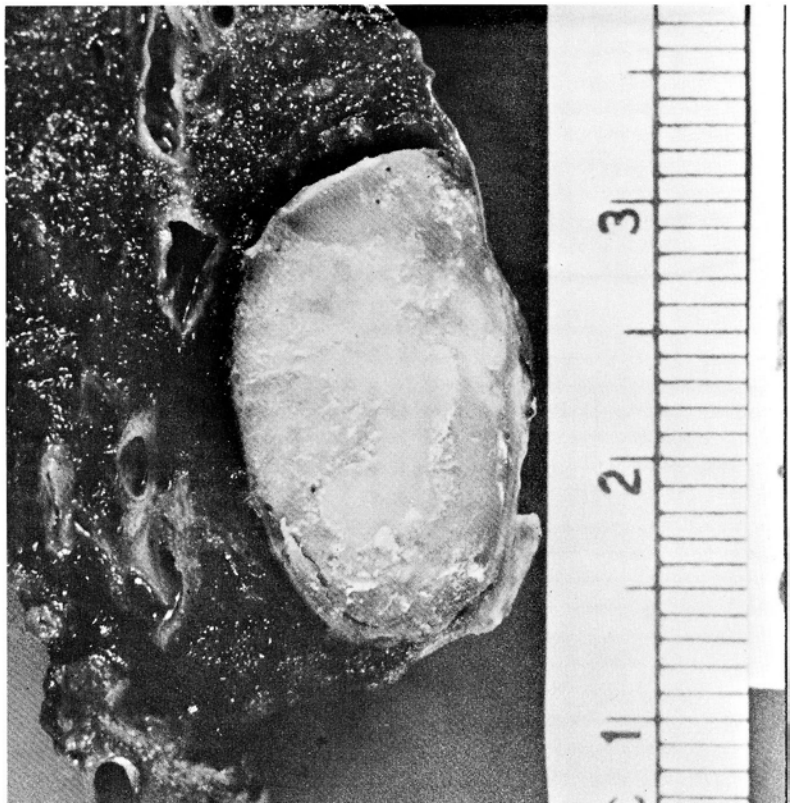


Fig. 2—Gross appearance of excised mass.



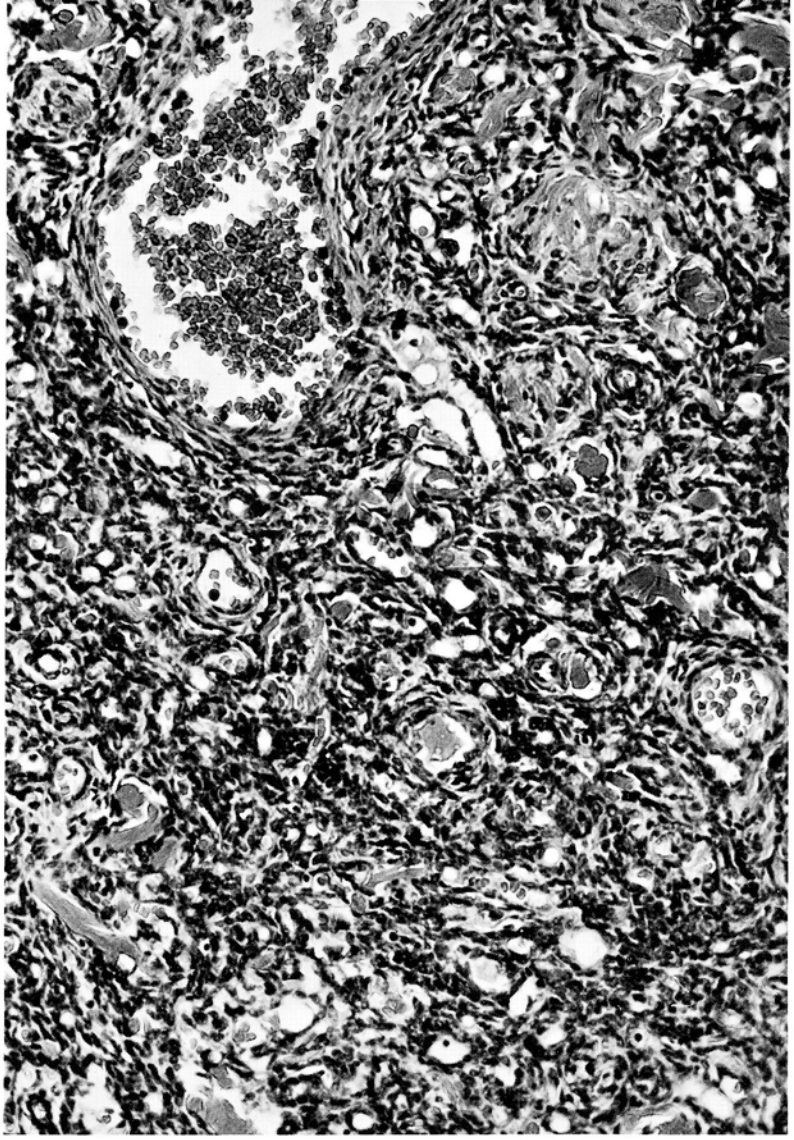


Fig. 3—Sclerosing hemangioma: Vascular spaces of varying size are lined by spindle-shaped cells. Some of the latter also occur in masses interstitially. There is focal hyalinization (X 200).

which contain erythrocytes. In some portions, however, the cells occur in bundles and the vascular characteristics of the lesion are more difficult to discern. In considerable part it has become hyalinized and there are scattered bundles and masses of hyaline connective tissue throughout. Within the hyaline tissue the rounded outlines of partly or subtotally sclerosed vessels can still be discerned. In one part of the tumor there is a large zone of hemorrhage. All transitions from the masses of spindle cells to well differentiated hemangioma with or without hyalinization are evident. This tumor can best be classified as a sclerosing hemangioma. The sex of the patient and the position of the lesion in the right middle lobe are common in sclerosing hemangioma.

There is no histological resemblance to the breast tumor that had been removed previously. This is quite ordinary carcinoma with some acinar and some solid nests of large irregular cells, many of which are in mitosis.

Sclerosing hemangiomas are known to be slow growing. The pulmonary mass must have been present at the time of the mastectomy one month previously. It must therefore be concluded that either a roentgenogram of the chest was not made, or the pulmonary lesions was not further investigated at the time.

