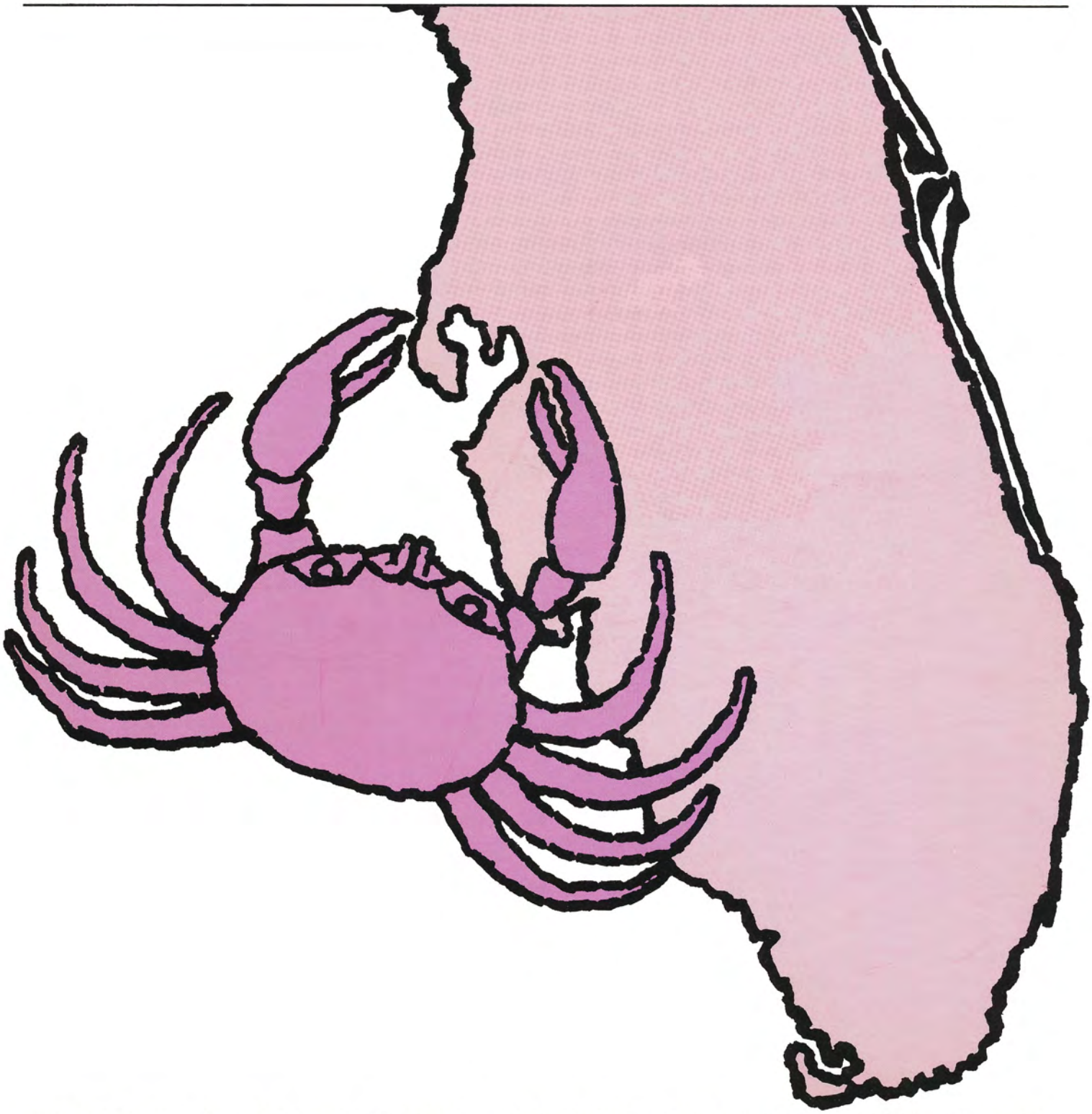
cancer seminar

VOLUME I NO. 4 SECOND SERIES



UNIVERSITY OF SOUTH FLORIDA • VETERANS HOSPITAL • TAMPA, FLORIDA

CANCER SEMINAR

SECOND SERIES, VOLUME ONE MAY 1981 NUMBER FOUR
Juan A. del Regato, Editor
Donna D. Pittman, Assistant Editor

CONTENTS

EDITORIAL OFFICE
VETERANS ADMINISTRATION MEDICAL CENTER
Department of Radiology
13000 North 30th Street, Tampa, Florida 33612

This second series of CANCER SEMINAR is printed by Joe B. Klay and Sons, Inc. in Tampa, Florida. J. A. del Regato, M.D., editor. Subscription rate is $15.00 per copy. Address all correspondence to the editorial office.

TUMORS OF THE LUNG AND MEDIASTINUM

The radiologic and histopathologic confrontation that characterizes these CANCER SEMINARS is the basis of the necessary continuous revision of our views in the utilization of these tools. Radiology has now been enriched by new approaches, and histopathology has been extended by electronics.

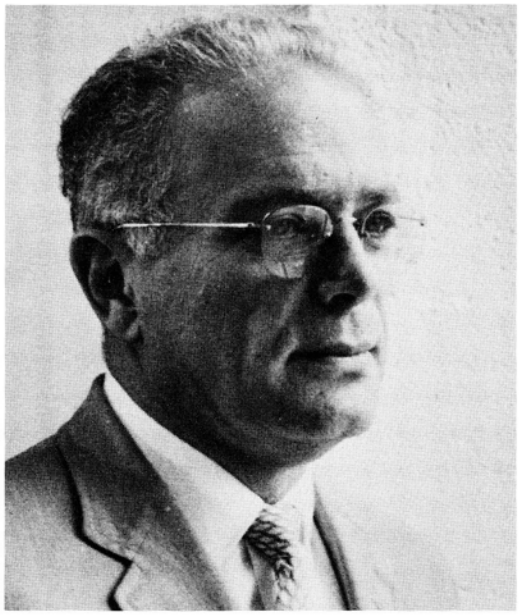
This CANCER SEMINAR on mediastinal and pulmonary tumors was held in the auditorium of the University of South Florida College of Medicine. Dr. Manuel Viamonte, Jr., one of the most distinguished research radiodiagnosticians of the present generation, proved his keen sense of clinical possibilities. Dr. Raffaele Lattes, whose world reputation as a tumor histopathologist is undisputed, displayed his didactic abilities and revealed his unusual insight into this group of tumors. Dr. Thomas B. Ferguson, a surgeon with unusual clinical capabilities, made the comprehensive discussion of the cases beyond the expertise of his partners in the seminar. Their presentations and discussion of each case were enriched by the opinions submitted by mail by a number of other observers and experts. Edited discussions and pertinent references complete these proceedings.

CANCER SEMINAR is a recognized educational and research exercise that contributes to the shaping of our views of these difficult problems. Originating in Colorado Springs where they were held for 24 consecutive years, they are now offered in Tampa under the auspices of the Departments of Radiology and Pathology of the University of South Florida. Through the initiative of Arthur D. Graham, M.D., Professor and Chairman of the Department of Radiology, and the most valuable counsel and support of Henry A. Azar, M.D. of the Department of Pathology, this new series of CANCER SEMINARS has been established. The contributors and dozens of participants have a great part in the shaping of these accounts. We are greatly indebted to all of them.

J. A. del Regato, M.D.
Tampa, Florida
June, 1981

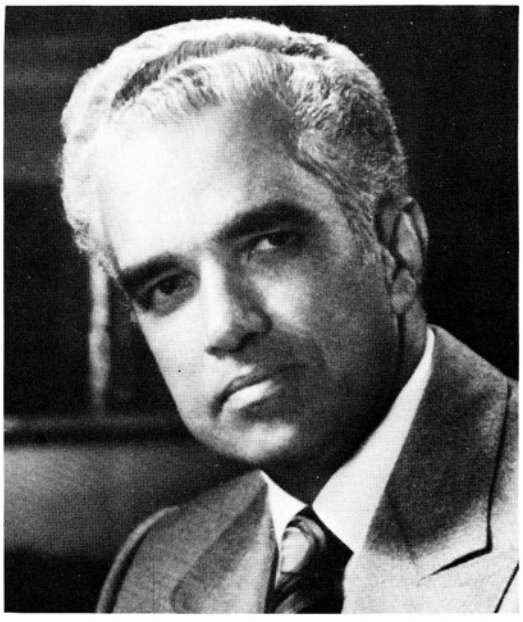
THOMAS B. FERGUSON, M.D.

Clinical Professor of Thoracic Surgery, Washington University School of Medicine, St. Louis, Missouri. A skillful surgeon, Dr. Ferguson is also a recognized authority in surgical oncology.



RAFFAELE LATTES, M.D.

Professor of Surgical Pathology, College of Physicians and Surgeons, Columbia University, New York, New York. Dr. Lattes is an internationally respected authority in pathology of tumors.



MANUEL VIAMONTE, JR., M.D.

Professor of Radiology, University of Miami School of Medicine, Miami Beach, Florida. Dr. Viamonte is one of the recognized leaders of research in diagnostic radiology.

1. ENDODERMAL SINUS TUMOR OF THE MEDIASTINUM

Contributed by T. T. Tang, M.D. and L. E. Kun, M.D., Milwaukee, Wisconsin

The patient was a 14-year-old boy in March 1977 when he complained of pain in the right side of the chest that was accompanied by fatigue, anorexia, cough, fever and chills.

Dr. Viamonte: Tomographic section was obtained with the patient supine with plane of section at the level of the anterior aspect of thoracic vertebral bodies. There is a large density occupying the lower two-thirds of the right lung with normal appearance of bony structures and left air soft tissue interfaces. The airway is patent, and the lesion represents an air space filling process. A second tomographic section obtained at the level of the anterior arch of the first and second ribs shows similar radiographic findings with additional evidence of pleural effusion.

If we assume that the patient had a diffuse process with slow evolution, we would consider an inflammation such as pulmonary pseudotumor. If the pulmonary process were of short duration, one must presume that the patient has a malignant tumor. The differential diagnosis would include an alveolar lymphoma and broncho-alveolar carcinoma. The latter is a tumor seen in older individuals.

Dr. Viamonte's Impression:

ALVEOLAR PROCESS:

1) INFLAMMATORY PSEUDOTUMOR
2) ALVEOLAR LYMPHOMA
3) ALVEOLAR CARCINOMA

Radiologic impressions submitted:

Lymphoma (Hodgkin's)	66
Tuberculosis	22
Pneumonia	27
Others	30

Dr. Viamonte: Most radiologists had the same interpretation, that it is an alveolar process, based on the fact that we see a patent airway. Alveolar processes in a fourteen-year-old child would include inflammation, and there could be tuberculosis and pneumonia. I would be against

Fig. 1—Tomographic section showing density in lower part of right lung.

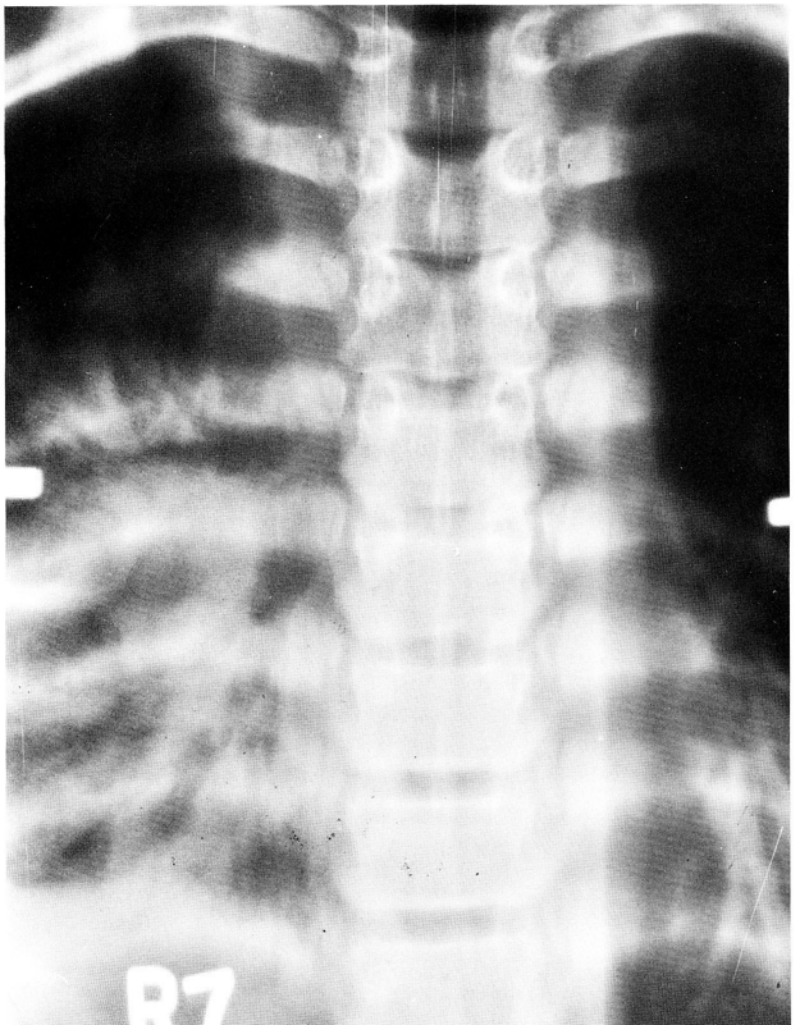
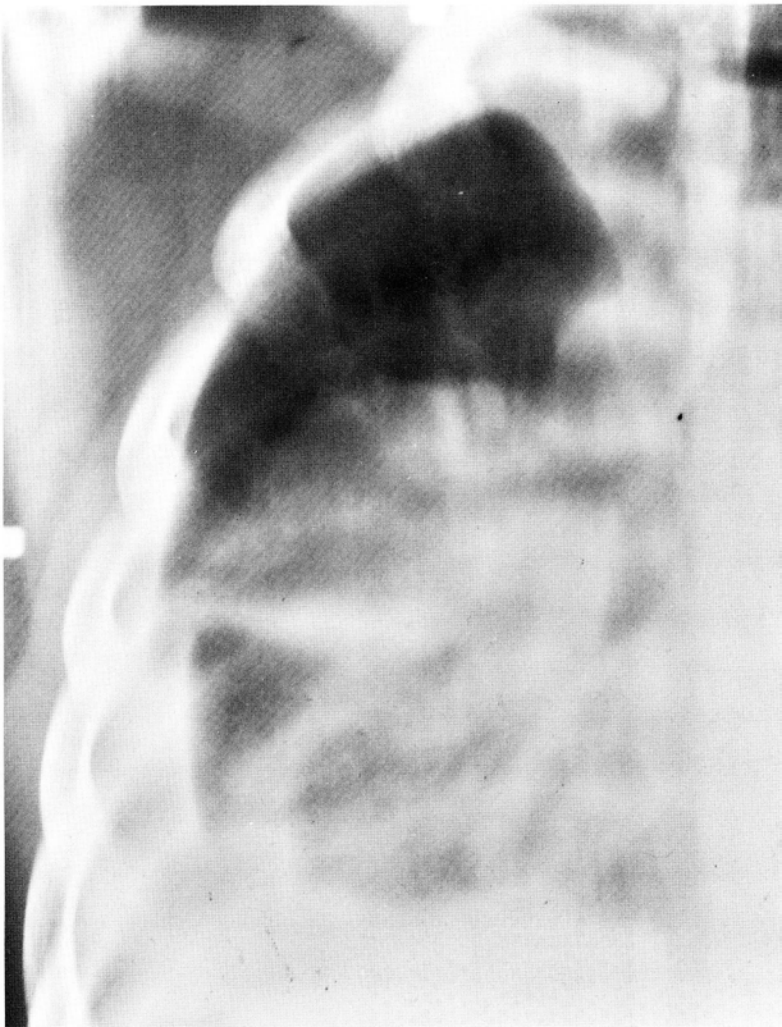


Fig. 2—Tomographic section showing evidence of pleural effusion.



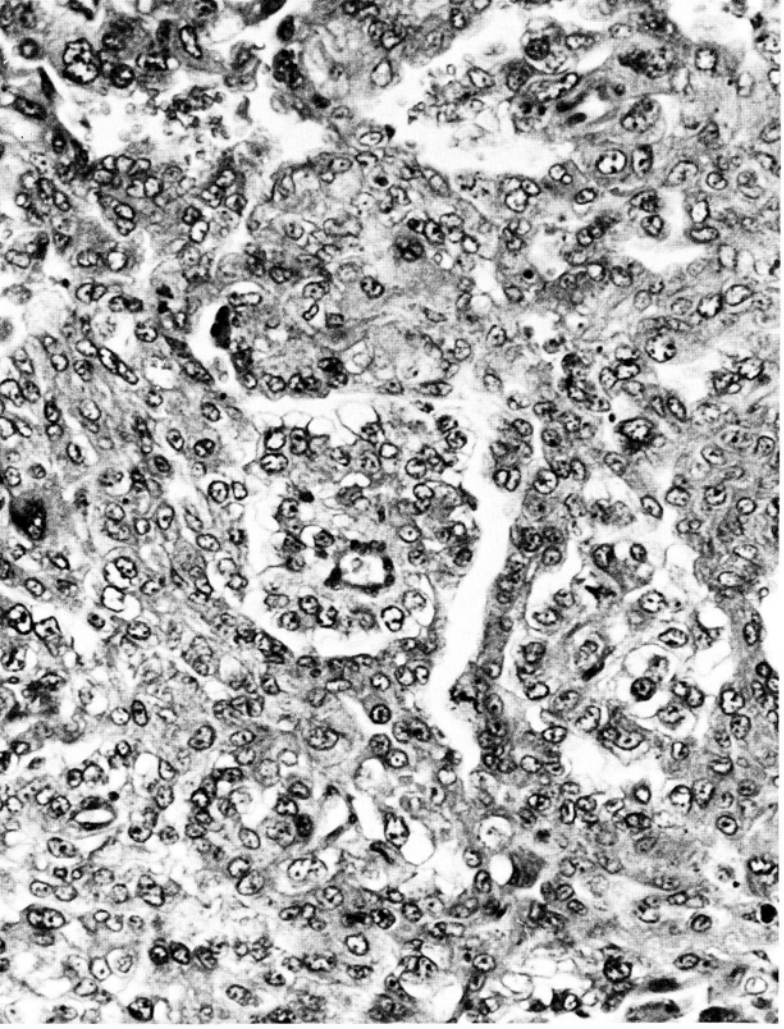


Fig. 3—Endodermal sinus tumor. Note glomeruloid structures (H + E, × 270).

tuberculosis because it is seen very infrequently; it is more often observed as an upper lobe disease in diabetics and debilitated adults. Any of the pneumonias or pseudotumors could certainly produce such a finding. In addition to lymphomas, I would add the broncho-alveolar carcinoma as a likely possibility.

Dr. del Regato: Drs. Arnold Friedman of New York and James Cox of Milwaukee offered an impression of Hodgkin's disease; Dr. Benjamin Felson of Cincinnati preferred Burkitt's lymphoma.

Operative Findings: On March 25, 1977 a thoracotomy was done. A large mass was found arising from the mediastinum and infiltrating the three lobes of the right lung. The tumor extended around the trachea and infiltrated the superior vena cava. A specimen was removed for biopsy.

Dr. Lattes: Histologically, this is a tumor that has the pattern of a partly papillary carcinoma and in which the tumor cells have vesicular nuclei, often arranged around a central vessel, sometimes imitating embryonal glomeruli. These cells have a clear cytoplasm that often makes a clear bubble towards the lumen. There are many mitoses and there a few bizarre large hyperchromatic nuclei which suggest the possibility of a choriocarcinomatous component. There is some PAS positive material, most of which appears to be extracellular. The clear vacuoles described before do not contain PAS positive material. The reticulin stains confirm the epithelial pattern described above.

Since this tumor was found in the mediastinum, it could well be a primary tumor of the thymus, rather than a metastasis. The pattern is that of the endodermal sinus carcinoma of Teilum, with areas suggesting the possibility of associated choriocarcinoma. We are dealing with a highly malignant tumor with an extremely poor prognosis.

Dr. Lattes' Diagnosis:

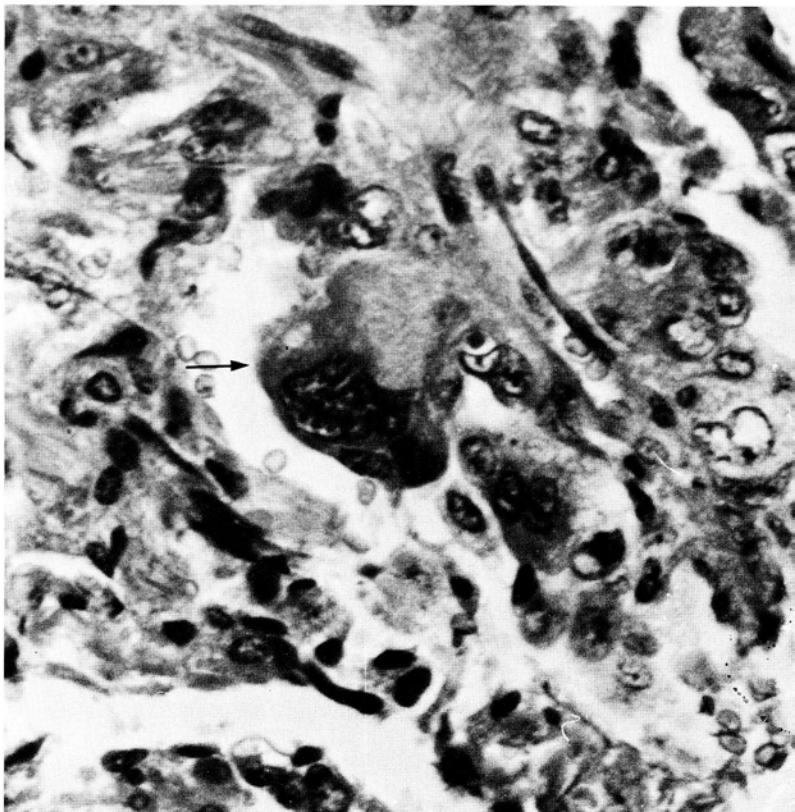
ENDODERMAL SINUS TUMOR (Teratocarcinoma?)

Histopathologic diagnoses submitted:

Embryonal carcinoma, metastatic	37
Clear-cell (papillary) adenocarcinoma	18
Malignant epithelial mesothelioma	15
Endodermal sinus tumor	05
Various other malignant tumors	18
Chemodectoma	03

Dr. Lattes: In my opinion, clear-cell (papillary) carcinoma is a highly specialized variant. I am sure that this is an epithelial, not a mesothelial, tumor. Chemodectoma is a tumor of the carotid or aortic body type, and it is benign.

Fig. 4—Detail showing a bizarre cell resembling a syncytial trophoblast (arrow) (H + E, × 530).



Dr. del Regato: Dr. M. R. Abell of Ann Arbor, Michigan made a diagnosis of embryonal carcinoma. Dr. Stephen E. Vernon of Los Angeles and Dr. Henry A. Azar of Tampa offered a diagnosis of clear-cell adenocarcinoma. Dr. Olga J. Dobrogorski of Cincinnati designated it as papillary adenocarcinoma. Dr. Robert R. Pascal of New York preferred rhabdomyosarcoma. Dr. C. Maso of Chicago offered choriocarcinoma, and Dr. Carlos Perez-Mesa of Columbia, Missouri, alveolar carcinoma.

Subsequent History: A diagnosis of embryonal carcinoma was rendered, and the patient was submitted to radiotherapy. From March to May 1977 he received 5100 R measured at the midplane of the chest in 38 days. Four weeks after completion of radiotherapy, a second thoracotomy was done, and mostly fibrosis of substitution was found with a few "suspicious" cells. Patient was put on Vincristine and Cyclophosphamide. In August 1977 he developed pain in the right upper abdominal quadrant; liver scan suggested metastases. He was put on Actinomycin D and Adriamycin. He is presently suspected of having a recurrence in the chest and continues to receive chemotherapy.

Dr. Ferguson: I rather suspect that the diagnosis before thoracotomy was in error; probably it was thought that this young man had some type of inflammatory process in the lung, perhaps an inflammatory process superimposed upon a congenital abnormality, such as pulmonary sequestration. There is some fluid present on the roentgenogram, and there is a suggestion of a widening of the mediastinum; both are accessible biopsy areas. I am not conversant enough with this particular tumor to tell whether such biopsy would prove fruitful.

I think it is important to point out that this is a mediastinal teratoma, a highly malignant tumor which already had infiltrated the lung, one of the more ominous ways in which malignant tumors can spread. In the literature, this is a very rare tumor; it is almost always fatal, but there have been bona fide biopsy proven cases reported cured by radiation therapy.

Dr. Mario Saldana, Miami, FL: Dr. Viamonte did not comment on the mediastinal mass. Also, where does Dr. Lattes think this tumor arose from; what is its origin?

Dr. Viamonte: The operative findings revealed that the tumor infiltrated the three lobes; I think that what we are seeing in the tomogram was the infiltration of the lung component. I had no lateral view, so it was impossible to establish whether or not there was a mediastinal component. On the other hand, after I submitted my impressions to Dr. del Regato, I saw an article published in the February 1978 issue of Chest (Garvey); in that article, Figure 3 shows a pattern identical to the one seen here. As a matter of fact, it is a tomogram showing a density in the lung; the air bronchogram is seen through the density. The commentary was that the patient had a mediastinal teratocarcinoma without lung involvement. The authors indicate that although in 1948 Felix Flashner was the first to describe the air bronchogram as a sign of alveolar disease, it is occasionally possible to have a mediastinal tumor compressing the lung but not enough to obliterate the airway. I believe that air bronchography means the airway is patent, and the lesion can be in the distal airway or in the mediastinum compressing the lung.