Dr. Liebow's diagnosis: SCLEROSING HEMANGIOMA

Histopathologic Diagnoses Submitted by Mail

Sclerosing hemangioma	18
Hemangiopericytoma	23
Hemangioendothelioma	15
Angiosarcoma	6
Mesothelioma	6
Hamartoma	16
Chemodectoma	9
"Tumorlet" (giant)	8
Others	33

Dr. Liebow: Most participants support the angioid origin of this lesion. Sclerosing hemangioma was diagnosed by many and hemangiopericytomas was considered by an even larger group. Hemangio-endothelioma and hemangiosarcoma likewise received some attention; these are always benign lesions. Most of these occur in women and most occur in the right lung, so this certainly fits the usual characteristic of this lesion. Mesotheliomas occur in the central parenchyma of the lung although just a few of them arise upon the pleura. The diagnosis of hamartoma has been made in some of these because they can entrap epithelium, and as the lesion becomes hyalinized does resemble what is commonly called hamartoma. However, further search will reveal the sclerosing angiomatous nature of this lesion. This lesion does not have the appropriate structure for a chemodectoma. I do not think this is a tumorlet in any sense. Maybe we should abandon the term "tumorlet" which means nothing more than a tiny little tumor. Tumorlets are carcinoid-like atypical proliferations which is what they were called before Dr. Whitwell called them tumorlets. This has been shown recently by electron microscopy which has demonstrated that they look like the cells that appear in the intestine. The same kind of cell that makes up the bronchial adenomas. It is of interest that a high proportion of those submitting diagnoses recognized that the lesion was of vascular origin, although interpretations varied. It should be stressed that the designation sarcoma is improper, since these tumors have proved to be benign with exception.

Dr. Regato: Dr. P.C. Dyke, of Denver, made a diagnosis of metastatic cystosarcoma phylloides. Dr. W.J. Frable, of Richmond, Virginia, preferred peripheral chemodectoma. Dr. R.M. Sherwin, of Colorado Springs, offered benign, spindle-cell mesothelioma. Dr. J. Rosai, of Saint Louis, preferred the designation of "tumorlet."

Subsequent history: On September 3, 1968, the patient was seen in good health.

Dr. Pool: I am in full agreement with the surgeon's approach of removing, soon after the radical mastectomy, this undiagnosed lesion in the lung. I think that the radiologist could not provide us with information that would make it safe not to operate. In my criteria, only a coin lesion that has a concentric ring of calcification about it or a lesion which is unchanged for several years in successive films is safe to observe rather than to remove. Furthermore, in association with mammary carcinoma a solitary lesion occuring in the lung is much more likely to be a new primary than a solitary metastasis. I recently reviewed nearly 400 cases of lung cancer in which aspiration biopsy was employed as a diagnostic method and this was positive in 80% of such procedures but I do not believe that it is wise to use aspiration biopsy in a coin lesion of this size and position because of the danger of spilling either cancer cells or tubercle bacilli or some yeast form into the pleura during the aspiration. You might use the aspiration biopsy when the chest was open through a purse-string on the surface of the lung if you wish to make the diagnosis to determine the amount of resection you want to do.

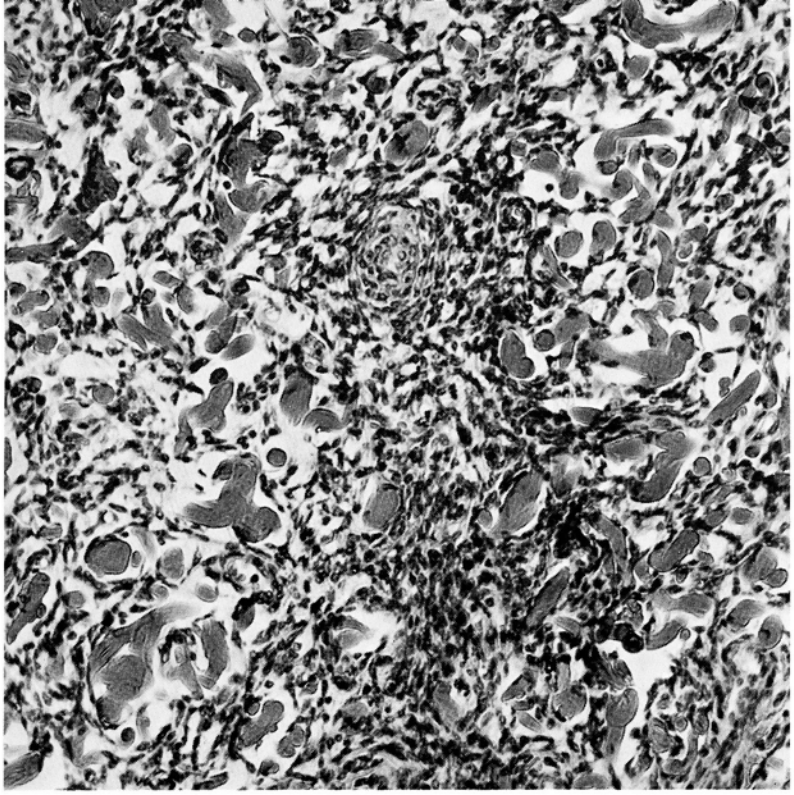


Fig. 4—Pseudolymphoma ("giant lymph node hyperplasia") of mediastinum: Lymphocytes concentrically arranged about a "reaction center". In the tissue separating these follicular structures there is a mixed infiltrate of lymphocytes, plasma cells and large mononuclear elements (X 200).