Dr. Lattes: In our experience, whenever the site of origin of a benign teratoma, malignant teratoma, or some gonadial tumors of the anterior mediastinum can be localized, they originate in the thymus gland. They are not thymomas, of course. When they are seen very small, there is thymic tissue around. The sections that I had in this instance did not show any thymus gland, but I am sure that would have been the case if it had been possible to examine it at an earlier stage.

Dr. James D. Cox, Milwaukee, WI: We had an opportunity to review 24 of these patients with malignant germinal tumors of the mediastinum. As many others have found out, the seminomatous variant is a rather readily curable tumor. In the Walter Reed material, we found two patients having embryonal carcinoma mixed with seminoma who were cured. We were unable to find any patient with choriocarcinoma or teratocarcinoma who had been cured by radiation therapy, surgery, or any means.

References

Cayley, C.K., Caez, H.J., and Mersheimer, W.: Primary bronchogenic carcinoma of the lung in children. Am. J. Dis. Child. 82:49-60, 1951.

Garvey, J. and Parmer, L.: Intrathoracic mass with air bronchogram. Chest 73:209-210, 1978.

Martini, N., Golbey, R.B., Hajdu, S.I., et al: Primary mediastinal germ cell tumors. Cancer 33:763-769, 1974.

Pedersen, H.: Tumors of the anterior mediastinum. Acta Pathol. Microbiol. Scand. (A), Suppl. 212, 1970.

Rosai, J. and Levine, G.D.: Tumors of the thymus (Fascicle 13). Atlas of Tumor Pathology, 2nd series, Armed Forces Institute of Pathology, Washington, D.C., 1976.

Sawyer, K.C., Sawyer, R.B., Lubchenco, A.E., McKinnon, D.A., and Hill, K.A.: Fatal primary cancer of the lung in a teenage smoker. Cancer 20:451-457, 1967.

Teilmann, I., Kassis, H., and Pietra, G.: Primary germ cell tumors of the anterior mediastinum with features of endodermal sinus tumor. Acta Pathol. Microbiol. Scand. 70:267-278, 1967.

2. BENIGN MEDIASTINAL CYSTIC TERATOMA

Contributed by S. E. Vernon, M.D., Los Angeles, California

The patient was an 8-month-old baby girl in June 1977 when she had fever and an episode of hemoptysis; she was found to have a consolidation of the right upper and middle lobes with an apparently loculated cavity of the apex. The hemoglobin was 8.4 gm percent, and there were 54 percent lymphocytes. The skin tests for tuberculosis, candida and mumps as well as the complement fixation for cocci were negative.

Dr. Viamonte: Frontal and lateral roentgenograms of the chest in this child reveal a large density with small air collections occupying the right hemithorax. The mediastinal structures are slightly shifted to the left. There is no evidence of calcification or of pleural or bony involvement. We see the minor fissure in the frontal view. The posterior margin of the lesion is sharp superiorly and indistinct inferiorly. If the lesion were in the lung, the right minor fissure should not be seen. Visualization of this structure indicates aeration of the anterior segment of the right upper lobe and the middle lobe. Consequently, the lesion is pleural based or mediastinal.

A mediastinal lesion such as a loculated mediastinal fluid collection would be unusual in this age group unless the patient had an empyema. There is no evidence of fluid in the right cardiodiaphragmatic sulcus. A mediastinal mass would not have a radiolucent component unless it contains fat or is in communication with the trachea or with the esophagus. Therefore, although initially the history suggests a pulmonary inflammatory process, the radiographic findings are more suggestive of a pleural or mediastinal lesion.

A mediastinal teratoma and a neurenteric cyst may contain air if the former communicates with the trachea or with the esophagus, and if the latter communicates with the duodenum or small bowel. We see no bony abnormalities to suggest neurenteric cyst. Therefore, an unusual form of mediastinal teratoma should be considered. A malformed lung such as cystic adenomatoid malformation could produce a similar radiographic finding.

Dr. Viamonte's Impression:

1) TERATOMA
2) EMPYEMA
3) CYSTIC ADENOMATOIC MALFORMATION

Radiologic impressions submitted:

Staphylococcus pneumonia	37
Tuberculosis	21
Adenomatoid malformation	34
Neuroblastoma	12
Cavitating teratoma	09
15 others	52

Fig. 1—Roentgenogram showing large density of the right lung with air collections.

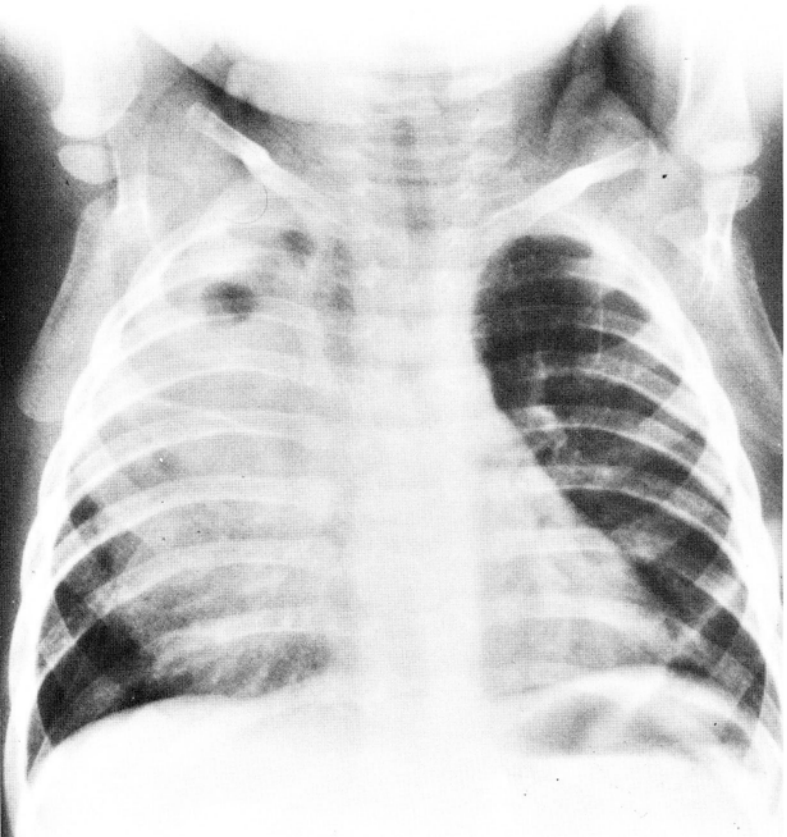
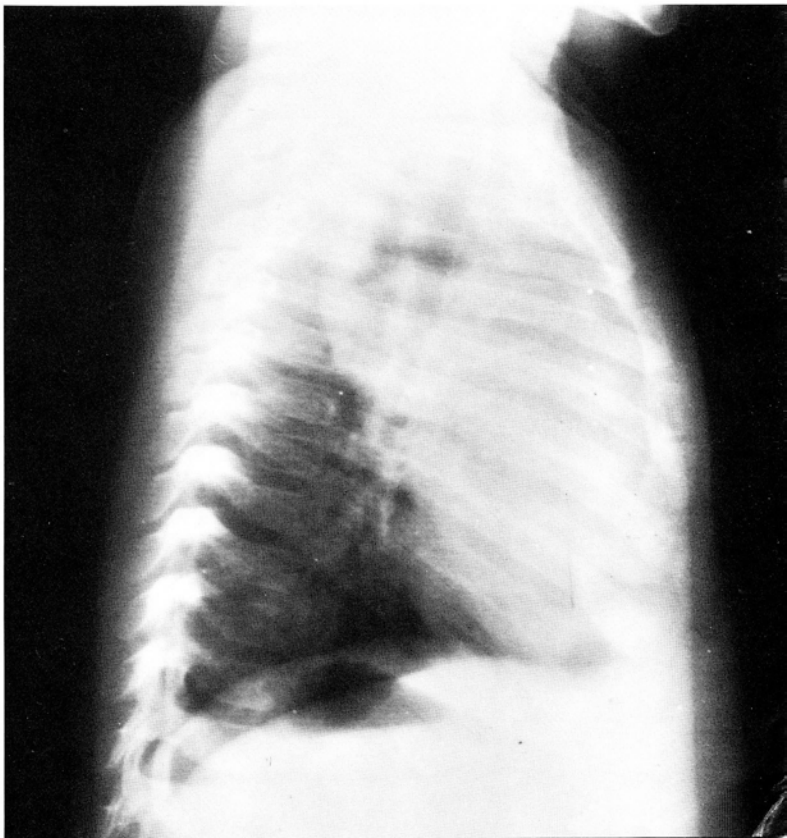


Fig. 2—Lateral roentgenogram showing sharp margin above and indistinct margin below.



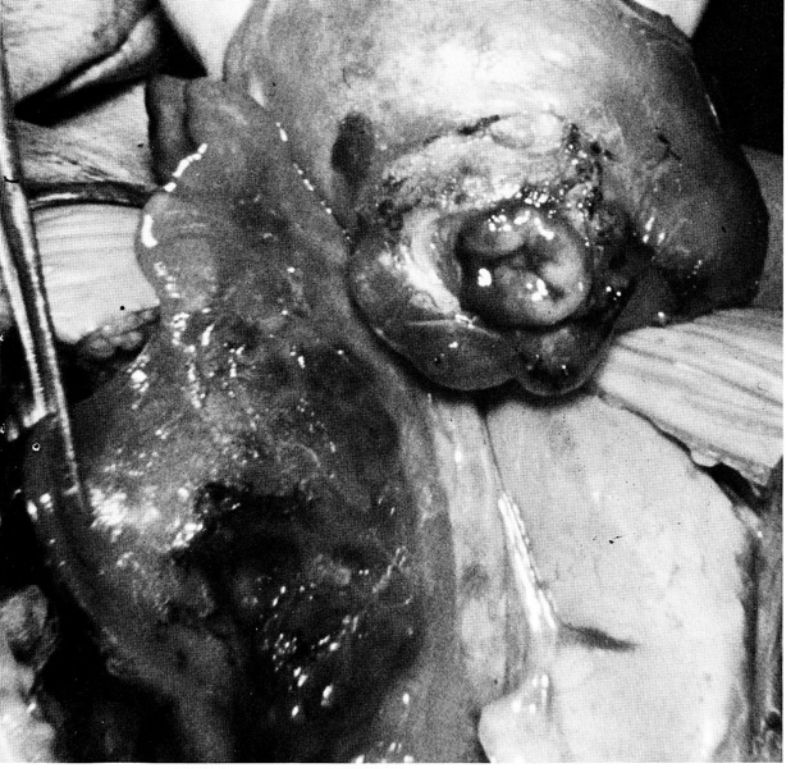


Fig. 3—Partly cystic lesion as it was removed from the lung.

Dr. Viamonte: The staphylococcus pneumonia and tuberculosis were offered due to the presence of air in the upper aspect of the lesion; also, they felt that the lesion arose in the lung. As I have indicated, however, the fact that we see the minor fissure makes it unlikely that the primary process is in the lung. Adenomatoid malformation of the lung is a good diagnosis, but again, the minor fissure sign favors an extrapulmonary rather than intrapulmonary lesion. I would not consider a neuroblastoma; it is an extremely large lesion that has no calcium, and it seems to have a cystic component. Cavitating teratoma is a possibility, but if it is a teratoma, it should not arise in the lung.

Dr. del Regato: Dr. John L. Pool of Connecticut admitted that the cavitation suggested a bronchial connection, whereas the deviation of the trachea allows placing the lesion as originating in the mediastinum. Dr. J. E. Crymes of Miami suggested lymphoma. Dr. Richard Thurer of Miami suggested a dermoid cyst. Dr. R. Otero of Tampa called it a teratoma.

Operative Findings: On July 13, 1977 a right lateral thoracotomy was carried out. A large, apparently encapsulated, mediastinal tumor was found and removed with resection of the thymus and part of the lung. The tumor measured 8 x 6 x 4 cm; it presented cystic areas containing as much as 100 cc of mucoid material.

Dr. Lattes: This is a good example of a benign cystic teratoma in which there are tissues representative of all the different layers of the embryo, including respiratory epithelium, columnar epithelium of the colonic type, gastric epithelium, neuroectoderm represented by glial tissue and ganglion cells, some smaller cells in the rosette-like pattern, smooth muscle, cartilage, adipose tissue, etc. I have not seen any area that would suggest malignancy.

In our experience, the benign and malignant teratomatous tumors of the mediastinum as well as the germ cell tumors originate within the thymus.

Dr. Lattes' Diagnosis:

BENIGN CYSTIC TERATOMA

Histopathologic diagnoses submitted:

Benign cystic teratoma	87
Mature teratoma	06
Immature teratoma	05

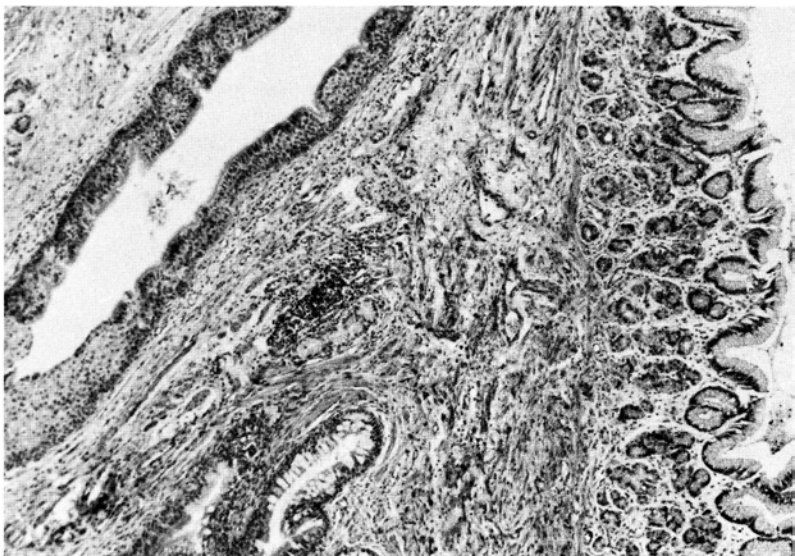
Dr. Lattes: It is a landslide in favor of the mature teratoma; only five misguided people thought it was immature.

Dr. del Regato: Most of our correspondents agreed on a diagnosis of benign cystic teratoma.

Subsequent History: The patient has been followed by Dr. Beverly Neyland of Las Vegas, Nevada: in November 1977 the patient was in apparent good health.

Dr. Ferguson: I would agree that this child should have been explored forthwith; with the radiographic findings as they were, exploration was the next step. Since the surgeon did not know exactly what the anterior mediastinal mass was, he did resect the thymus and even resected what we presume was lung tissue adherent to the mass. I think that it is proper to do so; the child certainly will not suffer any consequence by having the upper lobe removed.

Fig. 4—Cyst lining by mucosa of the gastric antral type. Note ducts lined by ciliated and transitional epithelium with occasional goblet cells, and scattered smooth muscle bundles (H + E, × 84).



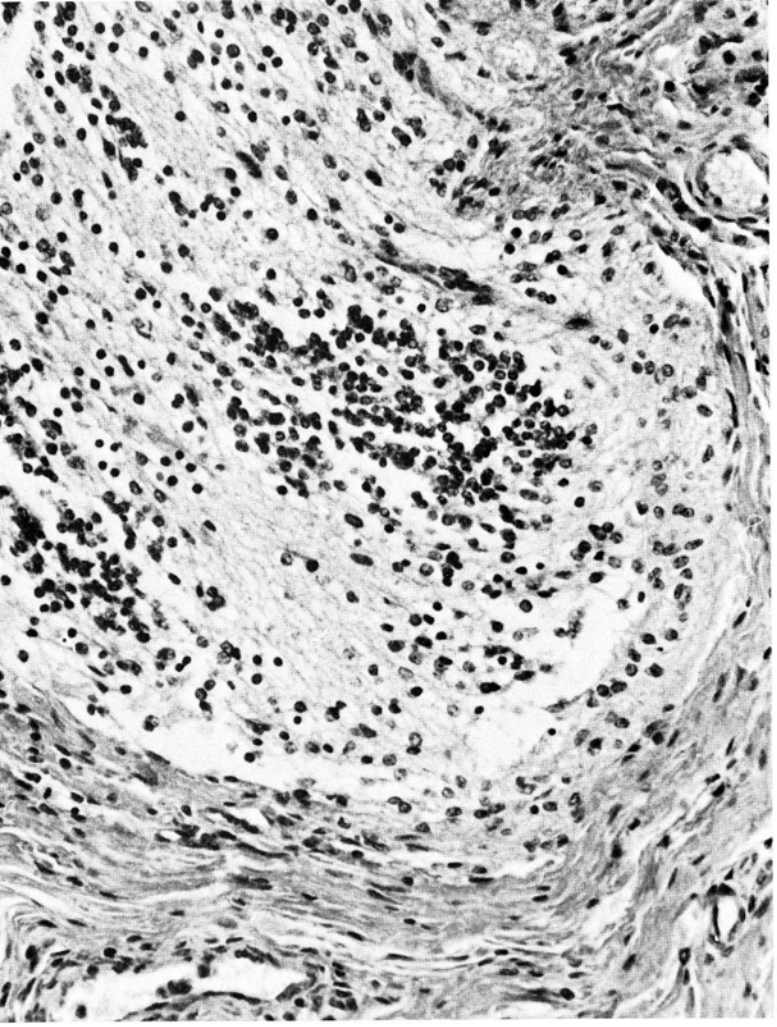


Fig. 5—Glial tissue (H + E, × 270).

In any series of mediastinal tumors, one third will be malignant. In children specifically, one half of the tumors will be malignant. As Dr. Cox mentioned, seminoma and some others have a very good prognosis, so this is not a desperate situation. In young boys under two years of age, Hodgkin's disease is more likely to be present than in females; in females, thymomas are more likely to be encountered.

Dr. John Pool, Wilton, CN: Recently, it has been shown that removal of the spleen in children changes the immunologic competence, making children, and perhaps adults, more susceptible to infection. Is there any information on the removal of the thymus gland in this child's age group with regard to immunological competence?

Dr. Ferguson: There has been a lot of work done on this, but I am not sure that it has proved any immunological deficit.

Dr. Henry Azar, Tampa, FL: At present, there is no evidence that prenatal or thymectomy done early in life interferes in a significant manner with development of immunity. Anything done to the thymus after birth may not interfere significantly with development of cell immunity.

Dr. del Regato: How about splenectomy?

Dr. Azar: Splenectomy seems to develop into susceptibility to certain infections later in life, but not so with thymectomy.

Dr. Lattes: Isn't it true, Dr. Azar, that it is very difficult to completely remove the thymus, even in doing a radical thymectomy? The distribution of the microscopic lobules of thymus in the neck has been studied. We really do not know whether a complete thymectomy at birth would affect immunological machinery because the thymus is not removed completely.

Dr. Azar: In most lower animals, early thymectomy does not appear to affect the cellular immunity. The same can be argued about the treatment of myasthenia gravis; some respond, and others do not.

Dr. Lattes: This patient was a female baby. It is interesting that the benign teratomatous lesions of the anterior mediastinum occur in both sexes, but the malignant teratomas, embryonal carcinomas, and most germinomas occur almost exclusively in the male.

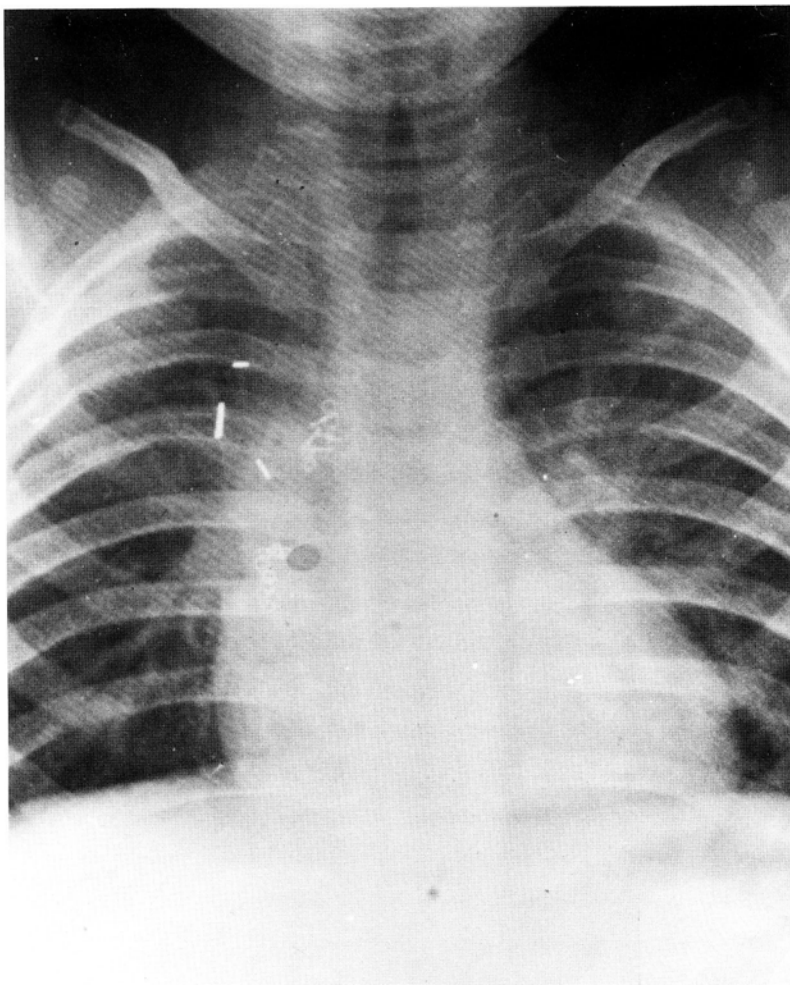
References

Garvey, J. and Parmer, L.: Intrathoracic mass with air bronchogram. Chest 73:209-210, 1978.

Schlumberger, H.G.: Tumor of the mediastinum. Atlas of Tumor Pathology, Armed Forces Institute of Pathology, Washington, D.C., 1951.

Willis, R.A.: Teratomas. Atlas of Tumor Pathology, Armed Forces Institute of Pathology, Washington, D.C., 1951.

Fig. 6—Post-operative roentgenogram, November 1977.



3. SEMINOMA OF THE MEDIASTINUM

Contributed by N. S. Rosenthal, M.D., Tampa, Florida

The patient was a 29-year-old man in February 1977 when he began coughing; he had lost 20 lbs. in weight under a reducing diet. On physical examination, there were no significant findings.

Dr. Viamonte: The chest roentgenograms reveal a large mediastinal mass occupying the anterior and middle mediastinum and surrounding the heart. It extends from the thoracic inlet down to the diaphragm. Left pleural effusion is noted and probably accounts for the separation of the air in the fundus of the stomach from the base of the left lung. The esophagus appears undisplaced and uninvolved. The bony structures appear radiographically intact.

A mediastinal mass in a 29-year-old man with left plural effusion should suggest first the possibility of a lymphoma. The most common form of anterior mediastinal lymphoma is nodular sclerosing Hodgkin's. The second most common process would be a teratoma or a metastatic testicular tumor. The testes should always be carefully examined when an anterior mediastinal mass is discovered in a young man. Germinomas may be histologically confused with thymomas.

Dr. Viamonte's Impression:

1) **LYMPHOMA**
2) **GERMINOMA**

Radiologic impressions submitted:

Lymphoma (Hodgkin's)	75
Teratoma	36
Thymoma	35
Seminoma	31
Various others	26

Dr. Viamonte: We mentioned thymomas; they would be down the list, primarily based on the pleural effusion. Most thymomas are benign; when malignant, they are infiltrating and certainly can produce pleural effusion. I put seminomas together with teratomas.

Dr. del Regato: Drs. J. Frank Wilson and James Cox of Milwaukee suggested a diagnosis of mediastinal seminoma. Dr. A. C. Speranza of Milwaukee and Dr. Richard Thurer of Miami preferred Hodgkin's disease. Dr. John L. Pool of Connecticut also suggested a seminoma.

Operative Findings: On March 23, 1977 a mediastinal biopsy was done.

Dr. Lattes: The fragment of tissue from this large mediastinal mass shows a partly necrotic tumor. Where it is well preserved, it exhibits a fairly homogeneous cell population with somewhat rounded large nuclei, fairly conspicuous nucleoli, and poorly outlined cytoplasm. Mitotic activity is high; there is no tendency toward glandular or any other type of differentiation.

Reticulin stains are in favor of an epithelial origin for this tumor. The tumor cells contain

Fig. 1—Large mediastinal mass surrounding the heart.

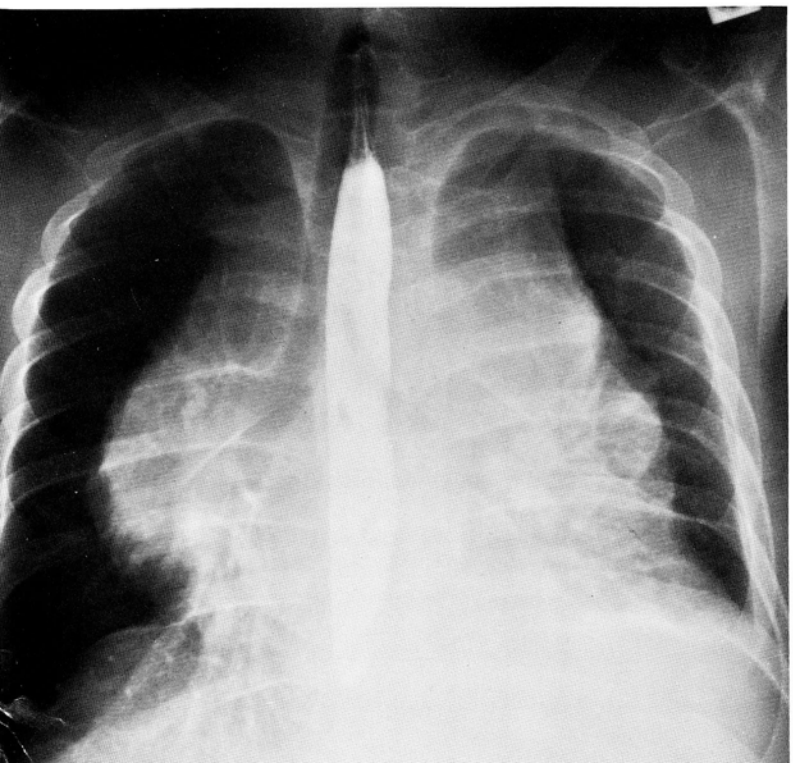
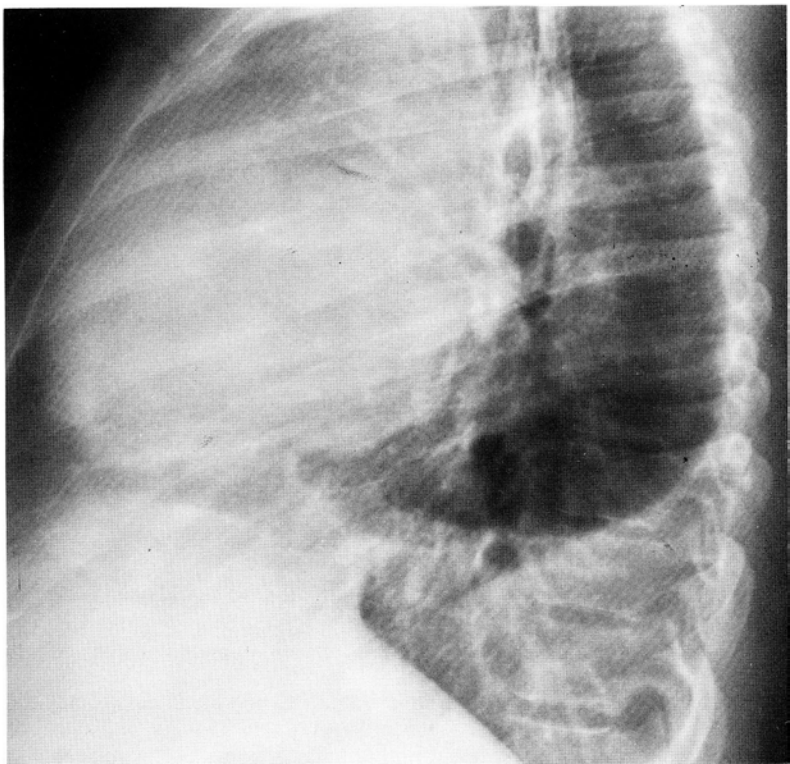


Fig. 2—The mass occupies the anterior and medial mediastinum.



PAS positive granules which are removed with diatase and are most probably glycogen.

Histologically, this tumor is consistent with a seminoma or dysgerminoma. They are not infrequently found as primary tumors of the mediastinum, are often limited within the thymus, and found almost exclusively in adult males. The various theories as to the presence of germ cell tumors in the thymic region have never been fully satisfactory, in my opinion.

Dr. Lattes' Diagnosis:

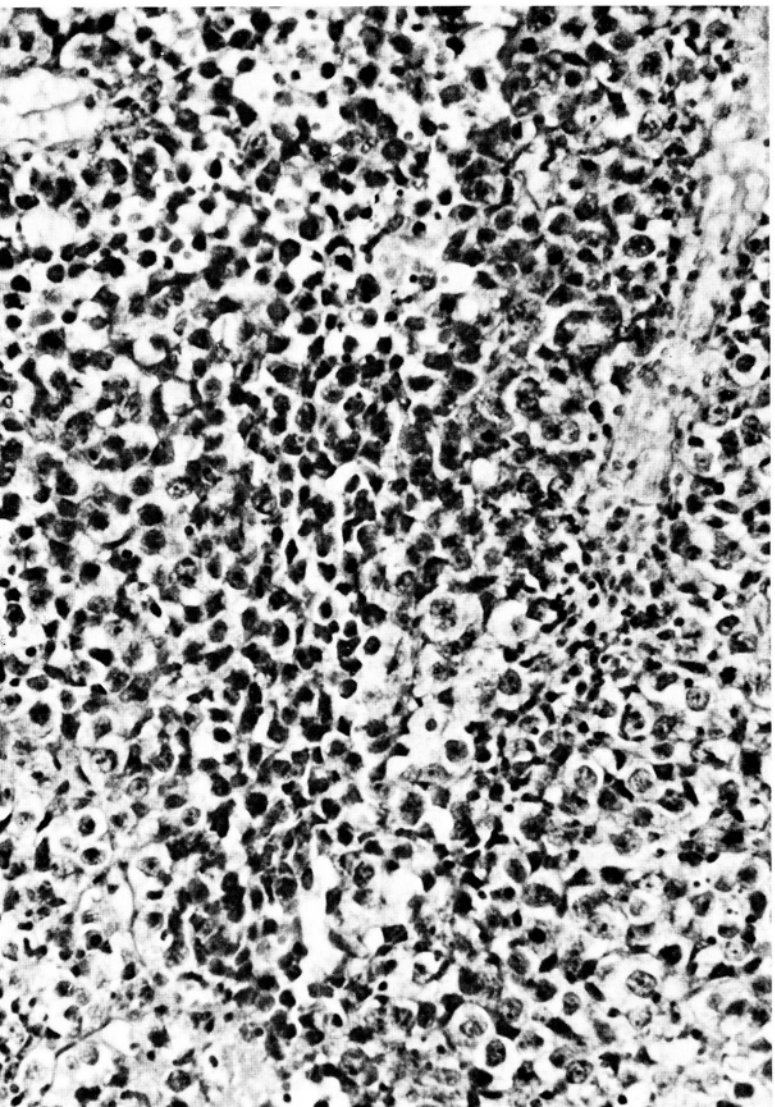
SEMINOMA

Histopathologic diagnoses submitted:

Seminoma	64
Thymic germinoma	09
Embryonal carcinoma	15
Anaplastic carcinoma	14
Thymoma	12
Others	10

Dr. Lattes: Seminoma and thymic germinoma are two ways of saying the same thing. Embryonal carcinoma and anaplastic carcinomas are terms that generally are used histologically, biologically, and clinically much more in malignant lesions with adenocarcinomatous areas, papillary areas, etc. Thymoma could be used only in the broadest possible sense; these are tumors in the thymus, but they are not tumors of thymic tissue. It might be acceptable to say that this is a thymoma of the seminoma type, but it is better to drop the term thymoma.

Fig. 3—Typical seminoma or dysgerminoma pattern (H + E, × 270).



Dr. del Regato: Sister Ignatius Owyang of Cincinnati and Dr. Henry A. Azar of Tampa also offered a diagnosis of thymic germinoma.

Subsequent History: Following a histopathologic report of germinal tumor, the patient was started on a series of radiotherapy applications. Having received only 1300 R in 1½ weeks, radiotherapy was discontinued, and the patient was transferred to Wilford Hall Hospital in Texas. He was put on Bleomycin with no response and with loss of weight. His condition worsened, and he was transferred to Travis Air Force Base in California. He was put on Actinomycin D and Bleomycin. He developed fever and seizures, and on September 21, 1977 he expired. Autopsy revealed bronchopneumonia and only a small focus of tumor in the mediastinum with large areas of necrosis. No metastases were found anywhere.

We owe this information to Dr. Nestor Legaspi.

Dr. Ferguson: With seminoma one should be as aggressive as possible. There is some evidence in the surgical literature regarding this disease that a very aggressive surgical approach combined with radiation gives better results than irradiation alone. I myself am uncertain and can find very little in the literature about the efficacy of chemotherapy as a primary modality. This patient only received 1300 rads, and it would be interesting to know why, since radiation therapy would be the preferred primary form of therapy. There are many examples in the literature of combinations of radiation therapy and chemotherapy, but I can find very few with chemotherapy alone. In the surgical literature, there are reports of 65 percent with one-year survival using all forms of therapy; one bright paper reported a 5-year survival of 50 percent in patients with seminoma.

Dr. Leonard Shukovsky, Tampa, FL: A planned course of 3000 rads was started. Then the patient was transferred to Wilford Hall because of his, his family's, and the attending physician's desire to have him taken care of in the military hospital. At Wilford Hall, they decided not to continue the radiotherapy and substituted it with chemotherapy. I think that was an unfortunate decision.

Dr. J. Maxey Dell, Gainesville, FL: I would like to ask Dr. del Regato to comment on the proposition of the surgeon, that he should always remove as much of the tumor as possible, which would make radiotherapy more effective.

Dr. Shukovsky: Milton Friedman has a very large series of patients treated with even lower voltages: any patient with seminoma who received over 2000 rads did not have recurrence. The same experience has been found at M.D. Anderson Hospital; in most of the major institutions now treating these tumors, no surgery is contemplated. The idea of the debulking operation should be reserved for tumors that are not very radioresponsive; lymphomas and seminomas are responsive and do not need debulking.

Dr. del Regato: Actually, I apply that to any kind of tumor that is radiosensitive and radiocurable. I feel that it is just as simple to irradiate the entire tumor, and I would not ask for any debulking. I think that very often, the surgical intervention, the ligation of vessels, and the interference with the physiopathology of the tumor might be disadvantageous. I would prefer to treat any patient who is theoretically radiocurable strictly by radiotherapy.

Dr. Lattes: It is generally not too much of a problem to recognize germinoma or seminoma in frozen section. There is another point about debulking: unless one has the whole tumor for histological examination, it is not possible to know that it is a pure seminoma. There are highly malignant teratocarcinomas with seminomatous areas, and the biopsy might show only seminoma. Some of the best results of radiotherapy alone might be due to the fact that the tumor was not a pure seminoma.

Dr. Shukovsky: In general the results are excellent. The cure rate for stage II seminomas is on the order of 90 percent.

Dr. John Pool, Wilton, CN: I think Milton Friedman's reports refer to seminoma in the testis, which is really quite different than seminoma arising in an anterior mediastinal teratoma. I would like to ask Dr. del Regato about the complications of radiation therapy. In the last few years, the experience I have had with a few of these enormous seminomatous tumors in the mediastinum is that after the radiation therapy, there is considerable fibrosis of the pulmonary tissue. We have not involved ourselves with the debulking procedure. However, could the debulking diminish the chance of pulmonary radiation injury? How do you protect the lung from damage?

Dr. del Regato: I sympathize with your unfortunate experiences. Of course, that depends on the quality of the irradiation. Actually, seminomas are just as radiosensitive as one could expect a tumor to be and as radiocurable as a lymphosarcoma. High MeV equipment can deliver thousands of rads in a few minutes; yet, to those young patients who might live long, there is an advantage in being treated over a long period of time. The cost these days is such that people are usually in a hurry, and these patients are treated too fast. My preference is to treat these patients over a long period, weeks of daily treatments. In a case like we are discussing where large fields are necessary, a large part of the lung can be irradiated with impunity; there may be no consequence whatsoever, or there may be a light pneumonitis, which properly managed would not result in great fibrosis, provided the treatment is well fractionated over a long period of time.

References

Cox, J.D.: Primary malignant germinal tumors of the mediastinum. Cancer 36:1162-1168, 1975.

Lattes, R.: Thymoma and other tumors of the thymus. An analysis of 107 cases. Cancer 15:1224-1260, 1962.

Rosai, J. and Levine, G.D.: Tumors of the thymus (Fascicle 13). Atlas of Tumor Pathology, 2nd series, Armed Forces Institute of Pathology, Washington, D.C., 1976.

Schantz, A., Sewall, W., and Castleman, B.: Mediastinal germinoma. A study of 21 cases with an excellent prognosis. Cancer 30:1189-1194, 1972.

4. MALIGNANT SCHWANNOMA OF THE CHEST WALL

Contributed by **H. S. Wilks, M.D.** and **R. M. Nalbandian, M.D.,** Grand Rapids, Michigan

The patient was a 70-year-old woman in June 1977 when she complained of pain in her left leg of several weeks duration. On examination she was found to have a large mass in the left side of the chest. Bronchoscopy revealed some distortion but no endobronchial mass.

Dr. Viamonte: The chest roentgenograms reveal a large, well-circumscribed extrapulmonary mass occupying the posterior half of the left lower hemithorax. Its upper, lower, and medial borders are sharp. There is minimal displacement of the heart to the right. The left

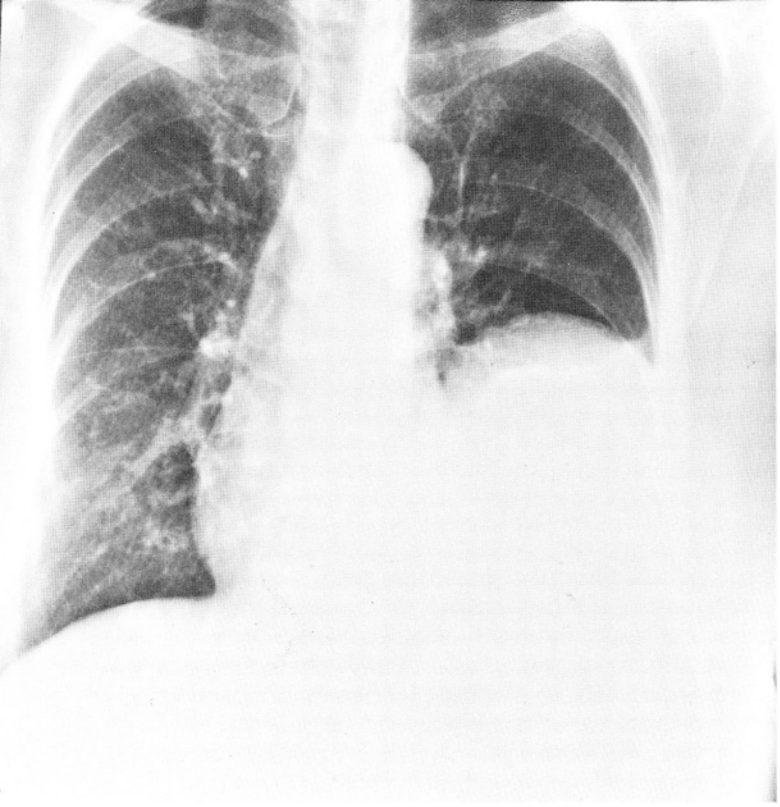


Fig. 1—Well circumscribed extrapulmonary mass.

heart border is indistinct due to the presence of the mass, which extends to it; there is no evidence of bone destruction.

The rounded upper border of the mass suggests a tumor rather than a fluid collection. It could arise in the lung, in the pleura, in the diaphragm, or represent a subdiaphragmatic process. Against a pulmonary origin is its superior and anterior rounded configuration. However, occasionally, large bronchopulmonary sequestrations may present like a spherical mass. Pleural tumors such as mesotheliomas (benign and malignant) may have a similar appearance; the malignant mesothelioma tends to be diffuse and is often manifested by pleural effusion. A diaphragmatic tumor would be an unlikely possibility due to the bulk of the lesion; the exceptions are lipomas. The fact that vessels are seen through the lesion (as noted in the lateral roentgenogram) might suggest a low density process. Computed tomography should be the definitive diagnostic test whenever a fatty tumor is suspected. A subdiaphragmatic process would be unlikely. Intrathoracic herniation such as is seen with a persistent left Bochdalek defect usually is followed by herniation of the kidney. The gross appearance of the lesion does not suggest a renal mass. A herniated left kidney with a tumor would be a very rare occurrence.

In summary, we believe we are dealing with a pleural tumor. In this age group, metastatic pleural lesions are more common than primary. However, they are most often manifested by scalloping of the periphery of the lung (due to multiple pleural implants) or by pleural effusion. We favor the diagnosis of a primary pleural tumor, possibly benign. The second possibility is a large diaphragmatic lipoma.

Dr. Viamonte's Impression:

1) **MESOTHELIOMA**
2) **LIPOMA OF THE DIAPHRAGM**

Radiologic impressions submitted:

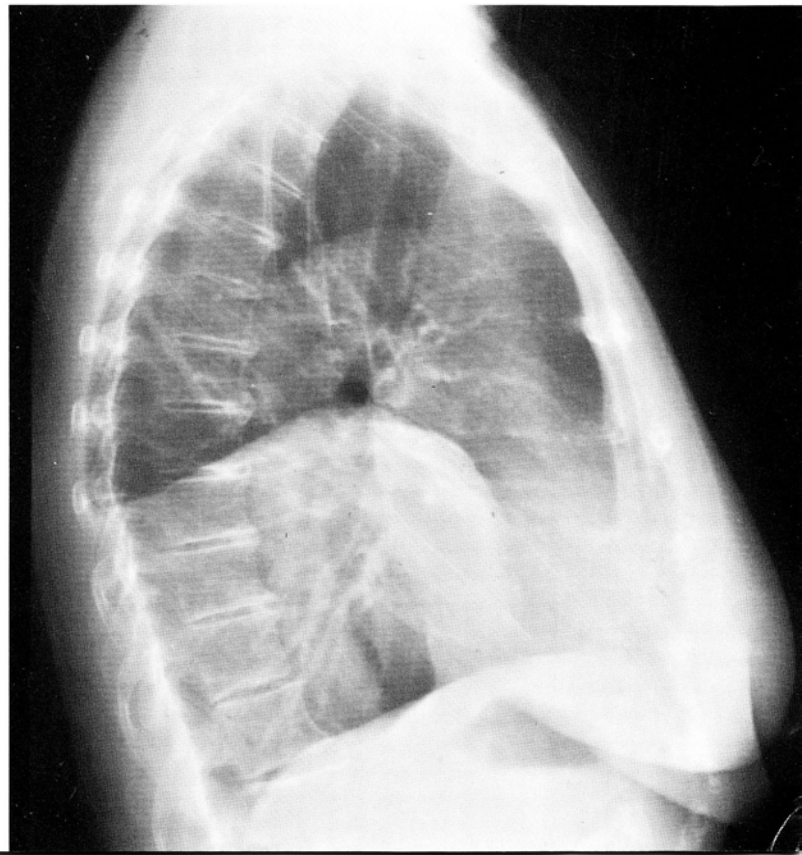
Mesothelioma	43
Diaphragmatic eventration	27
Metastatic tumor	16
Neural tumor	15
Bronchial carcinoma	15
Various malignant tumors	14
12 others	60

Dr. Viamonte: Eventration of the diaphragm would be a possibility, but it would be a very localized one. This tumor is too large and too solitary to be considered metastatic, but certainly that is a possibility. I would not consider bronchial carcinoma because the lesion appears to be extrapulmonary by virtue of its sharp superior medial and anterior margins.

Dr. del Regato: Dr. R. Otero of Tampa also offered a diagnostic impression of mesothelioma. Drs. Arnold Friedman of New York and J. F. Wilson of Milwaukee suggested a tumor arising from the diaphragm.

Operative Findings: On August 5, 1977 a thoracotomy was done with excision of the left

Fig. 2—Mass occupies the left lower hemithorax.



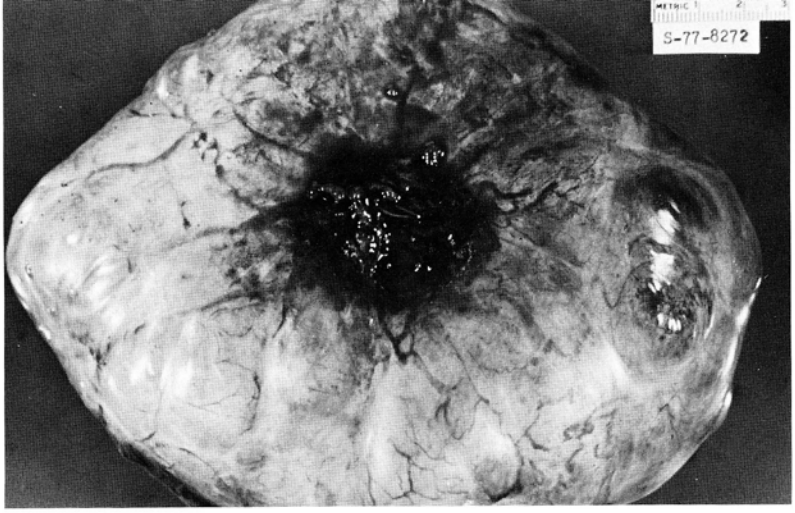


Fig. 3—Gross specimen showing circumscription of the tumor.

6th rib; an intrapleural tumor was found arising from the central tendon of the diaphragm; the specimen measured 18 x 15 x 8 cm. The tumor, 3 x 1.5 cm, had a glistening capsule; it was yellow-tan on cut section and had punctate calcifications.

Dr. Lattes: This tumor shows two different patterns. One is composed of wavy elongated bundles of cells associated with abundant eosinophilic material and showing occasional palisading of the nuclei. The other pattern is a very cellular growth of spindle-shaped cells, with elongated nuclei. Mitoses, however, are rare. The reticulin stains show that in the highly cellular component, reticulin fibrils are also arranged with a definite pattern; that is, they are not very frequent, and they seem to be arranged parallel to the long axis of the bundles. This is a feature observed not infrequently in Schwann cell tumors and also in smooth muscle tumors. Because of the two patterns described (one resembling neurofibroma and the other a malignant spindle cell tumor) and because of the reticulin arrangement, I believe it is probable that this is a malignant schwannoma originating in a preexisting neurofibroma.

The only possible alternative is, in my opinion, a fibrous mesothelioma. However, for the reasons stated above, I favor a Schwann cell origin.

Dr. Lattes' Diagnosis:

MALIGNANT SCHWANNOMA

Histopathologic diagnoses submitted:

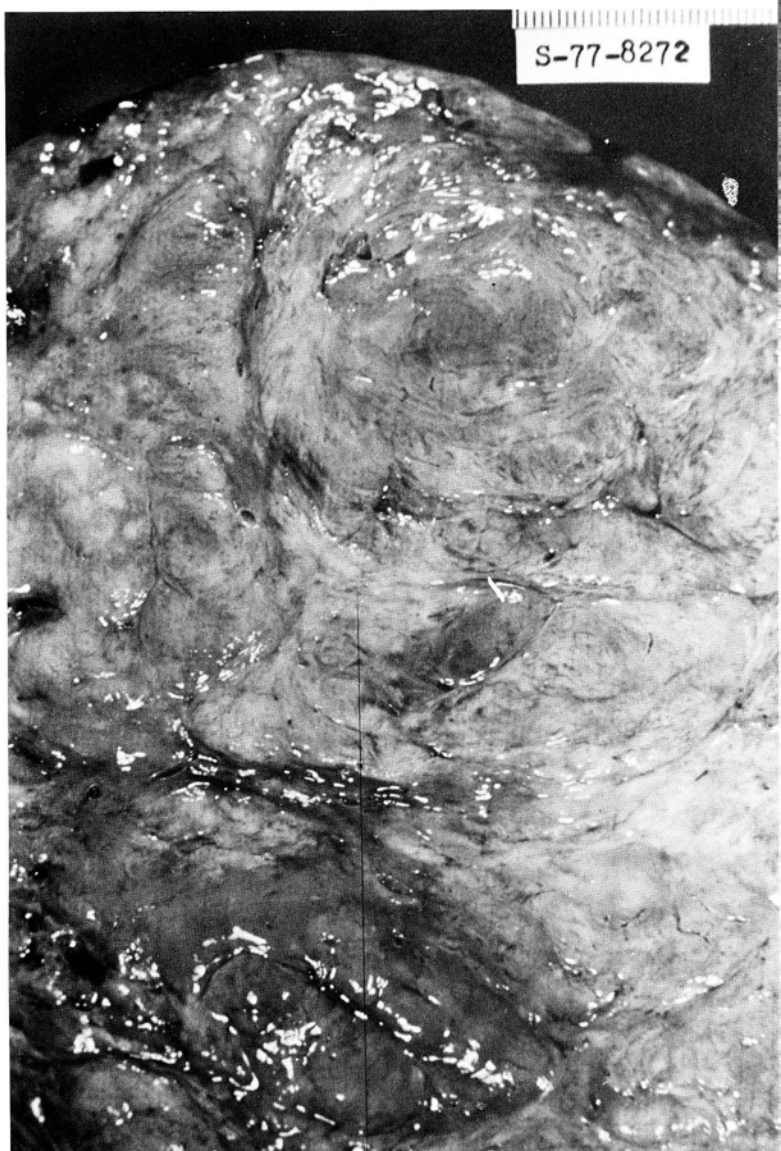
Neurofibroma	48
Malignant schwannoma	25
Mesothelioma	13
Various sarcomas	12
Thymoma	07
Others, benign	10

Dr. Lattes: Putting together neurofibroma and malignant schwannoma, it seems as if the majority of pathologists favored schwann cell origin. I think that it is malignant because in the sections that I had, there were areas that were too undifferentiated and anaplastic to fit into the category of benign neurofibroma. I sympathize with the diagnosis of mesothelioma; in some areas I would have made the same diagnosis. Perhaps I had the advantage of having more tissue available. It is certainly not a thymoma.