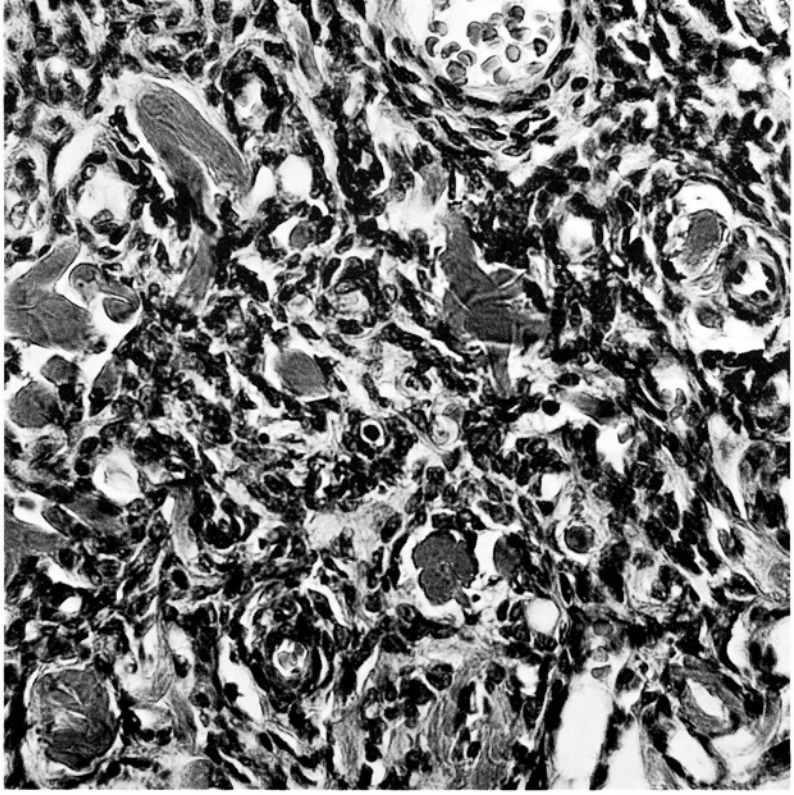


Fig. 5—Detail to show spindle-shaped cells, many of which are related to vessels. Focal hyalinization (X 400).

Dr. Liebow: I would like to ask Dr. Gottlieb whether or not a previous chest film was obtained in this patient.

Dr. L. Gottlieb, Salt Lake City, Utah: To my knowledge, no previous chest film was obtained on this patient. I spoke to her this week: she is feeling well with no ill effects; her only problem being that she gets quite anxious when I call to see how she feels.

Dr. Viamonte: Neither location, size nor configuration allows a distinction between benign and malignant solitary pulmonary nodules. The calcified rim around the nodule but concentric calcification, calcification in the center that may resemble popcorn, uniform stippled calcification, uniformly dense calcified nodules: all these are almost 100% benign and may be left alone. However, eccentric location of calcium may result from a granuloma or a benign nodule like hamartoma but also may be due to a carcinoma developing around a scar, so-called scar carcinoma. I believe that needle aspiration biopsy is a definite useful procedure and very simply performed with a thin needle. Needle aspiration biopsy with a 19 gauge needle in selected non-calcified nodules is very useful. For instance, I would not leave a nodule to be watched in a young individual. Slow growth of a malignant nodule may be seen occasionally; rate of growth will not favor benign versus a malignant lesion. As far as indication for needle biopsy in solitary pulmonary nodules, the best indication is when the nodule is small, when it is seen in a heavy smoker and the patient is a poor risk. Often we discover a solitary nodule that is not calcified and the elderly patient has severe emphysema, or may have borderline respiratory insufficiency, history of several heart attacks, etc. Are you going to explore this patient in order to tell if the nodule is malignant or benign or are you going to just watch and observe it? If one does a needle aspiration biopsy and proves that it is a malignant nodule, one will still have to evalute the indications for surgery. The incidence of dissemination along the tract is practically of no clinical significance. In dealing with large trochars like the Vim-Silverman needle or in doing aspiration biopsy through a mediastinoscope, it is true that often one may have seeding in the skin; we have had one such case with dissemination of the carcinoma into the chest wall. In the majority of instances, when a small needle is used and the lung is to be removed, I believe that the value of the procedure outweighs the risk. As far as spillage into the systemic circulation by the trauma, mechanical trauma produced with a needle always is a possibility. This is a very simple procedure, it has to be done under bi-plane fluoroscopic guidance because there is no way of hitting a 3 mm nodule unless you can see it; this is one of the tools that has fallen into the hands of the radiologist now.

Dr. Regato: I do not agree that needle biopsies are not harmful. Ackerman has demonstrated that there is seeding throughout the needle tract. On the other hand, depending upon the circumstances, this may be the proper risk to take particularly when the needle tract is likely to be removed by the operation. For over 35 years we have done needle biopsies for metastatic nodes in the neck which are to be treated by radiotherapy. Instead of doing incision biopsies, we have done aspiration biopsies with an 18 gauge needle using a 50 cc syringe, maintaining vacuum in order to bring in the specimen within the needle and avoid its being left in the tract and, also, taking the precaution of incising the skin where more often the specimen is left when the needle comes out. This is not new, it was originiated by Martin and Ellis over 30 years ago.

Dr. Viamonte: I would like to mention that in a large institution where thoracotomies are often done, the mortality varies from 15 to 20% in unselected patients.

Dr. Pool: I thoroughly agree that when you have a patient who is a poor risk and you are trying to find a

reason not to operate that this is a useful method in a patient suspected of carcinoma when several sputum cytologies have been secured and found negative. One must also remember, however, that if the aspiration biopsy is not positive for carcinoma, it does not rule out that possibility. I think that the figure of mortality for exploratory thoracotomies is nearer 5% than the figure mentioned.

Maria Viamonte, M.D., Miami Florida: Last year I visited the Karolinska Hospital in Stockholm, where I learned to use aspiration biopsy for everything and the results are excellent. Their technique and experience in the cytology are fantastic. The results are 98% positive in all cases of carcinoma of the lung.

Dr. Regato: One cannot quarrel with youthful enthusiasm (see bottom of page 80).

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14. *Sclerosing Hemangioma of the Lung*

Contributed by **J.L. Pool, M.D.** and **F. Foote, M.D.**, New York, New York

THE PATIENT was a 60-year old woman in July, 1968, when a pulmonary lesion was discovered on a routine radiographic examination of the chest; the patient had smoked cigarettes for 40 years. Physical examination and laboratory procedures were non-contributory.

Dr. Viamonte: A spherical nodule, one cm in diameter, is observed in the right base, just above the diaphragm. There is a suggestion of curvilinear calcification in its cephalic portion. However, partial calcification of the right 5th costal cartilage probably accounts for the calcification. A tomogram would have allowed recognition of the presence or absence of calcium in the nodule. If proven to be non-calcified, needle aspiration biopsy under fluoroscopic guidance is a technique by which the diagnosis of a malignant tumor can be made.

Basilar pulmonary calcified nodules are usually granulomas or hamartomas. Non-calcified pulmonary nodule may represent a non-malignant process (60%) or a pulmonary neoplasia (primary or secondary).

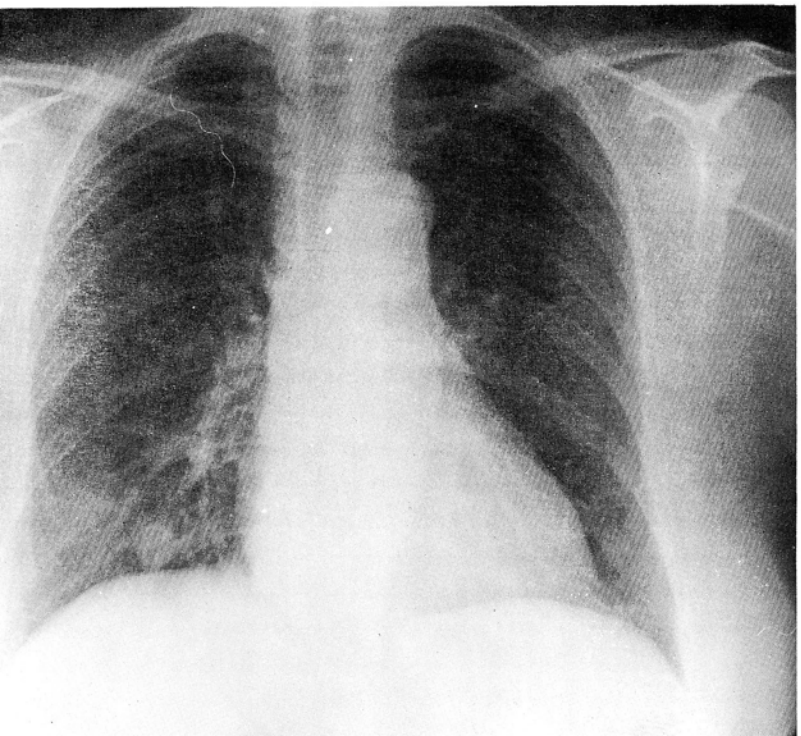
The history of smoking cigarettes for forty years would favor the possibility of a primary bronchogenic carcinoma.

Dr. Viamonte's Impression: 1) BRONCHIAL CARCINOMA, 2) GRANULOMA, 3) HAMARTOMA

Roentgenologic Impressions Submitted by Mail

Hamartoma	37
Bronchial carcinoma	18
Granuloma	16
Choristoma	13
"Scar" carcinoma	5
Others	12

Fig. 1—Spherical nodule of the right lung base.



Dr. Viamonte: Hamartoma is a possibility, but there is no calcium here and it will be a simple guess. Granuloma, obviously this could be. Choristoma is a term used to describe another tissue malformation, the normal proliferation of tissue elements that usually are not present in an area; I could not see any fibrosis or any underlying lung disease to suspect a "scar" carcinoma. I would think that because of the history this would most likely be a pulmonary neoplasm.

Dr. Regato: Dr. J.C. Lemon, of Denver, suggested a pulmonary varix, and Dr. M. Levine, also of Denver, a hamartoma.

Operative findings: On August 9, 1968, a thoracotomy was done and following frozen section a right lower lobe lobectomy was carried out.

Dr. Liebow: Although this tumor differs considerably from that of Case 13, detailed studies of more than forty such lesions has revealed that they are essentially the same. In fact the lesion in Case 14 is much more typical of the group. Here the predominant large rounded cells are interpreted as histiocytic, although many proliferated endothelial cells are also present. The former

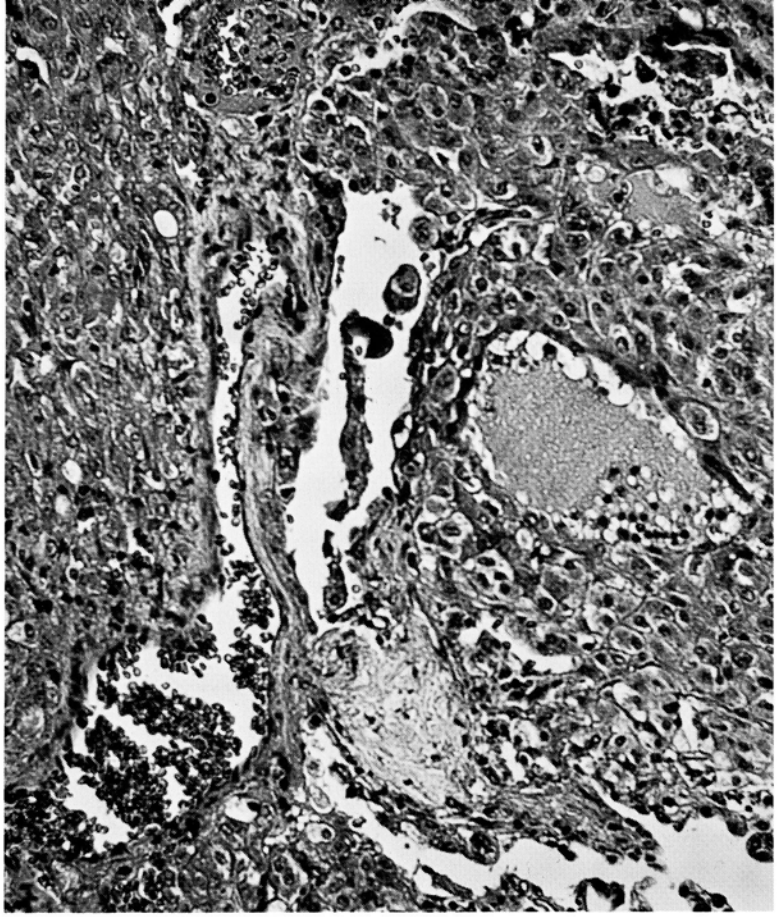


Fig. 2—Sclerosing hemangioma of the lung: Irregular vascular spaces. The channel at the left expands towards the bottom of the photograph to form a "bayou". The latter is lined in part by elongated endothelial cells, but in part also by large mononuclear cells. The latter occur in masses as the major component of the tissue. The cytoplasm of many is vacuolated (X 200).