Dr. del Regato: Dr. Stephen E. Vernon of Los Angeles also offered a diagnosis of malignant schwannoma and suggested that it arose from a neurofibroma. Dr. Robert R. Pascal of New York also submitted a diagnosis of schwann cell tumor but suggested that it is probably benign. Dr. Richard Johnson of Columbia, Missouri also suggested a low-grade malignant schwannoma.

This case had been submitted to Dr. M. R. Abell of Ann Arbor in August 1977 (680-LCD Univ. of Michigan), and he made a diagnosis of fibrous mesothelioma, so-called fibroma of the pleura, with benign and malignant areas. Dr. Abell indicated that he has a total of 14 such cases, that they occur primarily in women, have no association with asbestosis, and show very little tendency to recur.

Fig. 4—Cut surface showing lack of lobulation.



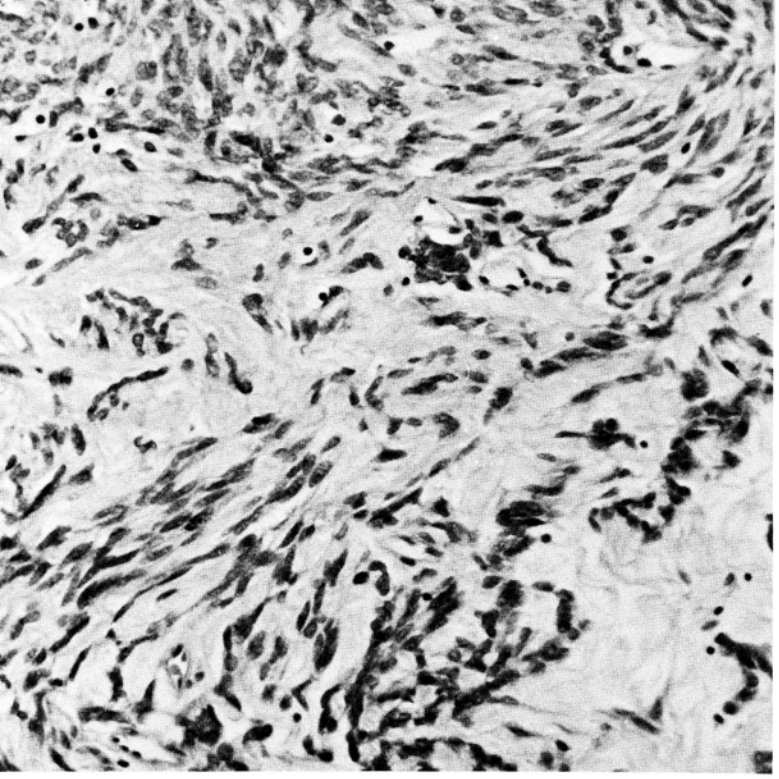


Fig. 5—Note atypical anaplastic spindle cells arranged in irregular whorls and wavy bundles (H + E, × 270).

Subsequent History: This patient has gained weight and has now come to live in Florida. On December 9, 1977 she was examined by Dr. F. R. Fabiani of Fort Lauderdale because of weakness and tremor of the left upper extremity. No evidence of recurrence or metastasis has been found, and the patient remains otherwise in good health.

Dr. Ferguson: I would make a diagnosis of mesothelioma over any other diagnosis because of the encapsulation, the fact that it was intrapleural, and its very small stalk, which is common in mesotheliomas of the benign fibrosis type. However, against its being a fibrous mesothelioma is the fact that these are often associated with hypertrophic pulmonary osteoarthropathy with which the patients have clubbing and a lot of joint pain; also, fibrous mesothelioma may be found in association with hypoglycemia.

References

Ackerman, L.V. and Taylor, F.H.: Neurogenous tumors within the thorax: a clinical and pathological evaluation of 48 cases. Cancer 4:669-691, 1951.

Foster, E.A. and Ackerman, L.V.: Localized mesotheliomas of the pleura. The pathologic evaluation of 18 cases. Am. J. Clin. Pathol. 34:349-361, 1960.

Green, J.D., Carden, T.S., Jr., Hammond, C.B., and Johnsrude, I.S.: Angiographic demonstration of arteriovenous shunts in pulmonary metastatic choriocarcinoma. Radiology 108:67-70, 1973.

Harkin, J.C. and Reed, R.J.: Tumors of the peripheral nervous system (Fascicle 3). Atlas of Tumor Pathology, 2nd series, Armed Forces Institute of Pathology, Washington, D.C., 1969.

Heller, R.M., Janower, M.L., and Weber, A.L.: The radiological manifestations of malignant pleural mesotheliomas. Am. J. Roentgenol. 108:53-59, 1970.

Oberman, H.A. and Abell, M.R.: Neurogenous neoplasms of the mediastinum. Cancer 13:882-898, 1960.

5. GANGLIONEUROBLASTOMA OF THE POSTERIOR MEDIASTINUM

Contributed by **K. Charyulu, M.D., S. Thomsen, M.D., H. Marchildon, M.D., M. Isikoff, M.D.** and **B. Rao, M.D.**, Miami, Florida

The patient was a 1-year-old baby boy in August 1977 when he was found to have a motor deficiency of the lower extremities. On examination there was positive bilateral Babinski and increased tendon reflexes as well as decreased muscle bulk below the knees.

Dr. Viamonte: There is a large retrocardiac mass that appears to be extrapulmonary due to its sharp superior, lateral and inferior margins. The base of the mass is larger than its lateral peripheral portion and faces the midline. There is widening of the seventh posterior intercostal space and long, smooth erosion of the undersurface of the posterior arch of the left seventh rib and upper border of the eighth rib, posterior arch. CT sections of the chest reveal irregular calcification of this mass and subpleural posterior extension.

This left paraspinal process involving the bone should represent a neurogenic tumor. On plain roentgenography, ganglioneuromas most often present this appearance. Neurofibromas often erode the adjacent ribs. In a patient of this age, the development of scoliosis is not expected. We have no lateral or oblique films to establish the presence or absence of widened intervertebral foramina. There is nothing in the history to suggest neurofibromatosis.

Computed tomography shows calcium within the lesion. Ganglioneuroma is the most frequent tumor of the sympathetic nervous system. On the other hand, neuroblastomas most often calcify and metastasize to other areas of the body. The history suggests the possibility of metastasis.

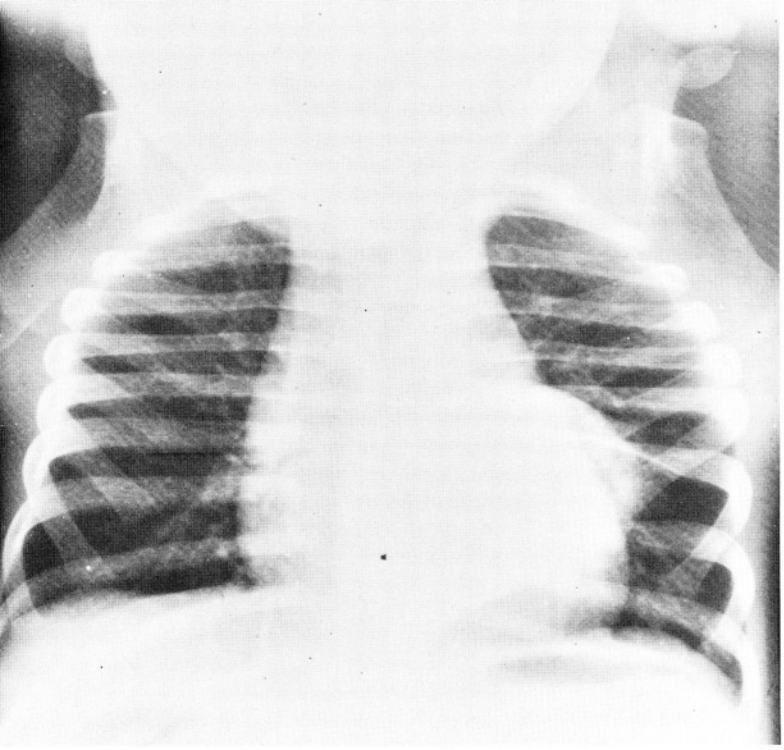


Fig. 1—Large retrocardiac mass.

Dr. Viamonte's Impression:

1) NEUROBLASTOMA
2) GANGLIONEUROBLASTOMA
3) NEUROFIBROSARCOMA

Radiologic impressions submitted:

Neuroblastoma	63
Neurofibroma	62
Ganglioneuroblastoma	21
Meningocele	19
Enteric cyst	15
Various others	10

Dr. Viamonte: A majority felt that this is a neurogenic tumor. Ganglioneuroblastoma is a good possibility: there is the ganglioneuromatous component by virtue of the gross appearance of the lesion and the blastomatous component by virtue of the calcification and infiltration. I would not consider meningocele. The CT in meningocele would not show the regular infiltration of a pleura; there would be a defect in the bone.

Dr. del Regato: Drs. J. E. Crymes of Miami and A. C. Speranza Miller of Milwaukee suggested neuroblastoma. Dr. J. D. Cox of Milwaukee refined his impression to ganglioneuroblastoma or ganglioneuroma.

Operative Findings: The myelogram showed an obstruction from T5 to T10. On August 24, 1977 a decompression laminectomy was done, and a mass was incompletely removed from the spinal canal.

Dr. Lattes: This tumor is a fairly good example of the malignant tumors originating from the sympathetic ganglia. It shows multiple focal areas of proliferation of cells of neuroblastic type, separated by almost acellular areas with a finely fibrillar pattern, and with multiple foci of necrosis and calcification. In this particular case, the tumor is not completely undifferentiated. It is not a classical neuroblastoma or sympaticoblastoma, but rather what has been called ganglioneuroblastoma, that is, a partly differentiated neuroblastoma or, if you want, a partly undifferentiated ganglioneuroma. The reticulin stains show a striking absence of reticulin fibrils except for the regions adjacent to the blood vessels, and the trichrome stain shows that the finely fibrillar felt-work between the groups of tumor cells is not collagen. It is known that it consists of the protoplasmic processes of the neuroepithelial cells. Statistically, this tumor, which is a partly differentiated neuroblastoma, should have a better prognosis than the completely undifferentiated neuroblastoma.

Dr. Lattes' Diagnosis:

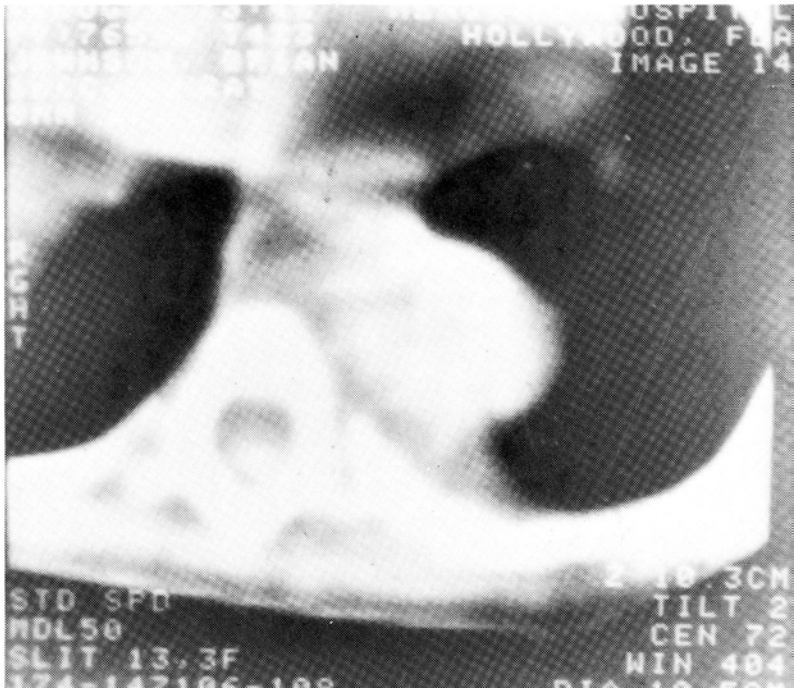
GANGLIONEUROBLASTOMA

Histopathologic diagnoses submitted:

Ganglioneuroblastoma	78
Ectopic astrocytoma	12
Neurogenous tumor	03
Embryonal rhabdomyosarcoma	03

Dr. Lattes: I do not think that this is an ectopic astrocytoma; there are unquestionable ganglion cells of different degrees and maturity. I have no objections to neurogenous tumor, except that it is a very broad term. I do not think that those who suggested embryonal rhabdomyosarcoma would have stuck to that diagnosis if they had access to differential stains. The sections that I had were classically ganglioneuroblastoma.

Fig. 2—CT section showing irregular calcification and subpleural extension.



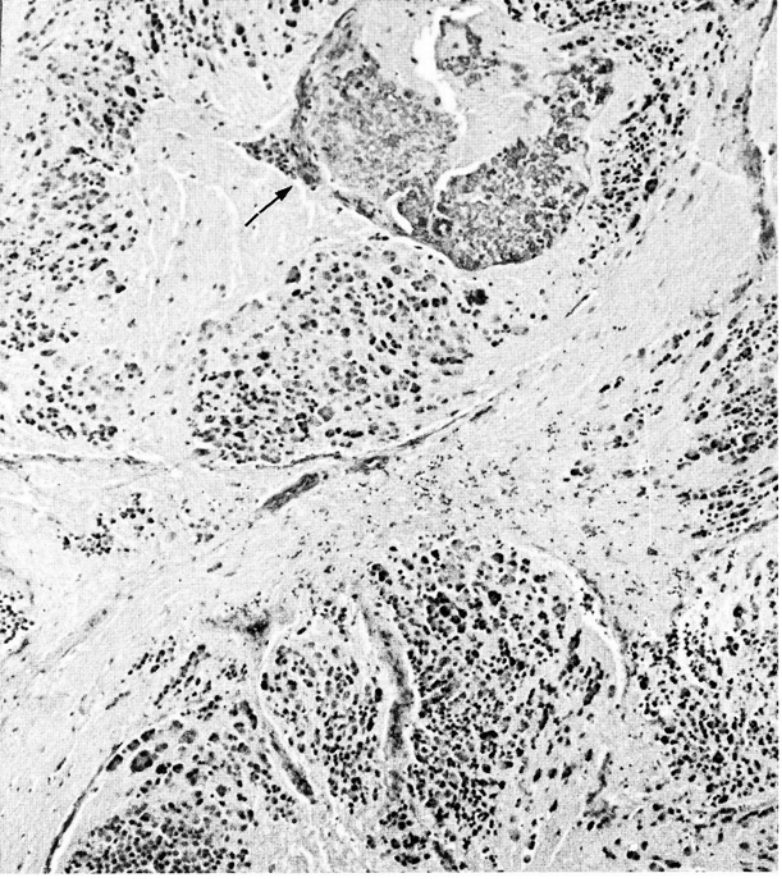


Fig. 3—Multiple clusters of immature neuroblasts in a finely fibrillar stroma. Note a conspicuous focus of necrosis and calcification (arrow) (H + E, × 84).

Dr. del Regato: Drs. D. Greider of Tampa and Olga J. Dobrogorski of Cincinnati also made a diagnosis of ganglioneuroblastoma.

Subsequent History: Post-operative radiotherapy was administered in the form of interstitial implantation of radioactive "seeds."

Dr. Ferguson: A solid tumor in the posterior mediastinum is neurogenic until proven otherwise. It is relatively easy to differentiate between the benign schwann cell tumors and the sympathetic nerve tumors. The benign schwann cell tumors usually occur in adults, have a very spherical appearance, and are asymptomatic. The sympathetic nerve tumors usually occur in younger people, are usually accompanied by symptoms, and are almost always effusive with very indistinct margins on top and bottom.

The younger the patient, the more malignant the tumor may be; calcium is more likely to make it malignant as is the fact that the child has neurological symptoms. All three of these are present in this child. These tumors do produce a vinyl mandelic acid (VMA). There has been a good bit written about the ability to diagnose these tumors by appropriate blood and urine tests. There are papers indicating, however, that this is not seen in a very high number of patients. By following the VMA levels, one can follow the course of a patient after the tumor has been resected. The neuroblastoma is probably the most common soft tissue tumor found in infants and children, although others say that it is rhabdomyosarcoma; both are frequent. In infants and children, 20 percent of the neuroblastomas will make an appearance in the chest. If one does a thoracotomy on a patient like this, it has been our practice always to do it in association with a neurosurgeon. It is very easy to get into the neural canal.

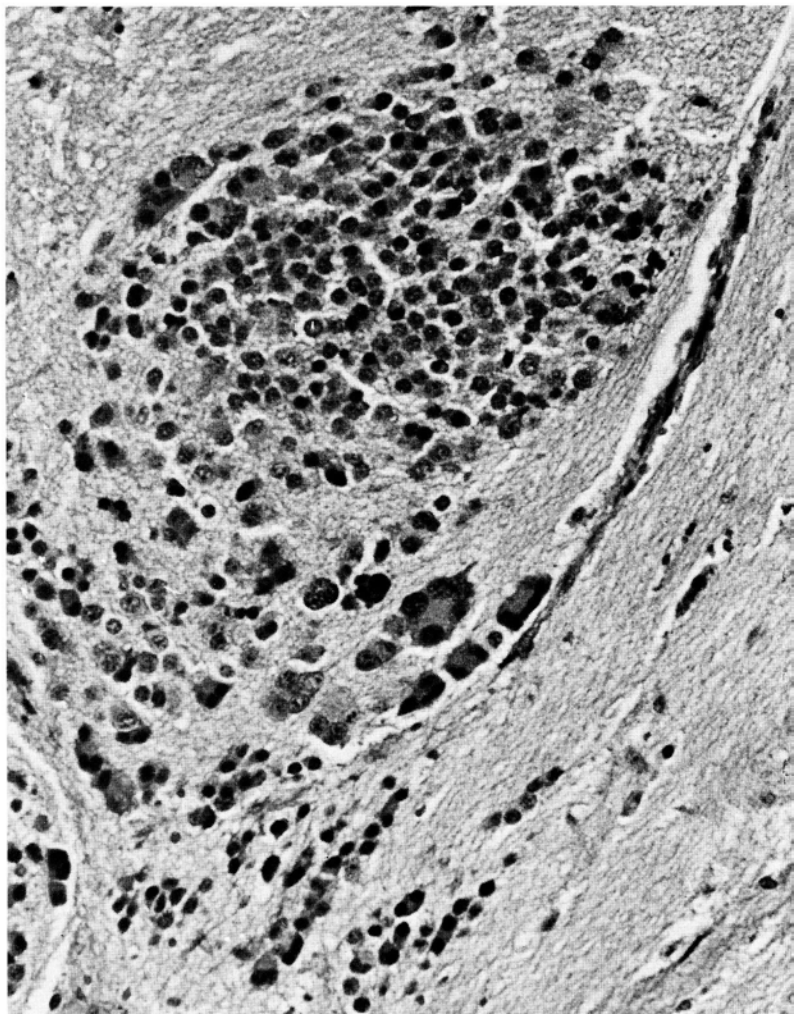
Dr. Komanduri Charyulu, Miami, FL: At the time of surgery, this tumor was found to have entered one of the intervertebral foramina in the spinal canal, and it was infiltrating the intercostal spaces. There was no clear margin of resection, and tumor was left behind in at least two places of the chest wall. Also, the tumor was stuck to the paravertebral gutter. One hundred twenty-five radioactive iodine seeds were implanted; the dose was about 4000 rads. Subsequently, the patient also received an additional 2400 rads in 12 treatments to the mediastinum. The child is now well about six months after the procedure. He was seen last month, and there were no sequellae.

References

Harkin, J. C. and Reed, R. J.: Tumors of the peripheral nervous system (Fascicle 3). Atlas of Tumor Pathology, 2nd series, Armed Forces Institute of Pathology, Washington, D.C., 1969.

Pachter, M. R. and Lattes, R.: Neurogenous tumors of the mediastinum. Dis. Chest 44:79-87, 1963.

Fig. 4—Detail showing occasional better differentiated neuroblasts, resembling ganglion cells (H + E, × 270).



6. THYMOMA WITH PREDOMINANT LYMPHOID PATTERN

Contributed by J. F. Wilson, M.D., M. Miller, M.D., M. W. Wilson, M.D. and J. V. Pilliod, M.D.,
Milwaukee, Wisconsin

The patient was a 37-year-old woman in May 1976 when she gave a history of upper left chest pain of seven months duration. Fungal and tuberculosis tests were negative. The SMA 12 was normal, but the sedimentation rate was elevated.

Dr. Viamonte: Roentgenograms of the chest reveal a lobulated mediastinal mass contacting the left heart border and extending into the anterior mediastinum. There is no evidence of calcification, excavation, hilar adenopathies or bone destruction.

In this age group with a lesion of this morphology, a thymic tumor should be the first diagnosis. Other possibilities include lymphoma, giant lymphoid hyperplasia, mesothelioma, and neurogenic tumor. The lesion is in the "home" of thymic tumors. The most likely diagnosis is a benign thymoma.

Dr. Viamonte's Impression:

1) **THYMOMA**
2) **LYMPHOMA**

Radiologic impressions submitted:

Lymphoma (Hodgkin's)	72
Thymoma	45
Carcinoma	31
Metastatic tumor	15
Others	28

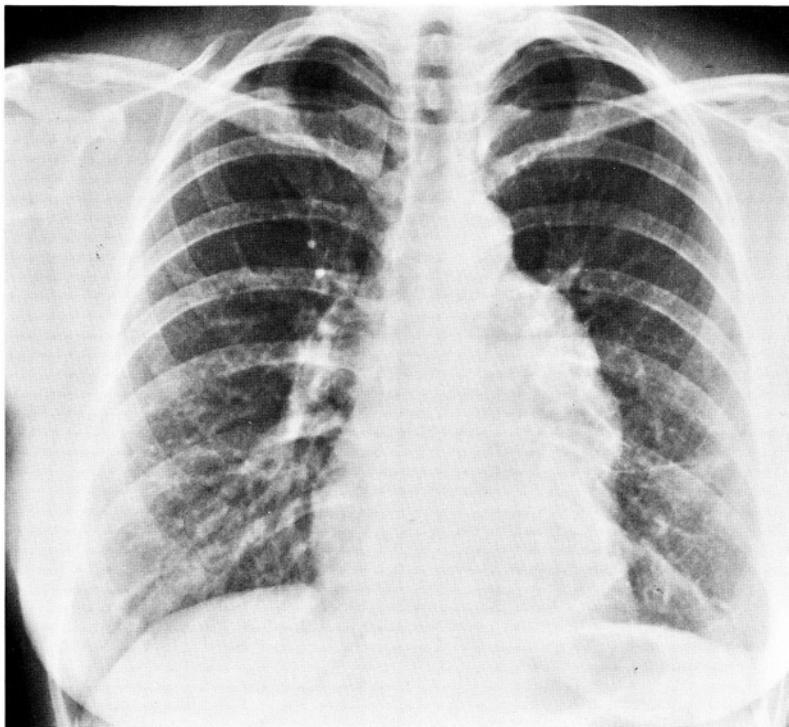
Dr. Viamonte: I favored thymic lesion because it is the most common lesion in this location. Thymomas of the anterior and middle mediastinum often present bilaterally; here, the lesion is primarily to the left of the heart and lobulated in outline. There is a type of carcinoma of the lung that presents as a primary mediastinal tumor, one which arises from the anterior segment of the upper lobes in the portion of the lung in front of the heart. That portion of the lung is actually impinging into the mediastinum, and a tumor arising in that location from either the right upper lobe or the left upper lobe can simulate a primary mediastinal neoplasm. Primary oat cell carcinomas may be undetected radiographically, and we may see only the mediastinal adenopathies; however, most of the oat cell carcinomas involve the middle mediastinum, often bilaterally.

Dr. del Regato: Drs. Benjamin Felson of Cincinnati and J. L. Pool of Connecticut as well as A. C. Speranza Miller of Milwaukee suggested a thymoma. Dr. Norman Rosenthal of Tampa diagnosed lymphoma.

Operative Findings: On May 28, 1976 a left postero-lateral thoracotomy was carried out. An antero-superior mediastinal mass was found adhering to the left upper pulmonary lobe; it was removed. It measured 9 x 7 x 4 cm and had a shaggy fibrous appearance with a uniform gray color and areas of necrosis.

Dr. Lattes: This is a tumor which originated either from the thymus or very close to it. In fact, remnants of non-neoplastic thymic tissue, some of which have epithelial lined cysts, can be seen at the periphery. The problem is then, what is the nature of what appears to be a predominantly lymphoid growth? This is not always an easy solution, especially in small fragments of tissue. In some places, the tumor grows into the thymic lobules. It is composed of an almost homogeneous population of cells of lymphoid type, but here and there some spindle-shaped cells can be seen as well as some cells which have a vaguely epithelial pattern. Fibrous trabeculae subdivide this tissue into distinct lobules, as is frequently seen in lymphoid thymomas. I believe, therefore, that we are dealing with a predominantly lymphoid thymoma rather than a malignant lymphoma. However, this is not an easy decision on the basis of a small amount of tissue, and I make it with some reservation.

Fig. 1—Roentgenogram showing mass over the shadow of the heart.