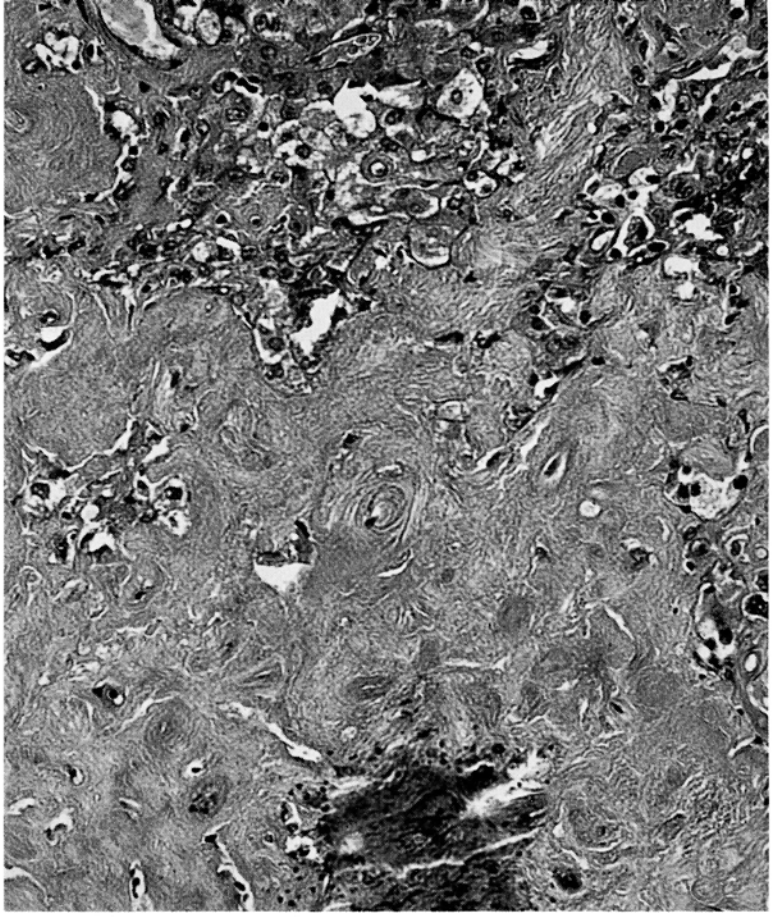


Fig. 3—Sclerosed remnants of vascular channels. These demonstrate the true nature of the lesion. At the top of the photograph there are numerous large mononuclear cells, some with vacuolated cytoplasm (X 200).

are believed to have accumulated in reaction to slow hemorrhage from the proliferated vessels of the hemangioma. The latter in part form large varicose thin-walled channels. From the fact that they may contain large monuclear cells in considerable numbers with both fat and hemosiderin in the cytoplasm, it may be suggested that their connection with the main vascular stream is in the manner of a bayou or backwater. The hyalinized "sclerosed" portions are very similar to those of Case 13.

It is noteworthy that the patient was female and that the lesion was in the lower portion of the right lung. This again corresponds to previous experience summarized from 32 patients as follows: 75% were women. In 60% of the patients, the lesion was in the right lung and in almost 30% in the right middle lobe.

Dr. Liebow's diagnosis: SCLEROSING HEMANGIOMA

Histopathologic Diagnoses Submitted by Mail

Metastatic carcinoma (renal, thyroid, liver, etc.)	51
Bronchial adenoma (carcinoid, oncocytoma, etc.)	21
Granular-cell myoblastoma	15
Chemodectoma	9
16 Others	31

Dr. Liebow It is apparent that this rather common benign tumor of the lung is not well known. Particularly distressing is the diagnosis of metastatic carcinoma these tumors are invariably benign. Hemorrhage has to be accounted for. Bronchial adenoma certainly would not have this stromal structure. One should find much more granular myoblasts than are present here to justify the diagnosis of granular-cell myoblastoma. It does not have the stromal arrangement nor the cellular characteristics of chemodectoma. Granular cell myoblastoma does occur in the lung, but only within bronchi and not as a peripheral lesion.

The question has been raised as to whether these lesions should be considered neoplasms. It is evident, however, that they represent proliferation of vessels and of endothelium, although much of their bulk may consist of the products of cellular response to hemorrhage. To lump these as "inflammatory tumors" including the plasma cell granulomas, seems improper, since the sclerosing hemangiomas have quite distinctive characteristics.

Dr. Regato: Dr. F. Foote, of New York, also made a diagnosis of sclerosing hemangioma. Dr. W.C. Black, of St. Louis, offered bronchial adenoma oncocytic type, a variant of carcinoid with peculiar large secretion granules; he felt that chromaffin paraganglioma is a differential diagnosis to consider. Dr. M.R. Abell, of Ann Arbor, preferred mucoepidermoid carcinoma of the bronchus. Dr. B. Castleman, of Boston, saw this lesion as a metastatic endocrine type of tumor, possibly a medullary carcinoma of the thyroid with an amyloid "shower." Dr. R.D. Schultz, of Denver, felt this was a metastatic renal tumor; whereas Dr. J.M. Woodruff, of Denver, felt it came from the liver; Dr. P.B. Conti, of Denver, from the adrenal, and Dr. J.B. Frerichs, of El Paso, saw it as a metastatic malignant mixed tumor of the salivary gland type.

Dr. Regato: Please notice that the last line says sixteen others.

Dr. Liebow: Yes, and I would like to know what these were because maybe somebody did diagnose a sclerosing hemangioma but you did not put it down.

Dr. Regato: Not one did!

Dr. Pool: Dr. Viamonte did not have the opportunity of seeing the tomograms which were quite extensively used by us and did not show any calcification. At operation the lesions was deeply situated in the lower lobe. The hilar nodes of that lobe contained considerable calcification which was difficult to free of the artery to the lower lobe; tapes were placed about the lower lobe vessels and the lesion was excised; it was reported as epidermoid carcinoma on frozen section and for that reason the lobectomy was completed. The division of the vein on the heart side of the tourniquet on the vein being carried out without releasing that tourniquet so that if malignant cells were mobilized by the surgeon, they would not be freed into the general circulation. Three months later the patient has no pulmonary complaints. I must add, however, that she had a cardiovascular arrest the night of the thoracotomy from which fairly good recovery has occurred.

Dr. J. Rosai, St. Louis, Mo.: The reason Dr. Black made the diagnosis of oncocytoma was that about a month ago we had a case almost identical to this that he studied by electron microscopy; they were endocrine cells with peculiar granules similar to those of bronchial adenomas of the oncocytic type.

Dr. Liebow: All of these patients on whom we have follow-up have had no evidence of recurrence. This lesion was first described in 1953 so the follow-up is quite extensive in a number of them. This is an entirely benign process. If electron microscopy had been done on this case, I think it would have shown beautiful phagocytic pneumocytes and endothelial cells.