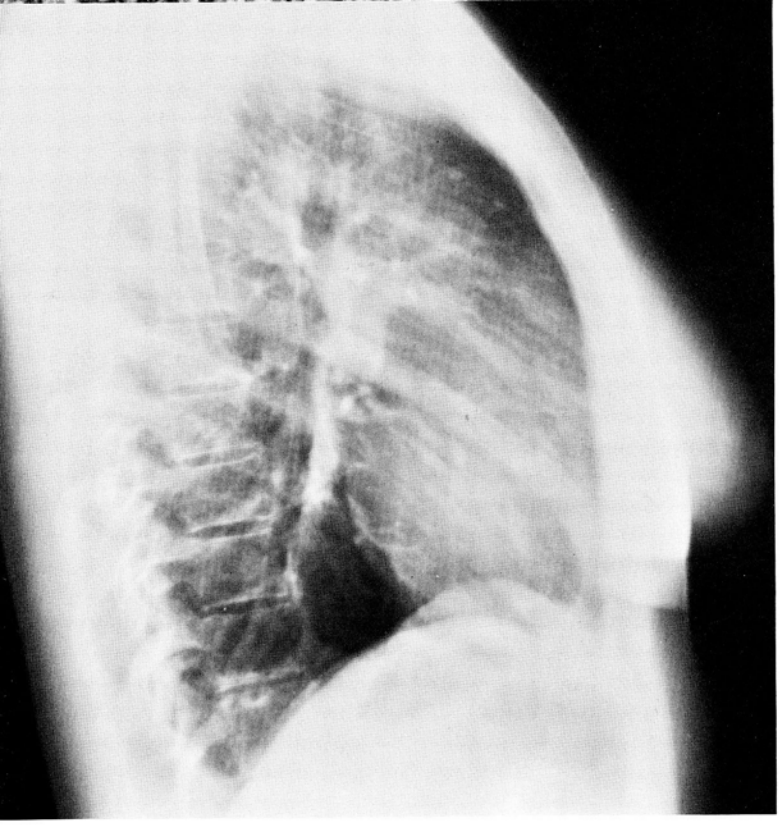


Fig. 2—Mass of the anterior mediastinum.

Dr. Lattes' Diagnosis:

THYMOMA (predominantly lymphoid)

Histopathologic diagnoses submitted:

Thymoma	69
Thymoma, lymphoid	24
Malignant lymphoma	07
Lymphoproliferative disorder	03

Dr. Lattes: I reviewed our material two years ago. Out of 248 thymomas in our files, the lymphoid type was the most common, followed by the mixed type in which there are different histological subtypes.

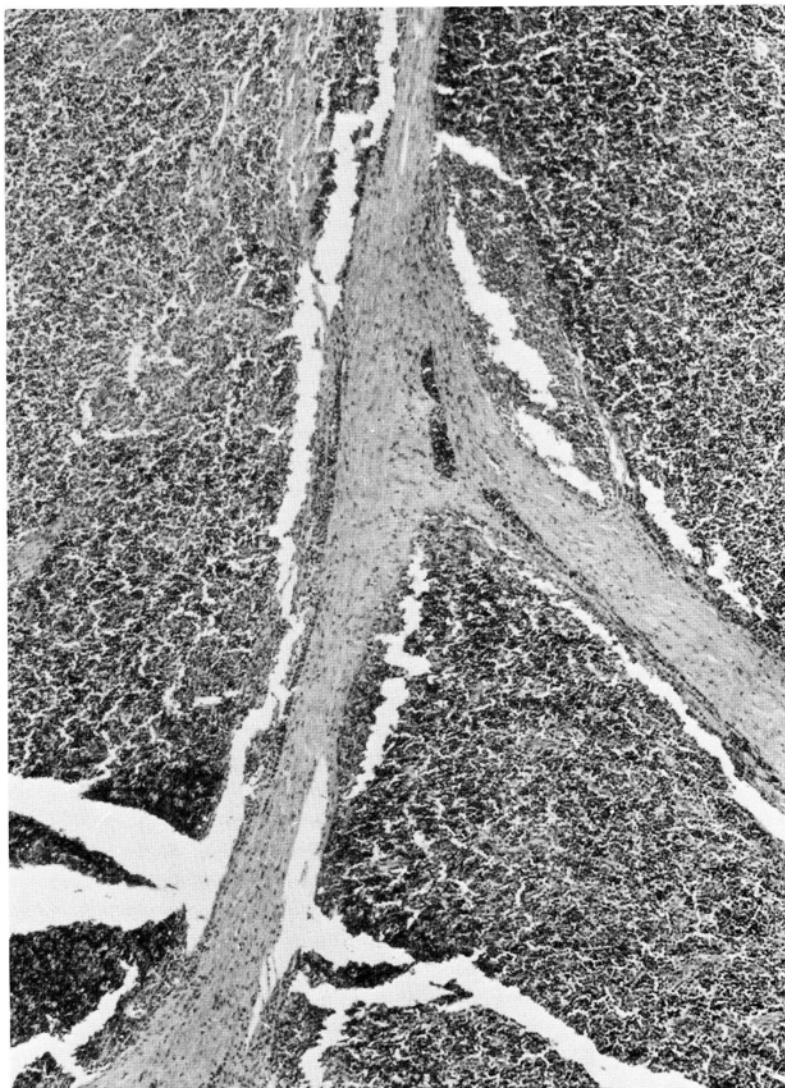
Dr. del Regato: Our experts agreed on the diagnosis of thymoma: Dr. H. Azar of Tampa qualified it also as predominantly lymphocytic. Dr. S. E. Vernon of Los Angeles noted that it had cystic degeneration. Dr. J. Shinner of St. Petersburg called it lymphoepithelial, and Dr. Robert R. Pascal of New York marked it as malignant.

Subsequent History: In October 1977 the patient was examined and appeared in good health. On February 17, 1978 she was examined by Dr. J. Frank Wilson, who found no abnormalities on physical examination or on roentgenograms of the chest.

Dr. Ferguson: The clinical appearance of the tumor is very important in the final diagnosis. When a biopsy is taken at the operation, one might get an area of lymphoid tissue that may be benign or malignant. At our institution, Dr. Ackerman, and later Dr. Bauer, insisted that the surgical pathologist come into the operating room, look at the tumor, and see what its local invasive or noninvasive characteristics are. This used to be a great concern to me because Dr. Ackerman never learned how to put on a surgical gown or mask. Dr. N. P. Bergh in Scandinavia has suggested that instead of calling these tumors benign or malignant, one should call them invasive or noninvasive; this indicates a departure, for he says that whether they are benign or malignant can be determined virtually on the basis of the clinical appearance at the time of surgery.

The point about myasthenia gravis is important: 20 percent of patients who have thymic tumors will have myasthenia gravis. Sometimes this is masked, so it is probably wise to do a test. This has more than academic interest. In both benign and malignant thymomas, the presence of myasthenia gravis adversely affects the prognosis. The diagnosis of Hodgkin's disease in the thymus is the best prognosis of any malignant lesion in the mediastinum. Dr. Bergh reported 17

Fig. 3—Predominantly lymphocytic thymoma, divided into lobules by fibrous tissue trabeculae (H + E, × 84).



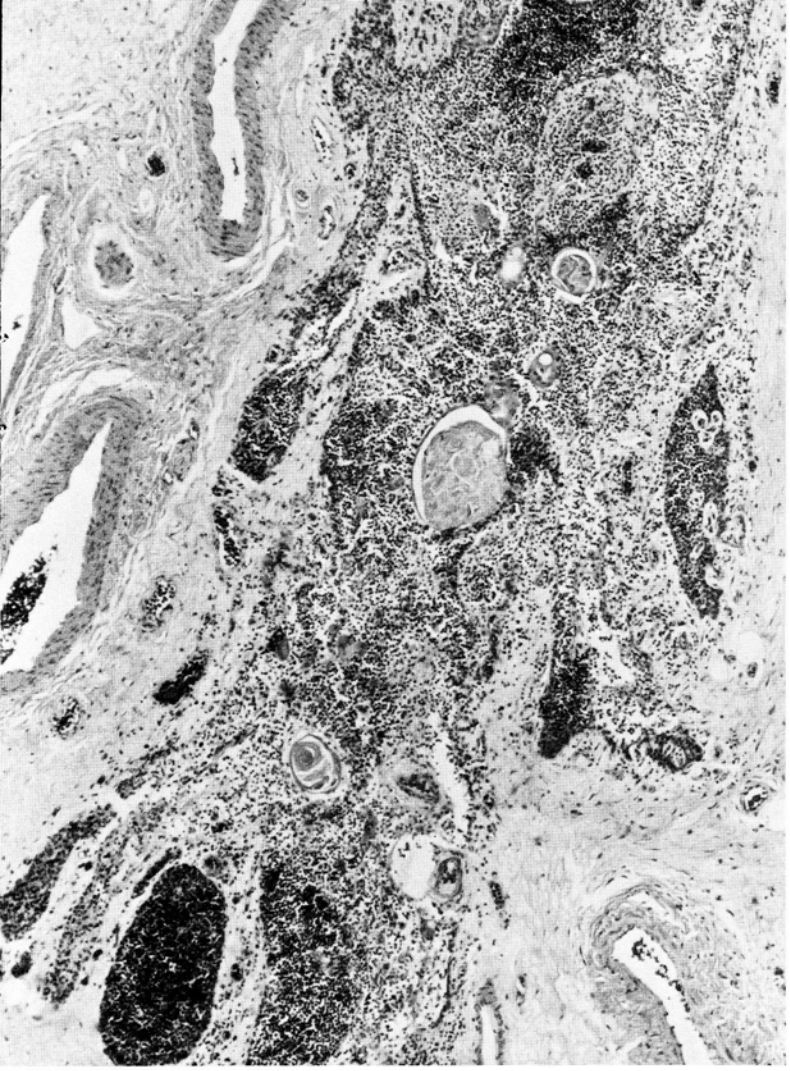


Fig. 4—Thymic tissue, showing atrophy, lymphocyte depletion, and fibrosis. There is no tumor in this microscopic field (H + E, × 84).

patients with Hodgkin's disease in the thymus gland. Of those treated with surgery and radiotherapy, there was a 100 percent survival rate for ten years.

Dr. Richard Thurer, Miami, FL: I wonder if Dr. Ferguson believes that mediastinoscopy has any role in the evaluation of mediastinal tumors in general and this type of lesion in particular? We believe that mediastinoscopy ought to be reserved for the accurate staging of primary lung tumors, but occasionally our medical colleagues expect us to do biopsy procedures on these lesions.

Dr. Ferguson: I think mediastinoscopy has absolutely no place in the diagnosis of any anterior mediastinal tumors; it is an inaccessible area and dangerous to get to. The nodes beneath the arch of the aorta on the left side are inaccessible, and the nodes anterior to the innominate artery, in front of the vascular structures, are relatively inaccessible. In my view, it is a dangerous procedure.

Dr. Viamonte: In trying to establish resectability of bronchial carcinoma and detection of nodal involvement, those subcarinal nodes seen to the right of the trachea can be detected beautifully by CT by virtue of the displacement of the fat normally surrounding the mediastinal structures. Linear tomography, which is a conventional way of enhancing the radiographic examination, should be complemented by CT in order to detect pericardial and contralateral involvement, or particularly a tumor extending into areas silent to the endoscope.

Dr. Maria Viamonte, Miami, FL: When we are called for a frozen section in a lesion like this, we sometimes see small lymphocytes. What is your experience with tumors that are composed of small cell lymphocytes? We worry about the possibility of leukemia.

Dr. Lattes: You are right. We have the same problems. In the presence of biopsies during the operation, which we consider controversial, we frequently advise to do nothing further until we study the biopsy material. We used to have the invaluable help of Dr. Margaret Murray, a tissue culture specialist who worked with Dr. Stout for more than 30 years. She was able to differentiate lymphomas and other small cell tumors from thymomas on tissue culture within 48 hours. Occasionally, a chest surgeon will decide to remove a well circumscribed, resectable mass, even if precise histological diagnosis has not been made yet on frozen section.

Dr. del Regato: Dr. Lattes, I know that histologically, there was no suggestion of this, but some of the radiologists suggested the possibility of Hodgkin's disease. I wonder if you would care to comment on the possibilities of Hodgkin's disease in the mediastinum, particularly of the thymus.

Dr. Lattes: That leads to a can of worms. There is a variant of Hodgkin's disease most commonly seen in the mediastinum, the so-called nodular sclerosing Hodgkin's with which everyone is familiar. There is a subvariant that seems to affect primarily the thymus gland; radiologically, it presents as a thymic tumor. Many years ago, Dr. Ewing warned that there are some lesions that look like Hodgkin's disease but are really tumors of the thymus. Later, Lowenhaupt suggested the term "granulomatous thymoma" for lesions of this type. About 18 years ago, I reviewed all of our thymic tumor cases and found a small group of these lesions that I felt sure were primary. These tumors had Reed-Sternberg cells and some other features of Hodgkin's but were associated with striking proliferation of the thymic epithelium. I did not want to say that they were thymomas, but I was not sure that they were Hodgkin's disease. More

recently we have reviewed our series of those original cases and others; more than half of those cases sooner or later developed signs of systemic Hodgkin's disease. The current thought, to which I subscribe completely, is that the granulomatous thymoma is a clinically low grade form of nodular sclerosing Hodgkin's disease, involving the thymus and causing it to proliferate in a peculiar way.

Dr. del Regato: I am glad you put that on the record. The fact is that years ago, these cases were discarded as not being Hodgkin's, even though they looked like Hodgkin's, because the patients were doing well after surgical removal. As you say, sometimes it takes years before they have another manifestation of the disease. The fact should be kept in mind that cases of Hodgkin's disease present two times out of three with a supraclavicular adenopathy which suggests a Virchow's node from a tumor possibly arising in the mediastinum.

Dr. James Cox, Milwaukee, WI: It is very common for Hodgkin's disease to involve the mediastinum (perhaps 60 to 70 percent of all patients). However, the nodular lymphoreticular tumors involve the mediastinum in probably no more than about 5 percent of the cases. The diffuse malignant lymphoreticular tumors, or so-called non-Hodgkin's lymphomas, do involve the mediastinum but much less frequently than Hodgkin's disease. If a mediastinal mass is seen, it might as well be called Hodgkin's disease because that will be right the majority of the time. Dr. Maria Viamonte suggested that in a child under the age of ten, it is almost always leukemia of the T-cell type.

Dr. John Pool, Wilton, CN: The thymus gland is H-shaped with two limbs in the neck, two limbs going down to the mediastinum, and the transverse piece going across the anterior mediastinum. The thymic tumors can lie in the neck, in the anterior mediastinum, or beside the pericardium all the way to the diaphragm. This is an important consideration for the surgeon when he is trying to remove a thymic tumor; he does not know whether it is going to be invasive or noninvasive. He should remove all fibrous areas extending to these four corners of the H. There is one other pathologic entity in the anterior mediastinum, the giant lymphadenopathy which I think Castleman described.

Dr. Lattes: What Dr. Pool refers to is a peculiar lesion composed of large masses of lymphoid tissue. They have peculiar germinal centers with center arterioles that look a little like the splenic tissue; they have been interpreted variously as a giant hyperplasia of the lymph node or an angiofollicular hyperplasia because of the vascular component. Many years ago, we suggested the remote possibility that they could be hamartomatous masses of lymphoid tissue because we were not able to prove that they were originally lymph nodes; they had been called hemolymph nodes or hypertrophy of hemolymph nodes, even though there is no such thing as a hemolymph node in the human species. When they are localized, the common denominator is that most but not all of them have been found in the mediastinum. They have been found retroperitoneally and in soft tissues away from where lymph nodes are, and they are perfectly harmless lesions. There is now a subtype that has been discussed and presented. In it there are a large number of plasma cells and an ameba-like substance associated with proteinemia which may disappear completely upon removal of the mass. It should not be confused with thymoma: we set it aside as pseudothymoma. It can be confused with thymoma because its peculiar germinal centers can be mistaken for Hassall's corpuscles; they are highly epitheloid germinal centers. My experience has been that they are uniformly benign.

References

Batata, M.A., Martini, N., Huvos, A.G., Aguilar, R.I., and Beattie, E.J., Jr.: Thymomas: clinicopathologic features, therapy, and prognosis. Cancer 34:389-396, 1974.

Bergh, N.P., Gatzinsky, P., Larsson, S., Lundin, P., and Ridell, B.: Tumors of the thymus and thymic region I. Cliniocopathological studies on thymus. Ann. Thorac. Surg. 25: 91-98, 1978.

Kreel, L.: Radiology of the thymus. Proc. R. Soc. Med. 66:157-158, 1973.

Lattes, R.: Thymoma and other tumors of the thymus. An analysis of 107 cases. Cancer 15:1224-1260, 1962.

Rosai, J. and Levine, G.D.: Tumors of the thymus (Fascicle 13). Atlas of Tumor Pathology, 2nd series, Armed Forces Institute of Pathology, Washington, D.C., 1976.

Salyer, W.R. and Eggleston, J.C.: Thymoma: a clinical and pathological study of 65 cases. Cancer 37:229-248, 1976.

Schantz, A., Sewall, W., and Castleman, B.: Mediastinal germinoma. A study of 21 cases with an excellent prognosis. Cancer 30:1189-1194, 1972.

7. MYXOSARCOMA OF THE CHEST WALL

Contributed by **S. D. Varma, M.D.,** Waukesha, Wisconsin

The patient was a 16-year-old boy in February 1977 when on routine roentgenogram of the chest, a symptomless mass was discovered occupying the left apex and extending to the

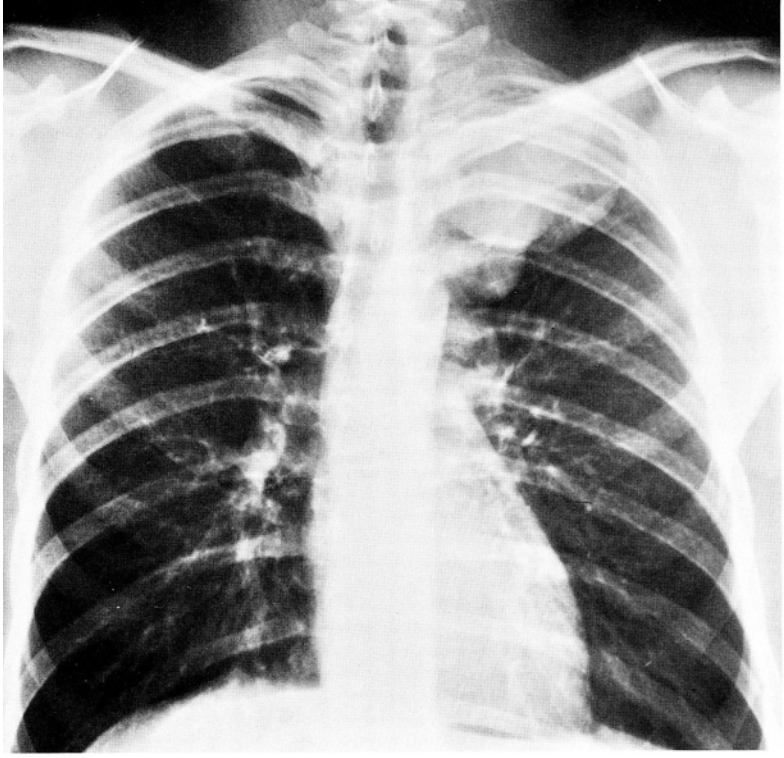


Fig. 1—Polylobated mass of the left apex.

mediastinum. There was a two month history of mild cough; physical examination revealed no abnormalities, no peripheral adenopathy.

Dr. Viamonte: The roentgenograms reveal a polylobated mass occupying the left apex and infraclavicular regions. Lobulations extend medially to the left hilus. The sharp inferior margin of the mass suggests the extrapulmonary origin of the lesion. The heart is not enlarged. No other thoracic abnormalities are noted.

CT examination shows a spherical mass with some spiculations in its outline. The two scans submitted do not provide any clue as to the composition or origin of the mass.

Differential diagnosis would be an extrapleural process. A tumor arising in the chest wall, such as neurogenic tumor, a primary or metastatic pleural neoplasia, or a rare mesenchymal tumor could produce the radiographic findings observed. A tumor arising in the base of the neck or extending into the base of the neck from the chest, such as a branchial cleft tumor or cystic hygroma, should also be included in the differential diagnosis.

Dr. Viamonte's Impression:

1) **NEUROGENIC TUMOR**
2) **MESENCHYMAL TUMOR (hemangiopericytoma?)**

Radiologic impressions submitted:

Neurofibroma	69
Mesothelioma	19
Hamartoma	12
Thymoma	12
A-V malformation	11
20 others	25

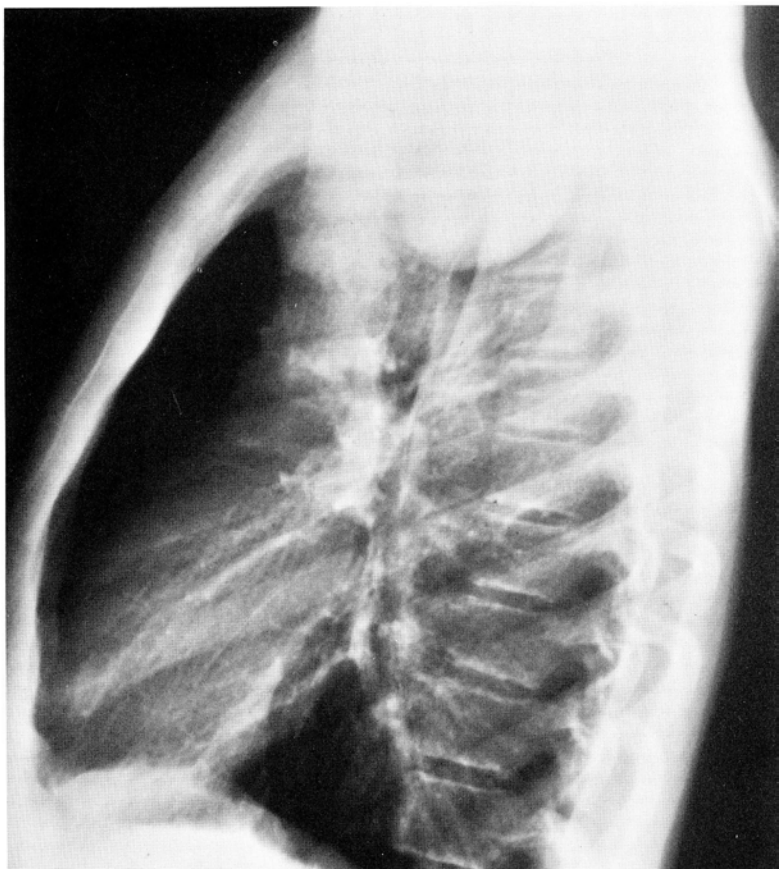
Dr. Viamonte: The majority of the radiologists felt that it could be a neurogenic tumor. They agreed with me that the lesion presents as an extrapulmonary tumor. Neurofibromas can present in many different ways. A hamartoma is usually a tissue malformation or benign tumor within the lung itself; I would not consider that as a possibility. The home of a thymoma is in the neck or the anterior mediastinum, not the paraspinal region. I would not consider an A-V malformation because there is no feeding artery or large vein draining the lesion.

Dr. del Regato: Dr. P. J. Hettle of Bay City, Michigan, Dr. J. F. Wilson of Milwaukee, and Dr. A. Friedman of New York suggested neurofibroma. Dr. Benjamin Felson of Cincinnati preferred sarcoma.

Operative Findings: On February 16, 1977 a thoracotomy was done. A tumor adherent to the mediastinal pleura was found coursing along the first rib but leaving the lung uninvolved. The lobulated mass was resected; one portion measured 7.5 x 6 x 4 cm and another, 6 x 4 x 2.5 cm with a total weight of 138 grams. The cut surface was gelatinous, yellow-tan and rubbery, yet crumbly.

Dr. Lattes: This is one of the most difficult cases in this Cancer Seminar. It will take me about five minutes to tell you that I am not sure

Fig. 2—Lateral view shows sharp contour.



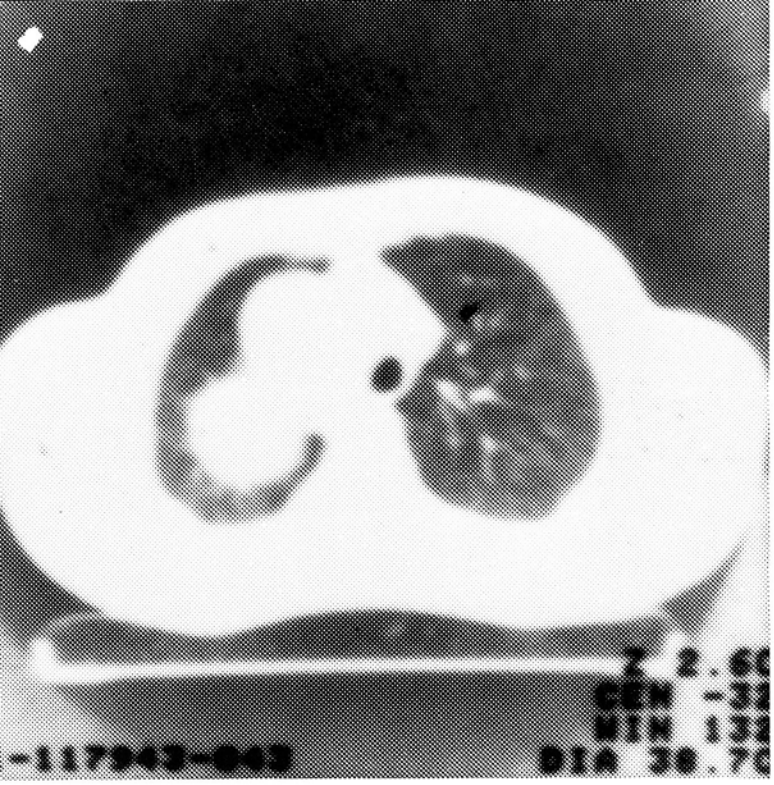


Fig. 3—Spherical mass is clearly seen.

what it is! This is a strikingly myxoid tumor. The term refers to the fact that the tumor cells, which are spindle-shaped and sometimes stellate in shape, are separated from each other by loose, finely fibrillar stroma with empty spaces, which might have contained a myxoid mucopolysaccharide ground substance. The trichrome stain does not show much collagen. The vascularity is striking, and that is contrary to what a true myxoma should show. There is a moderate amount of reticulin.

The tumor cells have generally a strongly acidophilic cytoplasm. More seldom they appear to contain small vacuoles. Some of the cells are ribbon-shaped, but I have not seen any that show acceptable cross striations. Likewise, I have not seen any good neurofibromatous area. The differential diagnoses to be considered are a liposarcoma, a sarcoma of the botryoid type, and a myxoid change in a neurofibroma. I believe it is a sarcoma, and even though I do not like and do not generally use the term, I believe in this instance, the term myxosarcoma is the least objectionable one.

Dr. Lattes' Diagnosis:

"MYXOSARCOMA"
(liposarcoma? sarcoma botryoides?)

Histopathologic diagnoses submitted:

Liposarcoma	57
Myxosarcoma	16
Myxomatous tumor	15
Myxomatous hamartoma	06
Various sarcomas	12
Various benign	10

Dr. Lattes: Several participants were impressed by the fact that since it is a sarcoma and it is myxoid, it should be liposarcoma or myxosarcoma. Myxomatous tumor is a beautiful diagnosis because it is absolutely noncommital. I do not think it is a hamartoma; I think it is a malignant tumor, a sarcoma.

Dr. del Regato: Sister Ignatius Owyang of Cincinnati offered myxomatous hamartoma. Dr. S. E. Vernon of Los Angeles preferred myxolipoma. Dr. E. L. Lee of Tampa and Dr. Marcus Beck of Columbia, Missouri offered myxoid liposarcoma. Dr. H. A. Azar of Tampa and Dr. W. J. Kirsch of St. Petersburg called it a well-differentiated liposarcoma.

Subsequent History: The patient received post-operative radiotherapy from March 30 to May 3, 1977; a total of 5550 R were administered to the mid-thoracic plane.

Dr. Ferguson: Liposarcomas are very rare tumors. There are only 50 reported cases in the literature of documented liposarcomas in the mediastinum; I have only seen one of these. Radiation therapy and chemotherapy are no good, as I understand it, and surgery is not good,

Fig. 4—Anaplastic spindle-shaped and stellate cells in a loose myxoid pattern (H + E, × 270).

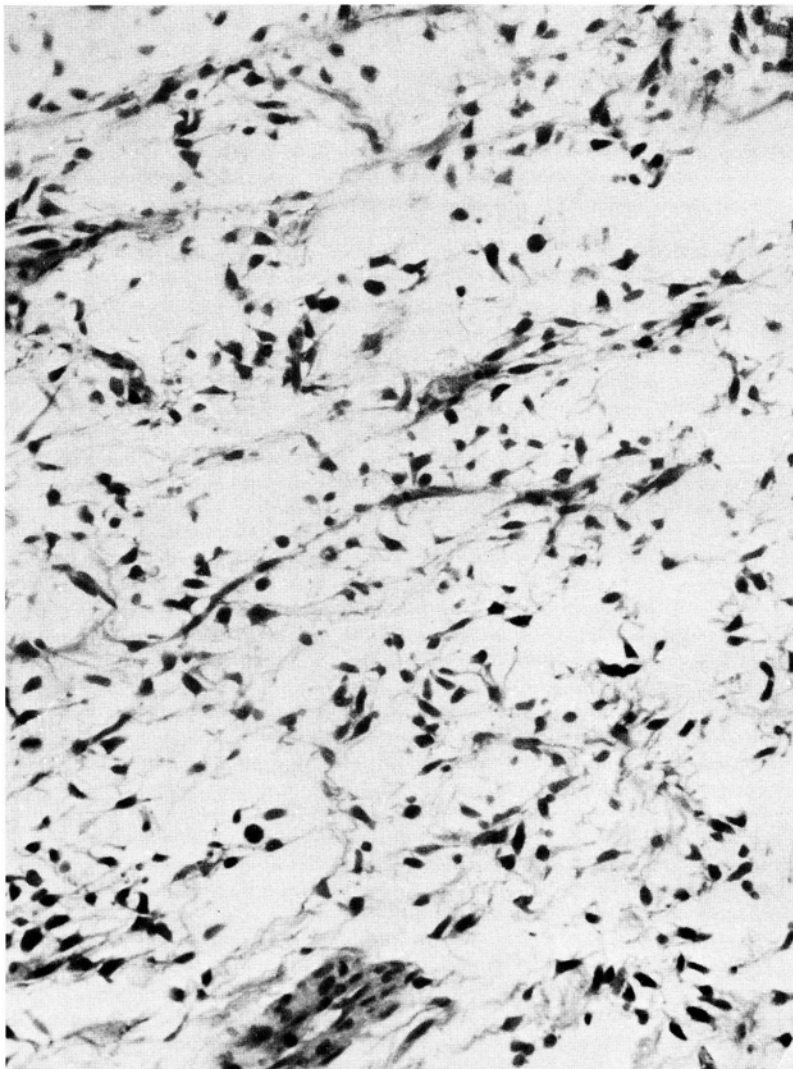


Fig. 5—Detail showing a suggestion of cross striations in the elongated cells in the center of the field (arrows) (H + E, × 530).

so the prognosis is bad. There has been a rare cure reported with surgery. One would hope that this young man represented such a case.

Dr. S. D. Varma, Milwaukee, WI: The patient was examined approximately a month ago and did not have any evidence of recurrence. He had developed a small nodule on the upper eyelid, which was removed and turned out to be a cyst.

Dr. Viamonte: In a large series of 300 liposarcomas published from the Mayo Clinic and Memorial Hospital of New York, only eight were from the mediastinum, so it is a rare tumor. The incidence of liposarcoma is one out of 120 lipomas, so in practical terms, if one sees a fatty tumor of the mediastinum in an asymptomatic adult, the chances are that it is a benign lipoma. I have been told that at surgery, the benign lipomas are sometimes infiltrating and not easy to resect; I wonder if it would warrant exploring every mediastinal lipoma since only a minority are liposarcoma.

Dr. Komanduri Charyulu, Miami, FL: Dr. Ferguson implied that these tumors are not radioresponsive. Perhaps Dr. del Regato would comment on the radiosensitivity of the tumors. There is some information in the literature that radiotherapy is curative in localized liposarcomas.

Dr. del Regato: A great deal of the valuable information that we have about radiotherapy of liposarcomas we owe to Dr. Lattes' mentor, Dr. Arthur Purdy Stout, a pathologist, not a radiotherapist. He also pointed out the fact that, contradictory to the radiobiological assumptions, the most radiosensitive and radiocurable of these tumors is the most differentiated. It is customary and useful to do post-operative radiotherapy in view of the fact that they often recur after excision and that they are easily radiocurable.

Dr. Leonard Shukovsky, Tampa, FL: I believe this tumor lends itself to the debulking procedure followed by radiation therapy. The M. D. Anderson series of soft tissue liposarcomas not in the mediastinum is fairly extensive. The control rate runs between 85 and 95 percent after an excisional procedure to remove the tumor in toto, without an attempt to curatively resect muscle groups or amputate limbs, and followed by high dosage radiation therapy.

Dr. del Regato: Well, actually, in the case of liposarcomas, particularly the bulky, gelatinous myxoid type, I might even agree to debulking without any intent of surgical cure but simply to remove the big mass. My objection in general is, however, to the procedure of debulking; I think it is a vogue that we are presently seeing and one that will die out.

References

Cicciarelli, F.E., Soule, E.H., and McGoon, D.C.: Lipoma and liposarcoma of the mediastinum: a report of 14 tumors including one lipoma of the thymus. J. Thorac. Cardiovasc. Surg. 47:411-429, 1964.

Staub, E.W., Barker, W.L., and Lanston, H.T.: Intrathoracic fatty tumors. Dis. Chest 47:308-313, 1965.

8. CHONDROSARCOMA OF THE CHEST WALL

Contributed by **L. E. Eynon, M.D.** and **J. D. Crissman, M.D.,** Cincinnati, Ohio

The patient was a 53-year-old man in May 1977 when he complained of dyspnea and cough; one year previously, he had been treated for a carcinoma of the prostate, receiving radiotherapy to the pelvis for a total of 6000 rads in 41 days. On examination he was found to have dullness and rales of the left pulmonary base and a palpable left submaxillary node. The SMA-12 was normal.

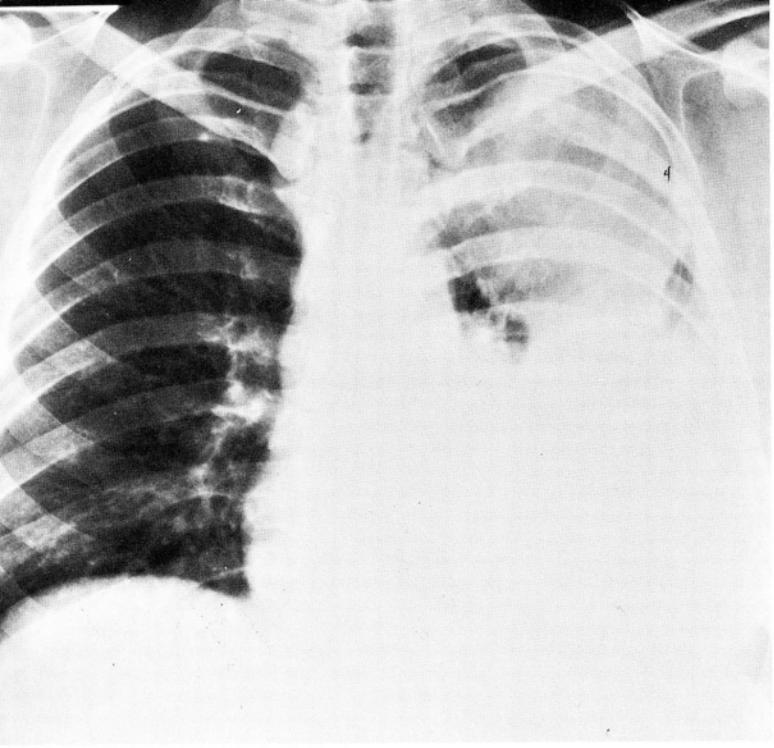


Fig. 1—Extensive mass in the upper part of the left lung.

Dr. Viamonte: Chest roentgenograms reveal an extensive, somewhat lobulated extrapulmonary mass which occupies the upper dorsal half of the left hemithorax and has an associated left pleural effusion. There is a right paratracheal mass suggesting adenopathy or tumor. The right lung appears radiographically unremarkable. There is destruction of the posterior arch of the left fourth rib.

The radiographic findings and the clinical history would suggest metastatic disease from the prostate. It is unusual to see localized bone destruction, a large extrapulmonary mass and right paratracheal adenopathies from metastatic prostatic cancer. As most of the mass appears extrapleural in location, a primary pulmonary malignancy would be unlikely. A primary bone tumor would produce all of the changes that are observed. The most common primary malignant tumor of the ribs is chondrosarcoma.

Dr. Viamonte's Impression:

1) CHONDROSARCOMA
2) METASTATIC CARCINOMA

Radiologic impressions submitted:

Metastatic carcinoma	64
Bronchial carcinoma	48
Plasma cell myeloma	31
Neurogenic tumor	09
Others	31

Dr. Viamonte: Bronchial carcinoma would be unlikely because the bulk of the mass is extrapleural. If you look at the lateral view of the chest, the anterior margin of the mass is very well circumscribed, so I would not consider a possibility of bronchial carcinoma of the left lung with extensive metastasis. I would not consider a plasma cell myeloma either, which is usually an expanding lesion with destruction and irregular trabeculation; a multiple myeloma would produce a multiple lytic lesion and would be unlikely to develop a very large extrapulmonary mass. We would certainly deal with a neurogenic tumor; this could be a neurosarcoma with pleural effusion, but we would have to explain the destruction of the rib and the paratracheal adenopathy.

Dr. del Regato: Drs. J. D. Cox of Milwaukee and J. E. Crymes of Miami suggested metastatic carcinoma of the prostate. Dr. Richard Thurer of Miami offered two lesions: mesothelioma and metastatic carcinoma. Dr. Arnold Friedman of New York suggested chondrosarcoma.

Operative Findings: On July 8, 1977 a left pneumonectomy was carried out with the removal of the 2nd, 3rd and 4th rib posteriorly. The mass surrounded the ribs and measured 8 cm in diameter, was light yellow with cystic areas and areas of necrosis.

Dr. Lattes: This is a strikingly pleomorphic tumor with areas of cartilaginous pattern and areas in which there are clusters of cells with little, if any, intervening ground substance and featuring abundant cytoplasm with clear spaces and vacuoles and bizarre nuclei. Some osteoid-like ground substance is also seen in some places. Among the larger cells, some of them would be acceptable as the so-called physaliferous cells of the chordoma, and some of them contain PAS positive material. Other cells show what could be interpreted as cross striations. Reticulin stains seem

Fig. 2—Mass associated with pleural effusion.

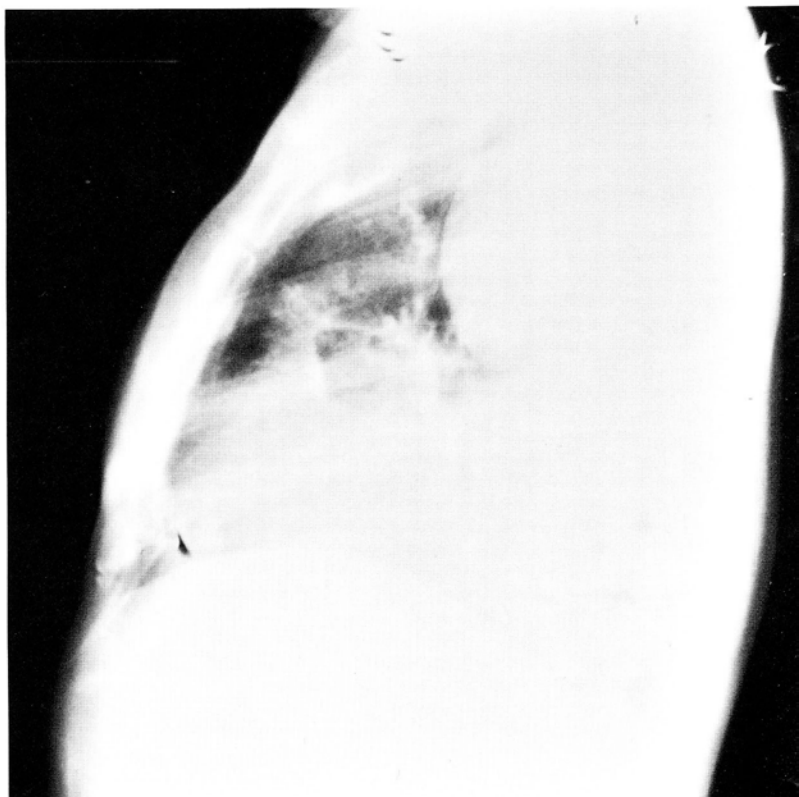


Fig. 3—Surgical specimen of pneumonectomy showing ribs removed in continuity.

to rule out an epithelial origin. We are then dealing with a tumor which, because of its anaplastic morphology and the moderate mitotic activity, is histologically malignant, produces osteoid-like and chrondroid-like ground substance, and has some of the features of the chordoma. However, chordomas are not generally found in this region. If the presence of cells with cross striations could be proven more satisfactorily, a diagnosis of malignant mesenchymoma would be in order.

Dr. Lattes' Diagnosis:

CHONDROSARCOMA WITH CHORDOMA-LIKE FEATURES

Histopathologic diagnoses submitted:

Chondrosarcoma	45
Osteosarcoma	24
Liposarcoma	16
Various malignant tumors	18
Others	06

Dr. Lattes: Chondrosarcoma and osteosarcoma are the most popular diagnoses. Liposarcoma is next, but with all these areas of osteoid and chondroid, we come down to the diagnosis of malignant mesenchymoma, which means a sarcoma featuring different tissue types.

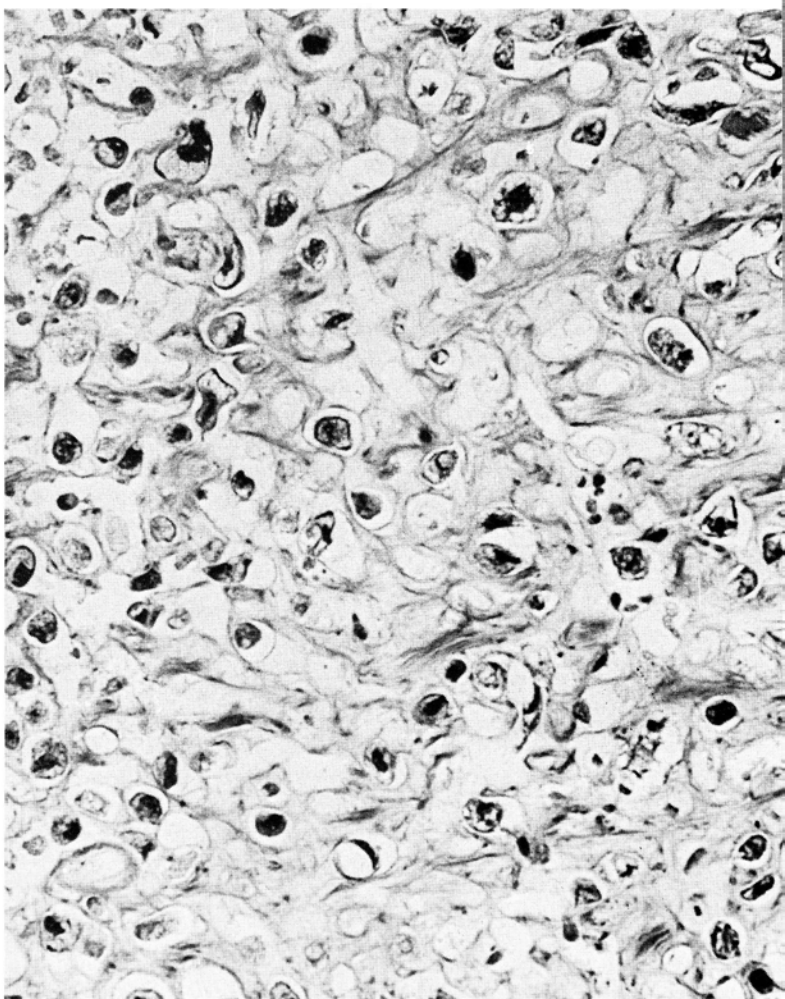
Dr. del Regato: Dr. O. J. Dobrogorski of Cincinnati and Dr. Jeno E. Szakacs of Tampa also made a diagnosis of chondrosarcoma. Dr. R. R. Pascal of New York preferred a noncommital undifferentiated malignant tumor. Dr. W. J. Kirsch of St. Petersburg offered malignant mesenchymoma. Dr. Carlos Perez-Mesa of Columbia, Missouri preferred an osteosarcoma, chondromatous type.

Subsequent History: Following operation, the patient received treatment with Adriamycin and DTIC in September, October, November and December 1977. In February 1978 he was receiving Adriamycin and reported doing well except for loss of hair.

Dr. Ferguson: There are a couple of confusing features of this case, such as the paratracheal mass on the right. I would imagine that was an extension of the tumor across the midline; it looked like an adenopathy. This patient should have had a mediastinoscopy because the mass is eminently accessible to the mediastinal scope; it could be a metastatic tumor from the prostate, or it could be conceivably from a chondrosarcoma, although in my experience, that would be a little unusual.

The other thing is why a pneumonectomy was performed. I am sure that the local situation would have to dictate what was done. I cannot tell what the extent of the lesion is on the roent-

Fig. 4—A frankly chondrosarcomatous pattern (H + E, × 270).



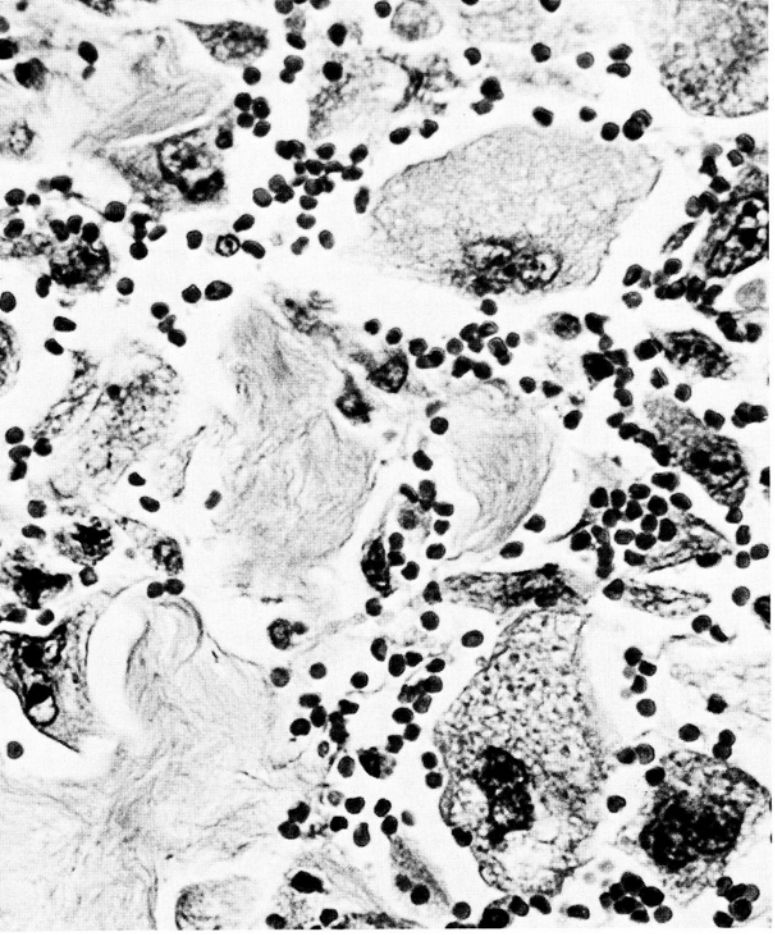


Fig. 5—Foamy, large cells resembling the physalipherous cells of chordoma (H + E, × 530).

genogram. If one does a pneumonectomy and takes a sizable portion of the chest wall, as was done here, the patient has a number of difficulties: one has to reconstruct the chest wall, which can be done and I assume was done in this case. Still, the patient who has a pneumonectomy and a chest wall resection is likely to have fluid leak from the hemithorax, and it makes it more likely that post-operative empyema could occur.

One-third of all the primary rib tumors will be chondrosarcomas. Because of the inability to get frozen sections of these lesions, we have taken the view that all patients who have rib tumors should have wide primary resection as the very first and only procedure. This is a more extensive tumor than most. What you should not do is cut into, or strip, the periosteum on the assumption that it is a fibrous dysplasia or a chondroma of the rib, only to find out that it is a chondrosarcoma; by then, the damage has already been done. What one should do is take out the rib that is involved with all the intercostal muscular tissue and the adjacent periosteum from the bottom of the rib above and the top of the rib below.

Dr. Victor Martinez, Tampa, FL: Are osteosarcomas more frequent in the ribs posteriorly? If a mediastinoscopy had been done and the node were negative, would you then have considered a needle biopsy through the chest wall to get the tissue type, or would you have gone ahead with the chest wall resection and pneumonectomy?

Dr. Ferguson: Osteogenic sarcoma of the rib is a fairly rare lesion. I think we do see chondrosarcomas more often anteriorly, but it does not surprise me that there is a posterior presentation of chondrosarcoma. If the patient had been found to have a metastatic disease from the prostate in the mediastinum, I would have done a needle aspiration biopsy, or even a needle biopsy, of the rib lesion to find out what it was. If this was chondrosarcoma in the right hilar region, I also would have biopsied the lesion on the left side but probably not operated on the patient. I would ask one question: having had all the extensive surgery that he did, why did the patient receive chemotherapy in addition? I am not aware that it was indicated.

References

Spjut, H. J., Dorfman, H. D., and Ackerman, L. V.: Tumors of bone and cartilage (Fascicle 5). Atlas of Tumor Pathology, 2nd series, Armed Forces Institute of Pathology, Washington, D.C., 1971.

9. PULMONARY BLASTOMA

Contributed by **J. C. Bolivar, M.D.,** Tampa, Florida

The patient was a 63-year-old man in August 1977 when on routine roentgenogram of the chest, a rounded mass was seen near the mediastinum in the upper part of the posterior portion of the right lower pulmonary lobe.