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15. *Sarcoma of the Lung*

Contributed by **D.A. Mulkey, M.D.**, Denver, Colorado
and **A. Nettleship, M.D.**, Fayetteville, Arkansas

THE PATIENT was a 56-year old man in October, 1965, when he complained of cough, hemoptysis and slight fever of recent onset; two years previously he had similar symptoms which had been diagnosed as due to "pneumonia" and treated by antibiotics; he had recovered. On physical examination there was a friction rub on ausculation of the left base laterally. No abnormalities were found on bronchoscopy; bronchial washings were negative for neoplastic cells.

Dr. Viamonte: A 5 x 7 cm non-calcified mass with slightly irregular outline is observed contacting the lateral chest wall, on this frontal projection of a left sided bronchogram. The bronchi of the lingula and of the anterior segment of the left lower lobe appear intrinsically normal and displaced medially. The medial third of the posterior arch of the left 9th rib is not well demarcated. No other abnormalities are observed.

Intrinsic pulmonary masses may displace, obstruct, invade, or surround the bronchi. When the bronchi appear displaced (as in this case) by a peripherally located mass, well demarcated in some areas (the cephalic portion) and indistinct in others (its medial and caudal portions), and with its base against the chest wall, the extra-pulmonary origin of the lesion has to be considered. The presence of cough and hemoptysis suggest bronchial involvement. Possibilities: 1) Pleural tumor with lung invasion. 2) Peripheral pulmonary lesion with lung invasion. Among the former, mesotheliomas, metastatic tumor, and sarcoma are the most likely possibilities. Locculated effusion is less likely in view of the location and appearance of the lesion and clinical history.

Similar symptoms two years previously followed by recovery would suggest pneumonia or recurrent pulmonary emboli with infarction. The presence of a friction rub on ausculatation and the apparent extrapulmonary location of the mass makes me suspect a malignant mesothelioma.

Dr. Viamonte's impression: 1) MALIGNANT MESOTHELIOMA, 2) PERIPHERAL PULMONARY TUMOR

Roentgenologic Impressions Submitted by Mail

Angiosarcoma	25
Malignant mesothelioma	24
Bronchiolar carcinoma	7
Alveolar carcinoma	6
Pulmonary infarct	6
Others	17

Dr. Viamonte: These are excellent possibilities. Pulmonary infarct usually does not present in this way, it would not distort the bronchial tree as we have seen here. The radiologists felt that we were either dealing with a sarcoma or a mesothelioma and that the second possibility that a peripheral pulmonary lesion may account for this abnormality.

Dr. Regato: Dr. J.P. Hodes, of Philadelphia, suggested the combined possibility of asbestosis and mesothelioma. Dr. M. Daves, of Denver, offered pseudolymphoma; Dr. L.O. Martinez, of Miami, preferred hemangiopericytoma and Dr. N. Goodman, of Denver, bronchiolar cell carcinoma.

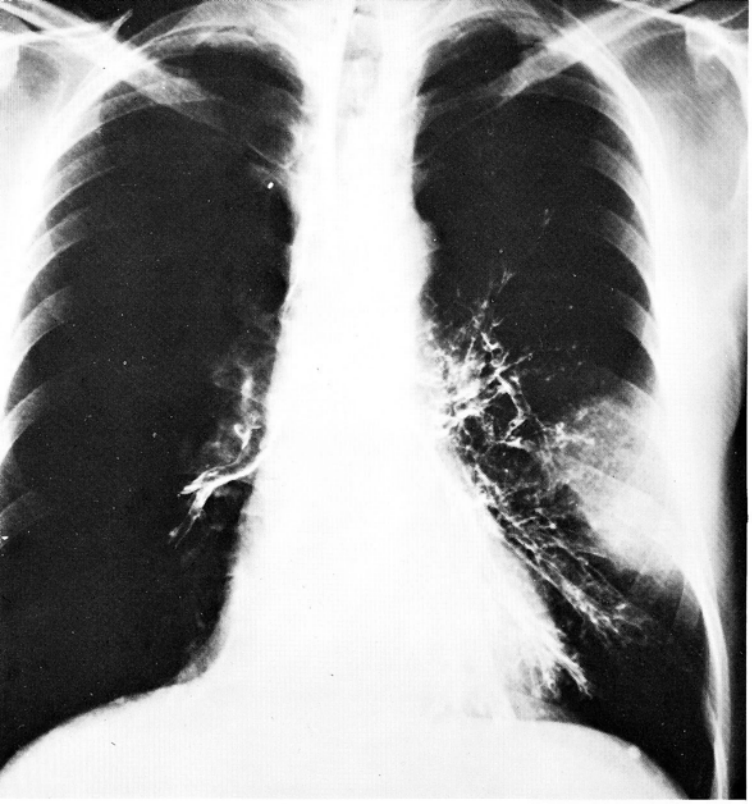


Fig. 1—Left side bronchogram showing mass against left lateral chest wall.

Operative findings: On November 1, 1965, a thoracotomy was done and a left upper lobe lobectomy was carried out. The lung contained a firm, well circumscribed lesion, 3 cm in diameter; an upper lobectomy was done.

Dr. Liebow: This lesion consists of somewhat variable but predominantly spindle-shaped cells in a homogeneous, faintly staining, acidophilic matrix. The vascularity of the mass varies, but some parts contain very few of the thin-walled vessels seen elsewhere. One large pulmonary artery has been invaded and a long polypoid mass of tumor tissue consisting of compacted masses of the component cells projects into the lumen. The Alcian stain is negative. In some places a reticulum stain demonstrates argyrophilic fibers to surround individual cells, but these fibers do not extend into the hyaline matrix where the latter is abundant. Mitoses are numerous and sometimes bizarre. Thus the tumor has the appearance of a sarcoma. Since such tumors often ultimately prove to be, in fact, carcinosarcoma, a careful search for an epithelial component was made. The tumor was not found to contain neoplastic epithelium, although in part the tumor cells did come into relation with normal epithelium of bronchi which had become invaded without destruction of the lining cells. The lesion is thus clearly within the parenchyma and the best diagnosis appears to be primary peripheral sarcoma of the lung. Such tumors, whether arising peripherally or, as they often do, as polypoid masses within proximal bronchi, have been generally considered to have a better prognosis than bronchogenic carcinoma (Iverson).