Dr. Viamonte: There is a well circumscribed spherical mass 5 cm in diameter in topography of the medial aspect of the right lung. It projects in the lateral view in the region of the posterior mediastinum. A discrete curvillinear calcification is noted. The remainder of the chest is radiographically unremarkable.

The differential diagnosis would include a hamartoma, a large bronchial adenoma, a circumscribed carcinoma of the lung, a pleural tumor, a mediastinal tumor such as a foregut

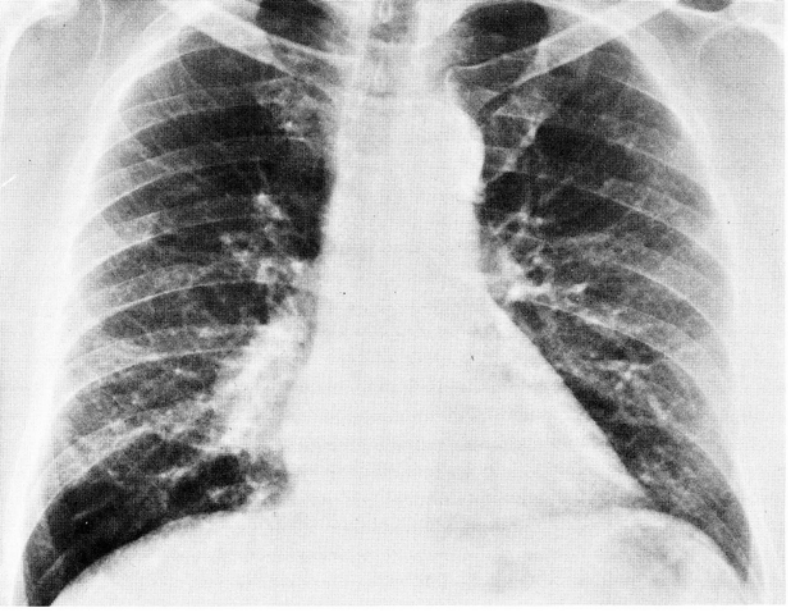


Fig. 1—Mass in medial aspect of right lung.

duplication cyst, a mediastinal mesenchymal tumor, and inflammatory pseudotumor. If the lesion appears calcified, a vascular process would also have to be included.

Dr. Viamonte's Impression:

1) **HAMARTOMA**
2) **HEMANGIOMA**
3) **ADENOMA**
4) **PSEUDOTUMOR**

Radiologic impressions submitted:

Bronchial carcinoma	60
Bronchial adenoma	31
Adenocarcinoma	12
Metastatic tumor	18
Bronchial cyst	15
Various others	42

Dr. Viamonte: Since this is a Cancer Seminar and the patient is a 63-year-old man, one has to consider a tumor of the lung. Bronchial carcinoma, adenoma, adenocarcinoma are the bulk of the primary lesions that were suggested. Metastatic tumor is a possibility.

Dr. del Regato: Dr. Normal Rosenthal of Tampa suggested a "neurogenic" tumor. Dr. J. Frank Wilson of Milwaukee offered an impression of inflammatory pseudotumor. Dr. Stuart Frenchman of Tampa preferred mesenchymal tumor.

Operative Findings: On August 12, 1977 a right lower lobectomy was done. The tumor was found in the upper portion of the lower lobe. The specimen weighed 200 grams and contained a mass 5 x 3.5 x 2 cm. There were no enlarged lymph nodes.

Dr. Lattes: This tumor is a highly cellular poorly differentiated tumor which infiltrates the lung. It is composed of sometimes rounded, more frequently oval-shaped or elongated cells with poorly outlined cytoplasm, vesicular nuclei which are sometimes indented and show considerable activity. The reticulin stains show scanty reticulin fibrils but without any particular pattern that might help in reaching a diagnosis. Trichrome stains show almost complete absence of stainable collagen. The trichrome stain, in addition, shows that the tumor cells are strongly acidophilic, but no obvious myofibrils or cross striations are seen. There are no glandular structures, but some epithelial lined irregular spaces can be seen.

Clinically and radiologically, this seems to be a primary lung tumor. Assuming that this is so, I can only suggest that this completely anaplastic tumor may be a predominantly sarcomatous variant of the so-called pulmonary blastoma, even though in the section available, a carcinosarcomatous pattern is not readily apparent.

Dr. Lattes' Diagnosis:

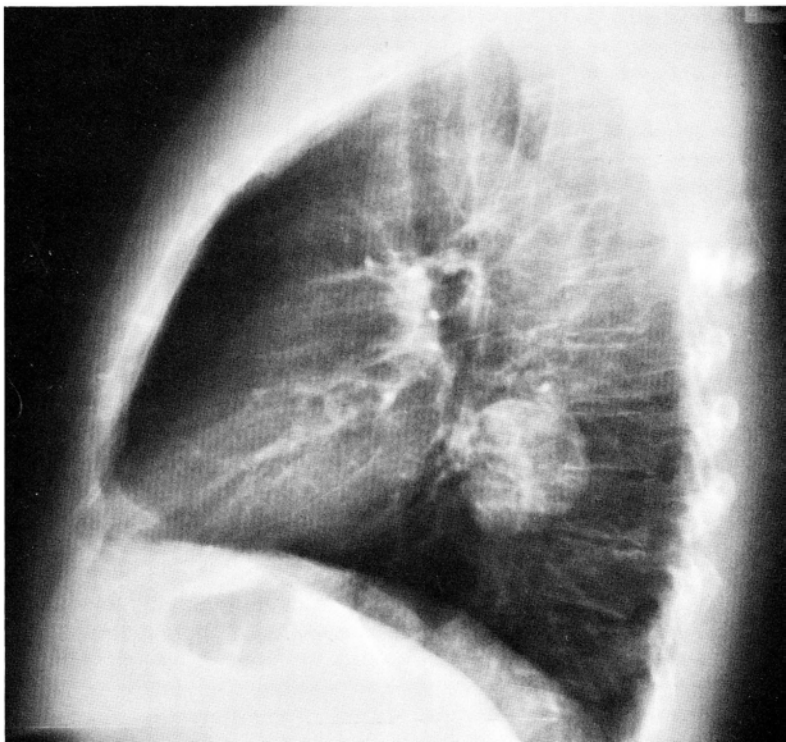
PULMONARY BLASTOMA, undifferentiated

Histopathologic diagnoses submitted:

Hemangiopericytoma	19
Mesothelioma	10
Sarcomas (leio-, rhabdo-, neuro-)	20
Malignant lymphoma	09
Undifferentiated malignant tumor	30
Others	07

Dr. Lattes: Hemangiopericytoma has been and still is a much used and abused term when we do not know what we are dealing with. This tumor really had no vascular pattern. In one of Dr. Stout's original papers on hemangiopericytoma, he stated that in that tumor, the cells grow outside of the blood vessels; however, that is also

Fig. 2—Well circumscribed mass in posterior mediastinum.



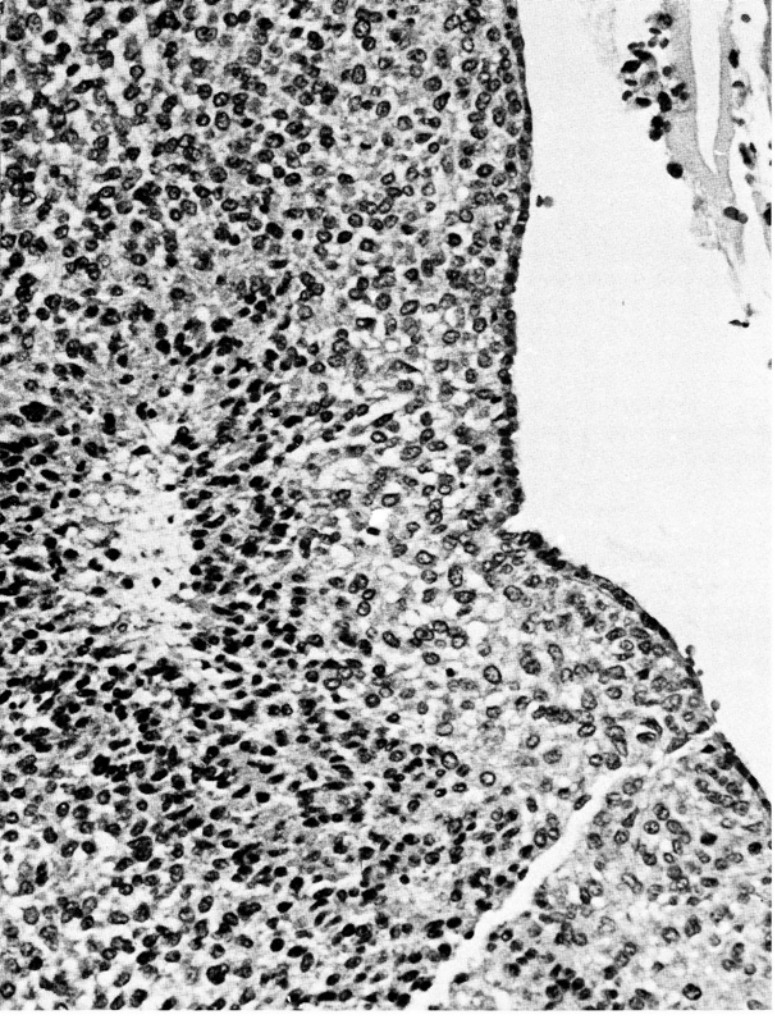


Fig. 3—An undifferentiated, highly cellular area, associated with a space lined by apparently neoplastic cuboidal cells (H + E, × 270).

true for most tumors except endothelial tumors. There are two things against mesothelioma: that this grows inside the lung and that it does not look like one. If there is a sarcomatous pattern, it is probably only one phase of what is really a biphasic tumor. The reticulin stain gave me the lead towards the high probability of pulmonary blastoma. The cell type is not that of a malignant lymphoma.

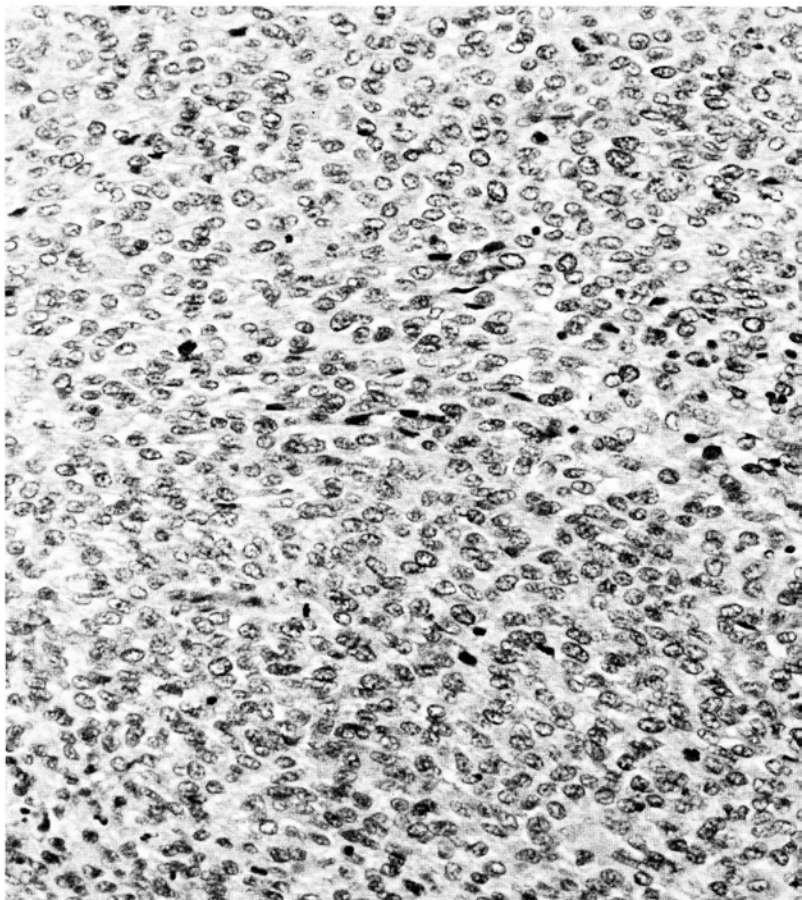
Dr. del Regato: Dr. S. E. Vernon of Los Angeles offered a diagnosis of undifferentiated malignant neoplasm. Dr. J. Lincoln Tamayo of Tampa rendered a diagnosis of large cell malignant neoplasm. Dr. Marianne Wolff of New York saw this case in consultation (in the absence of Dr. Lattes) and made a diagnosis of malignant tumor, possibly leiomyosarcoma or synovial sarcoma. Drs. Jeno E. Szakacs of Tampa and Carlos Perez-Mesa of Columbia, Missouri offered malignant melanoma.

Subsequent History: The patient has returned to his regular work. The roentgenogram of the chest shows no abnormalities beyond the surgical defect.

Dr. Ferguson: This case lends itself very well to aspiration needle biopsy for cytologic diagnosis. In this particular case, the lesion is fairly close; it is probably in the posterior basilar segment of the right lower lobe. One would wonder if this lesion could be seen with fiberoptic bronchoscopy. Dr. Stuart Sagel of the department of radiology at Washington University uses a brush biopsy to obtain diagnosis in solid tumors of this variety, but it has not been great. The yield of brush biopsies, even with biplane radiographic techniques, is fairly low. Needle biopsy of a lesion like this is a great help to the surgeon because if it is known that malignant cells are present, it is so much easier to do what is needed.

We have done over 1200 aspiration needle biopsies in the past five and a half years at Barnes Hospital and have a spectacularly good diagnostic rate with malignant tumors of the lung. Our cytopathologist is unwilling to give more details about the cells other than whether they are malignant or benign; of course, this is one drawback. In most instances where an aspiration needle biopsy has been done in patients subsequently found to have cancer, the diagnostic accuracy rate has been 92 percent. In many cases, we do an aspiration needle biopsy of a lesion without resorting to bronchoscopy, sputum cytology, or other indirect methods. I realize that this is a departure from standard diagnostic techniques. If one is willing to accept and the patient understands the risk, then this is a very good technique for diagnosis. There will be about one patient in five who will have a pneumothorax

Fig. 4—A purely "sarcomatous" area (H + E, × 270).



and only one patient in ten who will require any sort of treatment for that pneumothorax.

I have had one patient with pulmonary blastoma. It is quite rare, and it is usually found in individuals younger than this patient. They are said to have a better prognosis than ordinary bronchogenic carcinoma.

Dr. Manuel Carta, Tampa, FL: We were under the impression that this could be a metastatic melanoma. We decolorized the slide, restained it for melanin, and it came out positive. It was not very much; there was a fine granular black pigment within some of these cells.

Dr. Lattes: Did you see brown pigment before you decolorized the stain?

Dr. Carta: It was questionable. It was very fine here and there, and that was why we thought of the possibility; in addition, there were some rather large, plump eosinophilic cells that we could not place in any particular category. Therefore, we said this could be a melanoma.

Dr. Lattes: I have had very discouraging results in decolorizing a slide and then doing a Fontana stain for melanin. When it is decolorized, any pigment is also bleached out. You see some brown pigment, and you wonder if it is melanin or something else. In the lung, where there are occasionally grains or anthracotic pigment, I am always a little skeptical about an occasional black granule after a Fontana stain. A Fontana stain will cause that brown pigment to become black if there is amoniacal silver precipitate in the form of metallic silver. I would like to see it; anyway, the final answer would be an electromicroscopic study showing melanin. If there is tissue fixed in formalin anywhere, it would be worthwhile trying because melanin could still be demonstrated.

Dr. James D. Cox, Milwaukee, WI: If electron spin resonance studies were done on the formalin fixed tissue, it would pick up even tiny quanitities of melanin, and it is highly specific.

Dr. Maria Viamonte, Miami, FL: I had a case in which we saw two types of pigment with different shades of yellow. We decolorized the slide before it was restained for melanin, and it gave a false positive stain, for it was a hemangiosarcoma, not a melanoma.

Dr. Mario J. Saldana, Miami, FL: Dr. Lattes, could you please explain the relationship between this tumor and carcinosarcoma of the lung? What is your concept of this and carcinosarcoma?

Dr. Lattes: Carcinosarcoma is a concept that has been challenged many times. It has been said that pulmonary blastoma is an embryonal variant of carcinosarcoma and that it repeats in a neoplastic form. In the original anlage of the lung, it is difficult to clearly distinguish between what are going to be mesenchymal cells of the supporting tissue and what are going to be lining cells of the bronchioles.

In general, carcinosarcoma of the lung has not been very popular as a diagnosis in the last ten years or so; the current thought is that they are basically carcinomas, with areas of spindle cell metaplasia imitating a sarcoma. Most carcinosarcomas of the breast, larynx, and trachea are probably basic carcinomas with spindle cell areas. However, for the female genital tract and blastoma of the lung, the term carcinosarcoma is probably justifiable. A blastoma of the lung has been compared with a Wilm's tumor of the kidney. A Wilm's tumor is a tumor of the embryonal blastema of the kidney, and it is difficult to draw a line between those cells programmed to become epithelial and those to become supporting tissue.

Dr. Viamonte: Some pleural tumors can present radiographically as if they were intrapulmonary; those are the pleural tumors arising from the fissures. We have seen mesotheliomas and pleural fibromas that present as solitary pulmonary nodules and which, at surgery or pathology, have proved to be pleural in origin.

Dr. John Pool, Wilton, CN: It is important for all clinicians to realize that if an aspiration biopsy is done of an undiagnosed radiologic shadow, which is a mass within the lung parenchyma, and there is not a histologic diagnosis, cancer has not been disproved. A negative aspiration biopsy means that a diagnosis has not been established.

Dr. Henry Azar, Tampa, FL: When a diagnosis is found to be difficult by microscopy, the chances are that the results of electromicroscopy will also be poor. I was very optimistic when I started, but we have serious limitations of sampling in electromicroscopy, except for specific situations in which we know it can help tremendously. A melanoma is one of the toughest that I have encountered personally.

Dr. Lattes: Yet, if there were some pigment, it is worth trying.

Dr. Cox: I would just like to clarify my comment about electron spin resonance studies of melanin pigment; they are highly specific. The electron spin characteristics are picked up after being influenced by a high energy magnetic field. A laboratory at our institution is doing it, and they have confirmed the ability to diagnose with extremely small amounts of pigment in amelanotic and melanotic tumors in both animals and humans.

Dr. Farhad Moatamed, Salt Lake City, UT: If it is a melanotic melanoma, one can think ahead and add something to incubate it immediately after tissue removal. These melanotic melanomas lack certain enzymes for conversion of pigment; the conversion is helped by incubation.

References

Fung, C.H., Lo, J.W., Yonan, T.N., et al: Pulmonary blastoma: an ultrastructural study with a brief review of literature and a discussion of pathogenesis. Cancer 39:153-163, 1977.

Spencer, H.: Pulmonary blastoma. J. Pathol. Bact. 82:161-165, 1961.

10. CARCINOID OF THE LUNG

Contributed by **D. J. Rothwell, M.D.,** Milwaukee, Wisconsin

The patient was a 57-year-old woman in August 1977 when she complained of cough. Bronchoscopic examination and biopsy were negative. A large pelvic mass was present.

Dr. Viamonte: The roentgenograms reveal a 2.5 cm spherical mass almost contacting the right heart border. There is no calcification within this nodule. The heart appears minimally enlarged. The remainder of the chest is radiographically unremarkable.

The most common tumor in this age group is a bronchial adenoma. Negative bronchoscopic examination would rule out a bronchial carcinoma and a bronchial adenoma. Hamartoma, granuloma, inflammatory pseudotumor (sclerosing hemangioma, plasma cell granuloma, etc.), fibrous histiocytoma are likely diagnostic possibilities. Solitary metastasis from extrapulmonary malignancy should also be considered.

Dr. Viamonte's Impression:

1) **NON-EPITHELIAL TUMOR**
2) **METASTATIC TUMOR**

Radiologic impressions submitted:

Bronchial carcinoma	37
Bronchial adenoma—carcinoid	31
Aneurysm—Varix	57
Hamartoma	12
Adenocarcinoma	07
Metastatic tumor	12
Others	31

Dr. Viamonte: Most participants felt that it should either be a carcinoma or a bronchial adenoma; I would agree with these diagnoses. However, relying upon the clinical history and the negative bronchoscopic examination and biopsy, I suggested that this would be an extrabronchial process. There is nothing in the lesion to

Fig. 1—Spherical mass almost in contact with right heart border.

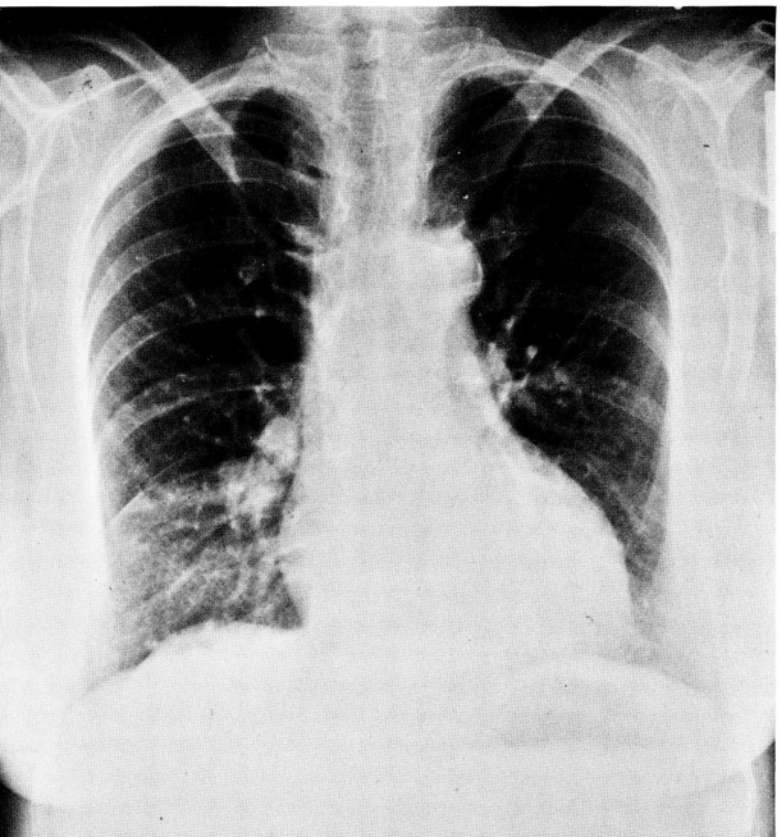
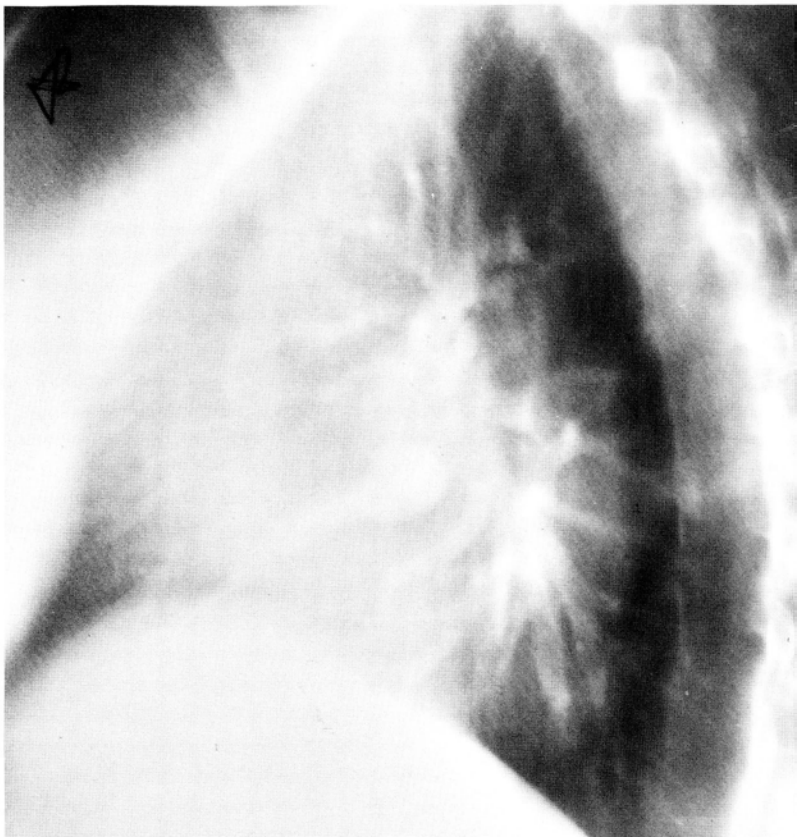


Fig. 2—Spherical mass without calcification.