Dr. Liebow's diagnosis: SARCOMA OF THE LUNG

Histopathologic Diagnoses Submitted by Mail

Malignant mesothelioma	41
Hemangiosarcoma	9
Hemangiopericytoma	8
Rhabdomyosarcoma	11
Leimyosarcoma	13
Other sarcomas	21
Others	27

Dr. Liebow: Malignant mesothelioma was the most popular. Howeer, I think this is most unlikely in view of the position of the lesion, the histologic structure and the fact that it is not diffuse. Whether this is a hemangiosarcoma is questionable. I do not think it is a hemangiopericytoma; the cells are much larger than those of hemangiopericytoma. It would be very difficult to specify the particular type of sarcoma unless one found a specific structure for rhabdomyosarcoma, leiomyosarcoma; for the most part, this requires electron microscopy.

Fig. 2—Sarcoma of the lung: Whorls of large spindle-shaped or rounded cells (X 200).

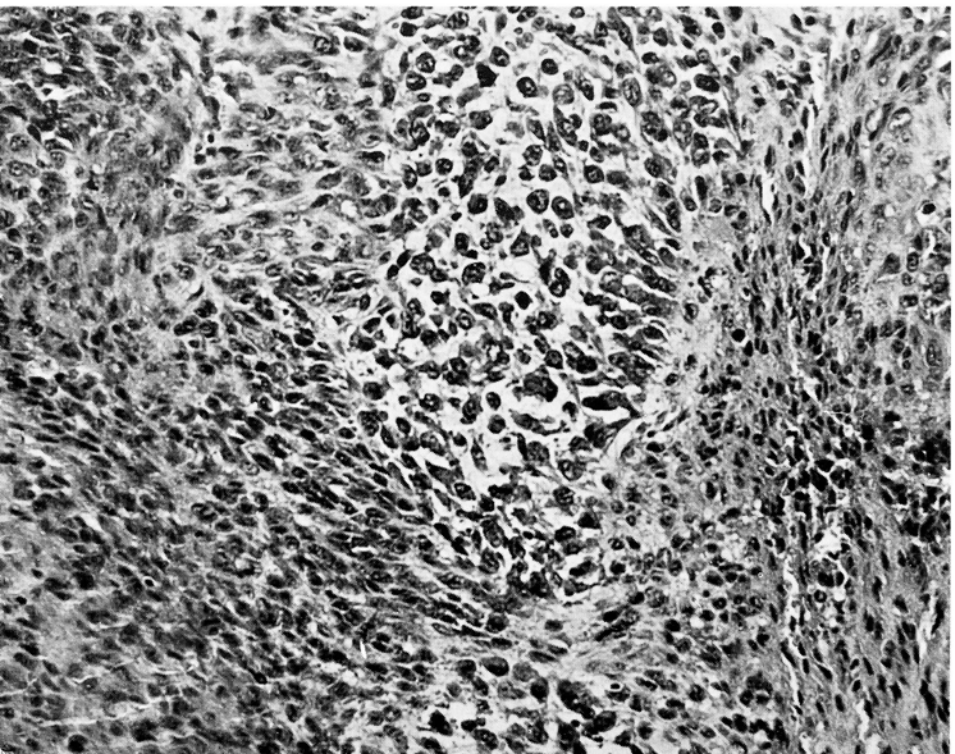
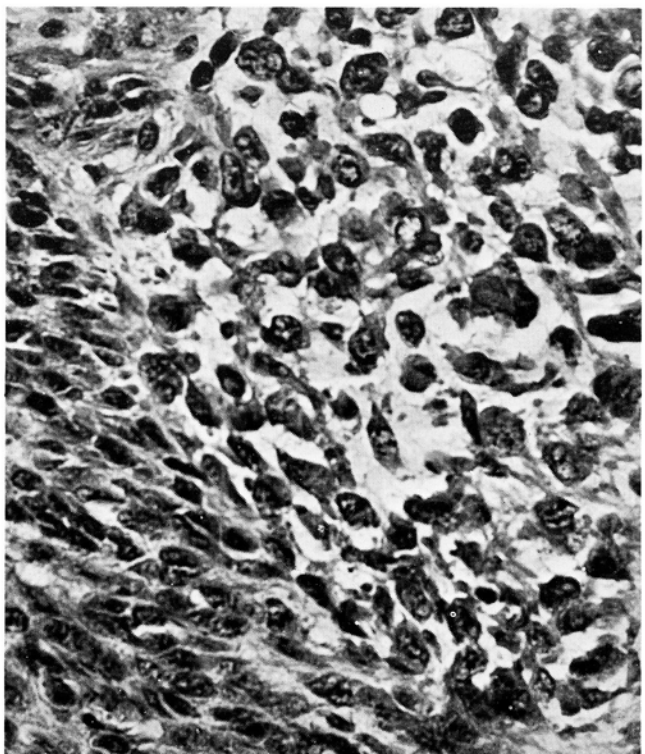


Fig. 3—Detail of Fig. 2. Gradual transition from spindle-shaped to rounded cells (X 400).



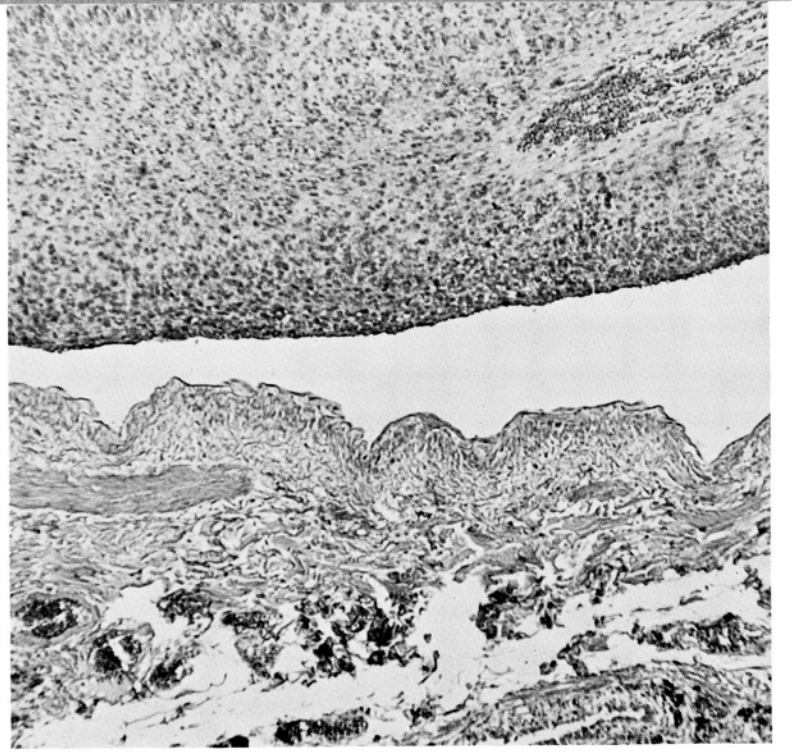


Fig. 4—Tumor thrombus within large pulmonary artery. One wall of the latter lies below the mass of tumor cells (X 45).

Dr. Regato: Dr. B. Castleman, of Boston, and Dr. R.W. Morrisey, of San Antonio, made a diagnosis of mesothelioma. Dr. M. Wheelock, of Miami, preferred leimyosarcoma; Dr. R.E. Stanford, of Denver, rhabdomyosarcoma; Dr. J.M. Woodruff, of Dener, malignant schwannoma; Dr. J.H. Coffey, of Fargo, mesenchymoma. Dr. M.R. Abell, of Ann Arbor, suggested metastatic melanoma, and Dr. S.H. Choy, of San Francisco, squamous-cell carcinoma simulating sarcoma. Dr. D. Mulkey, of Denver, who submitted the case, made a diagnosis of embryoma.

Subsequent history: Within weeks following the thoracotomy the patient developed tumefactions of the right side of the thyroid gland and right axilla as well as some infiltration of the skin of the chin. On December 22, 1965, he underwent a right subtotal thyroidectomy; the tumor removed was 6 x 4 x 2.5 cm, firm, white, occupying most of the gland and microscopically identical with the pulmonary lesion. On February 2, 1966, the lesions of the axilla and chin were excised; their character was identical with the lesions of the thyroid and lung.

Dr. D. Mulkey, Denver, Colo.: The patient was treated with methotrexate initially and finally with thio-tepa and actually had no improvement in his course. He went on to die about six months after development of his initial lesion. At the time of death he had multiple skin lesions similar to ones which were biopsied on the chin, axilla, abdominal wall, elbow, scrotum and in the groin. At the time of death his liver was palpable and he had a bilirubin of 8 mgm%. An autopsy was not obtained.

Dr. Regato: Did you have the impression that this was a lesion of the lung?

Dr. Mulkey: That was the impression.

Dr. Regato: And your diagnosis was embryoma?

Dr. Mulkey: This diagnois was made through the epithelial elements which Dr. Liebow pointed out and also the sarcomatous elements which were seen.

Dr. Pool: I have no reflections to communicate on this case but I would just like to say how much I have enjoyed being exposed to the wisdom of the pathologists and radiologists.

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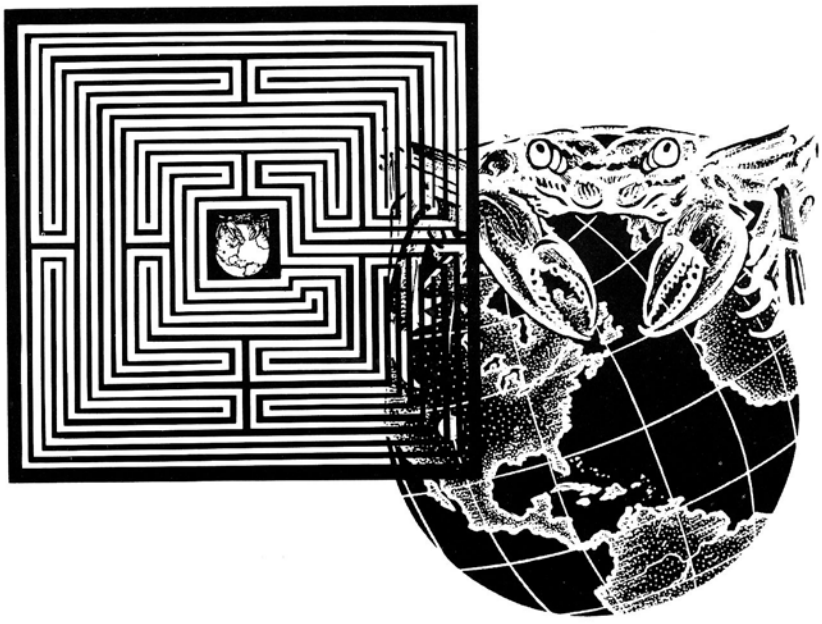
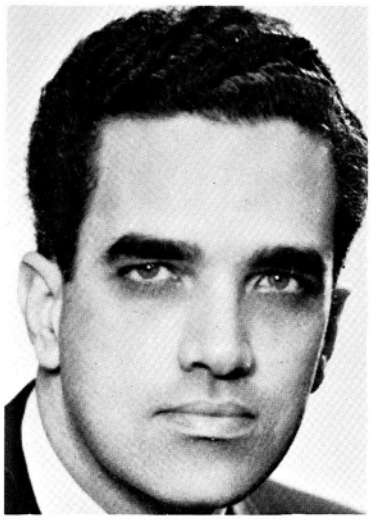
Maria Viamonte, M. D.



OUR GUEST SPEAKERS

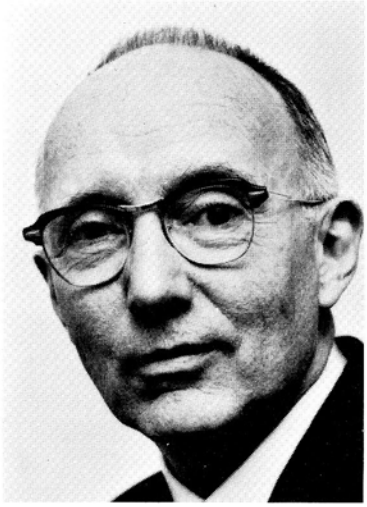


Manuel Viamonte, Jr., M.D.

Director of the Department of Diagnostic Radiology, Mount Sinai Hospital of Greater Miami and Professor and Chairman, Department of Radiology, University of Miami Medical School, Florida. Dr. Viamonte is one of the outstanding young radiodiagnosticians in the nation. He has won awards for his work in lymphangiography and angiocardiography.

Averill A. Liebow, M.D.

Professor and Chairman of the Department of Pathology, University of California School of Medicine at San Diego. Dr. Liebow is an acknowledged authority in pulmonary pathology and a dedicated teacher in his specialty.



John L. Pool, M.D.

Attending Surgeon, Thoracic Service, Memorial Cancer Center, New York City and Assistant Clinical Professor of Surgery, Cornell University Medical College, New York. Dr. Pool is a dedicated contributor to the literature of his specialty and a man with experience in the field of tumors of the lung and mediastinum.