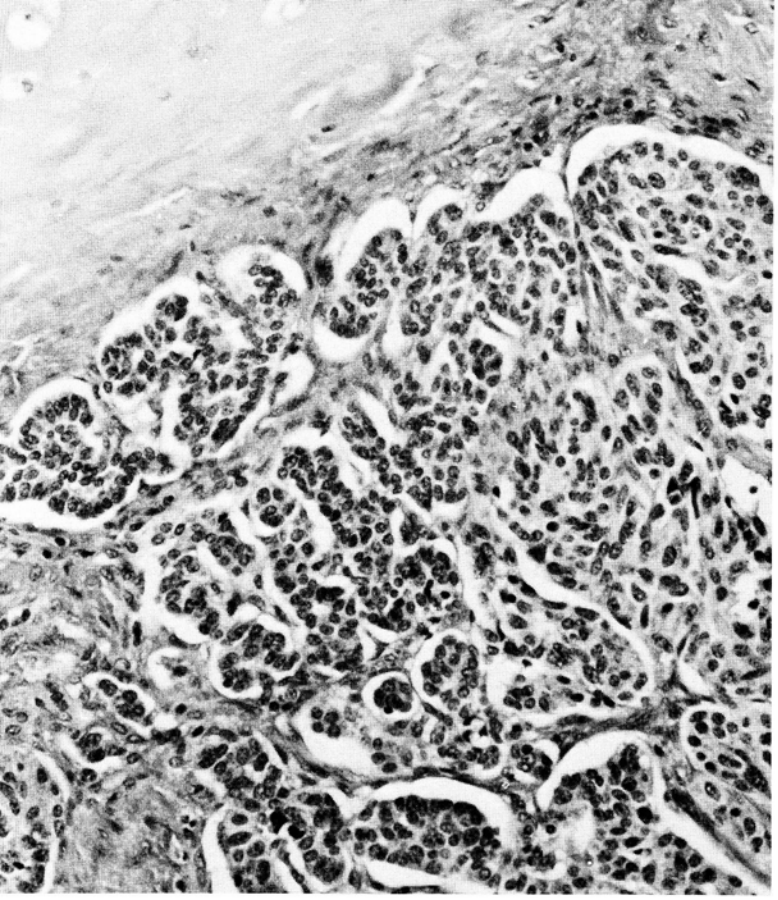


Fig. 3—Typical carcinoid pattern, and a portion of bronchial cartilage (H + E, × 270).

suggest varix or an aneurysm. I have never seen an isolated aneurysm of a pulmonary artery look like this. Hamartoma certainly is a possibility.

Dr. del Regato: Drs. Benjamin Felson of Cincinnati and J. F. Wilson of Milwaukee suggested a bronchial adenoma; Dr. A. C. Speranza Miller of Milwaukee offered carcinoid.

Operative Findings: A preliminary removal of a pelvic mass 12 cm in diameter resulted in a microscopic diagnosis of leiomyoma. On September 29, 1977 a thoracotomy was done; the right middle and lower lobes were removed. A tumor 2 x 1 x 1 cm was found, apparently not involving the major bronchi. A frozen section was reported as small cell carcinoma. The tumor was reddish-gray, soft and friable; a removed lymph node did not show tumor.

Dr. Lattes: This tumor is closely associated with the wall of two bronchi and large blood vessels; therefore, it originated in the region of the hilus. It is composed of slightly elongated, sometimes rounded cells which appear poorly differentiated but which show minimal, if any, mitotic activity. In some places, the cells are arranged in definite epithelial-like nests.

An examination of this tumor under ultraviolet light showed a faint autofluorescence. This is not absolutely diagnostic but strongly suggestive of carcinoid. Grimelius stains show argyrophilic granules.

Dr. Lattes' Diagnosis:

CARCINOID TUMOR

Histopathologic diagnoses submitted:

Carcinoid tumor	64
Paraganglioma	24
Various malignant tumors	19
Others	03

Dr. Lattes: A paraganglioma would mean a tumor of the carotid body or the aortic body; the paraganglioma belongs to that system but has a different pattern with larger cells, more compactness and much more striking vascularity than this one.

Dr. del Regato: Dr. J. Shinner of St. Petersburg also made a diagnosis of carcinoid tumor. Dr. Olga J. Dobrogorski of Cincinnati submitted paraganglioma. Dr. Lewis B. Woolner of Rochester, Minnesota was consulted originally (5819495); he rendered a diagnosis of carcinoid tumor.

Subsequent History: In the beginning of February 1978 the patient was examined and found in good health.

Dr. Ferguson: The carcinoid tumor was first described by Laenec in 1831. In the past, thoracic surgeons have been warned that when they see a tumor with a deep red mulberry appearance in the bronchus, they should assume that it is a bronchial carcinoid and biopsy it very gently or not at all, for these patients can bleed vigorously from the biopsy site. By the same token, the tumors can be submucosal. I would suspect that what happened in this case is what I have seen in a number of cases in recent years: the fiberoptic bronchoscope is used. The fiberoscope is a great instrument which has extended our diagnostic capabilities tremendously, but it has some drawbacks; one of them is the very small size of the biopsy tissue obtained. Even if a bronchial carcinoid is on the mucosal side of the cartilage, it may still be under the epithelium, and the tumor may not be reached with very small biopsy forceps. This tumor is reported to be more predominant in women, but in most of the series reported in the literature, bronchial carcinoids are equally divided between males and females.

References

Bonikos, D. S., Bensch, K. G., and Jamplis, R. W.: Peripheral pulmonary carcinoid tumors. Cancer 37:1977-1998, 1976.

11. INFLAMMATORY PSEUDOTUMOR OF THE LUNG

Contributed by J. F. Wilson, M.D., Milwaukee, Wisconsin

The patient was a 44-year-old woman in April 1975 when the roentgenogram of the chest revealed the presence of a well-delimited, symptomless mass in the right lower pulmonary lobe. Bronchial washings and brushings were negative.

Dr. Viamonte: The roentgenograms reveal a 2.5 cm spherical, noncalcified nodule with indistinct margins just behind the right heart border. The remainder of the chest is unremarkable.

Dr. Viamonte's Impression:

1) **ADENOMA**
2) **HAMARTOMA**
3) **GRANULOMA**
4) **PSEUDOTUMOR**

Radiologic impressions submitted:

Adenocarcinoma	61
Bronchial adenoma—carcinoid	60
Hamartoma	34
Granuloma	12
Sequestration	12
Others	50

Dr. Viamonte: There is a predominance of opinions on neoplasia. Hamartomas and granulomas certainly can look like this case, but sequestration would be ususual. There are two types of bronchopulmonary sequestration, the intra and the extralobar. The intralobar most often occupies the posterior basilar segment of lower lobes and is therefore in contact with the diaphragm. This lesion is a little high for an intralobar sequestration. The extralobar type, or the so-called accessory lung, also is found between the lung and the diaphragm, sometimes entirely intra-abdominal. Some of the extralobar sequestrations have been described as close to the upper lobes, so I would think this is a very rare possibility.

Dr. del Regato: Drs. J. D. Cox of Milwaukee, J. E. Crymes of Cincinnati and R. Thurer of Miami felt that this picture suggested a primary adenocarcinoma. Dr. A. C. Speranza Miller of Milwaukee preferred a granuloma, and Dr. Benjamin Felson of Cincinnati suggested a pseudotumor.

Operative Findings: On May 23, 1975 a thoracotomy was done, and a right lower lobectomy together with the hilar nodes was carried out. The tumor measured 2.5 cm in diameter; it was well-delimited but not encapsulated. The lymph nodes were found negative for tumor.

Dr. Lattes: This growth is made up of a mixture of elongated cells with poorly outlined cytoplasm and vesicular sometimes lobated nuclei arranged in bundles and whorls and inflammatory cells, most of which appear to be lymphocytes and/or plasma cells. Occasional foam cells are seen. The cytoplasm of the tumor cells as seen with a trichrome stain is finely granular in places.

Fig. 1—Noncalcified nodule with indistinct margins.

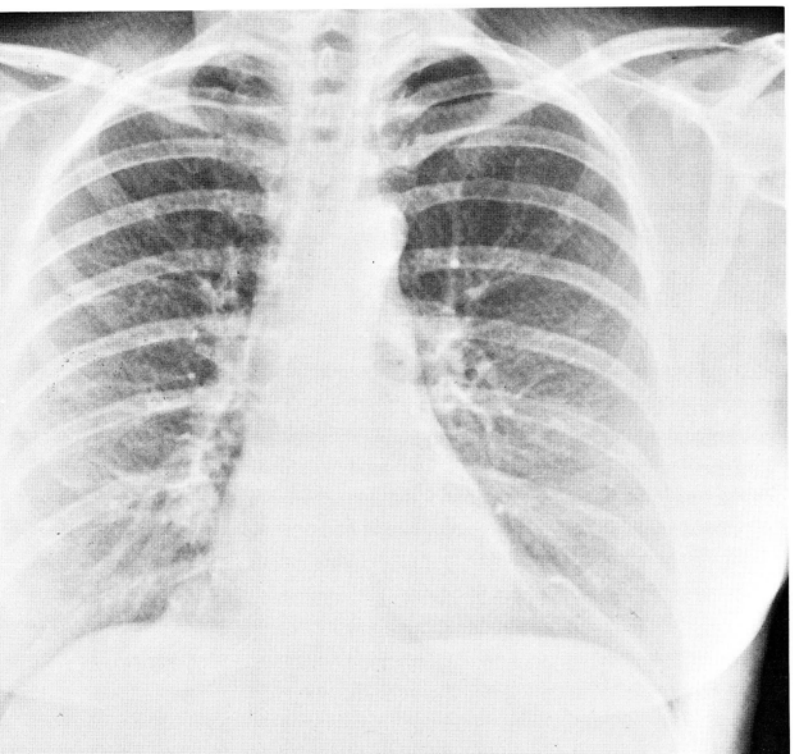
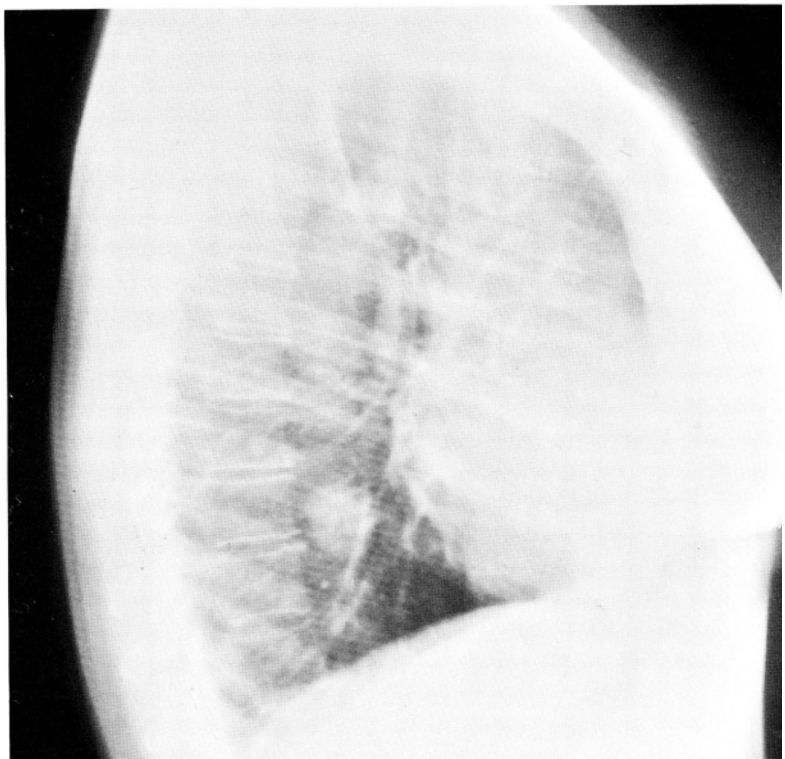


Fig. 2—Spherical mass behind the heart.



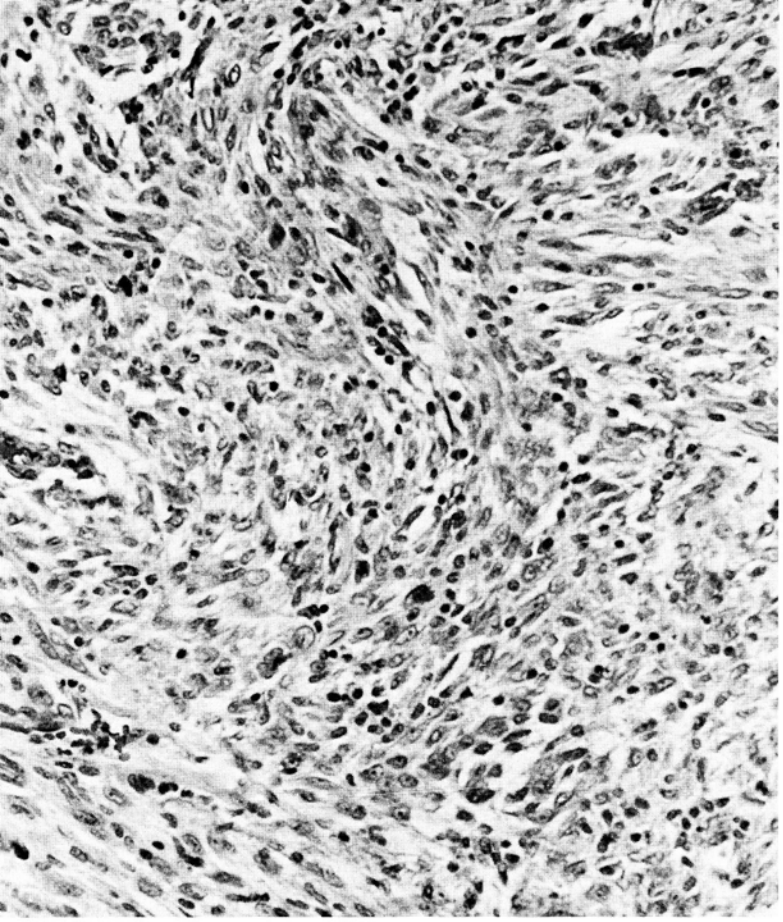


Fig. 3—An admixture of fibroblastic and histiocytic cells with a sprinkling of inflammatory cells (H + E, × 270).

I believe that this is not a metastatic leiomyosarcoma or schwannoma, but rather one of those sarcoma-like lesions that occurs in the lung, and which have been variously called inflammatory pseudotumor, fibrous histiocytoma, fibroxanthoma, sclerosing hemangioma, etc.

Dr. Lattes' Diagnosis:

INFLAMMATORY PSEUDOTUMOR

Histopathologic diagnoses submitted:

Plasma-cell granuloma	30
Benign fibrous histiocytoma	27
Leiomyoma	13
Various sarcomas	10
Benign lesions	12

Dr. Lattes: I predicted some of the terms: plasma cell granuloma, benign fibrous histiocytoma. I feel very strongly that this is not a sarcoma. I occasionally have walked into that trap, thinking that this could be a leiomyoma with inflammatory infiltration, but I believe that they are essentially fibrous histiocytic reactive lesions. In my opinion, this is essentially a reactive lesion which simulates a neoplasm and is harmless.

Dr. del Regato: Dr. J. Shinner of St. Petersburg also made a diagnosis of pseudotumor. Dr. H. A. Azar of Tampa and Sister Ignatius Owyang of Cincinnati offered fibrous histiocytoma, inflammatory type. Dr. C. Maso of Chicago suggested spindle cell adenoma. Dr. D. Greider of Tampa preferred fibrosarcoma.

Subsequent History: On November 17, 1977 the patient was examined and found in good health.

Dr. Ferguson: As Dr. Pool has already said regarding needle aspiration biopsy of these and other granulomatous lesions, a negative biopsy means little. In our area of the country (the midwest), the incidence of histoplasmosis is very high. In patients with a benign inflammatory lesion like histoplasmoma, the combination of the x-ray appearance, negative aspiration biopsy and a fairly high density on the CT scan provides us with enough information for the intestinal fortitude to follow these patients, rather than take out every circumscribed pulmonary nodule just to prove the thesis that it may be cancer. So far, we have eleven patients with three to four year follow-up. We have every reason to believe that this will be of help.

Dr. John L. Pool, Wilton, CN: I wonder if Dr. Viamonte could tell us how he explores a coin lesion, if I may use that phrase, as it comes into these last two or three cases we have seen. What radiographic options are available?

Dr. Viamonte: It has been shown that although the CT is quite specific in recognizing calcium in pulmonary nodules, linear tomography appears more sensitive in depicting calcium in small nodules. We have had experience with the faster CT scanners which allow exposure of two to eighteen seconds versus the old scanners which required two and a half minute exposures. Respiratory motion interfered with delineation of the lesion. Even with the faster scanners, uniform discrete calcifications have been missed by computer tomography.

In evaluation of the patient with a solitary pulmonary nodule, assuming that no excavation or cavities are seen within it, it is important to know whether or not it is the only lesion present in the chest. Here is where I believe linear tomography complements the information of conventional tomography.

If the nodule appears quite dense on plain film, we leave it alone; it should be a granuloma or a uniformly calcified hamartoma, particularly in endemic areas of tuberculosis and histoplasmosis. If the nodule does not appear very dense and shows no evidence of calcification on plain films, linear tomography may show more nodules in about 15 percent of the cases. If there are no other nodules detected with linear tomography,

the nodule is a surgical one. One has to individualize: is it a nodule in a 90 year-old person, or is it in a young individual? Further radiological workup is going to be subject to the clinical decision. In our area, we have a 72 percent medicare population, and most pulmonary nodules are considered surgical because small cancers have been removed successfully in octogenarians.

If the person is in the so-called high risk category, then it is worthwhile trying to make a tissue diagnosis. Fiberoptic mediastinoscopy is popular in our area, and I believe that it has the highest yield in perihilar nodules. If the nodules have a peripheral location, needle aspiration biopsy has a higher yield and lower morbidity. If by any of these methods we have proven that the lesion is a carcinoma and the patient has no extrapulmonary malignancy, computer tomography is extremely valuable. The effectiveness of computerized tomography exceeds that of linear tomography in its detection of certain areas: around the pericardium, the great vessels, the mediastinum, below the diaphragm, the region of the adrenal glands, around the celiac axis, and occasionally the liver. When we use computerized tomography, we do not limit the examination to the chest; we include some sections of the upper abdomen because there may be subdiaphragmatic involvement, particularly with lymphomas.

Dr. James M. Dell, Gainesville, FL: Dr. Felson has said that he has never seen a carcinoma containing calcium unless the calcium had been engulfed by the growth of the nodule. However, he did not say how to tell the difference between a peripheral calcification that had been engulfed and one that had not been engulfed.

Dr. Viamonte: The nodules that we consider absolutely benign and should be left alone are those that have either dispersed uniform calcification (the little dots throughout the nodule), or concentric rings of calcium within the nodule. If the nodule is eccentrically calcified, particularly if it is located in an area where there is fibrosis in the upper lobe, it could be called a colliding carcinoma.

References

Cheng, W. K. and Douglas, F. G.: Pseudolymphoma of the lung with prolonged follow-up. Chest 73:245-246, 1978.

Titus, J. L., Harrison, E. G., Clagett, O. T., Anderson, M. W., and Knaff, L. J.: Xanthomatous and inflammatory pseudotumors of the lung. Cancer 15:522-538, 1962.

12. PULMONARY CARCINOID TUMOR

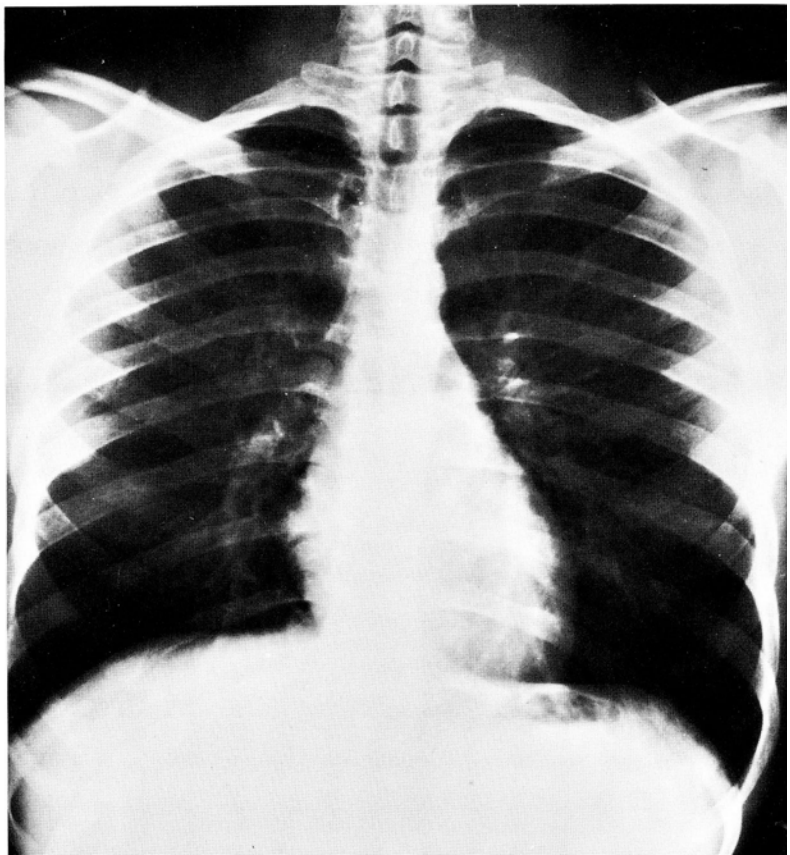
Contributed by **S. J. Rakoff, M.D.,** Bronx, New York

The patient was a 17-year-old man in January 1977 when he developed dyspnea and stridor. Physical examination revealed no abnormalities; bronchoscopy showed a mass in the right bronchus intermedius.

Dr. Viamonte: The frontal chest roentgenogram shows a small, round mass at the bifurcation of the right main stem bronchus. There is no atelectasis, obstructive emphysema or pneumonia. A frontal tomogram of the chest at the level of the right hilus reveals a 1.8 cm spherical, sharply demarcated mass at the bifurcation of the right main bronchus. The mass appears to be attached to the medial aspect of the bronchus intermedius. There are no other abnormalities noted.

Although unusual, a bronchial adenoma should be considered based on the morphology of the lesion. In this age group, papillomas and foreign bodies should also be considered. The age group would be against endobronchial metastasis. Also, the morphology of the lesion suggests a tumor arising from the bronchial mucosa.

Fig. 1—Rounded mass with bifurcation of right main stem bronchus.



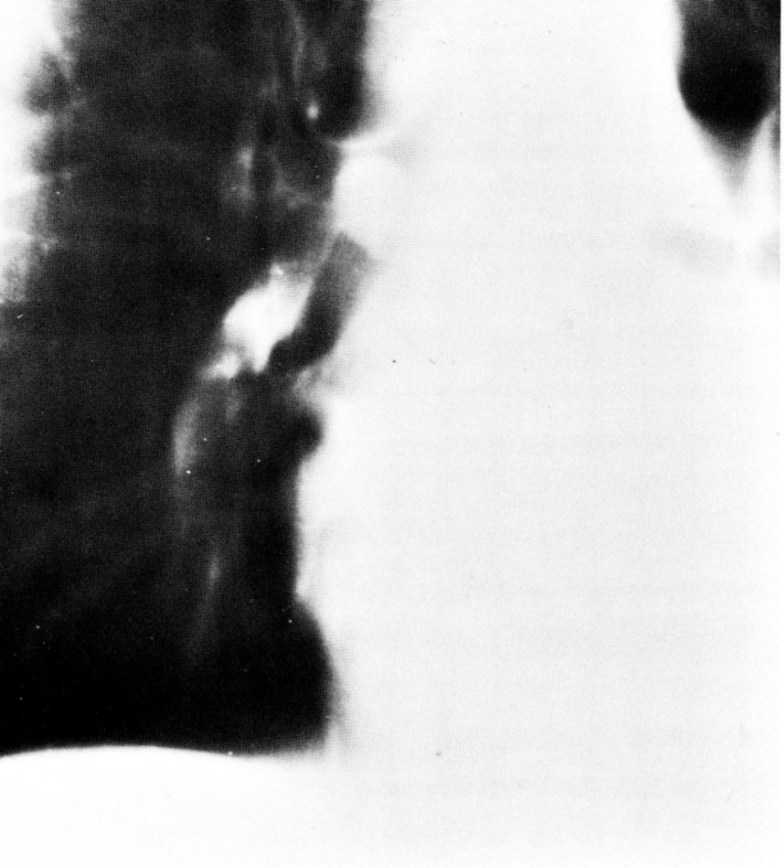


Fig. 2—Lateral view of the mass at the level of the right hilus.

Dr. Viamonte's Impression:

BRONCHIAL ADENOMA

Radiologic impressions submitted:

Adenoma—carcinoid	120
Papilloma	15
Lymphoma	06
Bronchial carcinoma	06
Metastasis	05
Others	15

Dr. Viamonte: I am delighted to see that the majority of radiologists felt that this is an adenoma, carcinoid type. Endobronchial lymphoma could occur, but it would be unlikely in this age group. It would also be unlikely for it to be a bronchial carcinoma.

Dr. del Regato: All of our correspondents agreed on a diagnosis of "benign" bronchial tumor. Dr. P. J. Hettle of Bay City, Michigan called it an adenoma. Dr. John L. Pool of Connecticut preferred a cylindroma and Dr. Stuart Frenchman of Tampa, a carcinoid.

Operative Findings: On January 31, 1977 a thoracotomy was done through the 5th right costal interspace. Through a longitudinal incision of the bronchus intermedius and after ligation of blood supply, a sleave resection of a fleshy tumor was done together with the right upper pulmonary lobe. The tumor measured 1.4 x 1.4 x 0.4 cm. Five peribronchial nodes were found negative for tumor.

Dr. Lattes: This tumor is closely associated with the cartilage of a large bronchus. It is composed of a highly cellular tissue in which the tumor cells are rounded with moderately abundant cytoplasm and are arranged in poorly outlined nests separated by some fibrous and vascular traveculae. Occasionally, a rosette-like arrangement can be seen.

I think that this is a tumor belonging to either the paraganglioma or the carcinoid variety. In my opinion, it is more likely that we are dealing with a carcinoid tumor. Also, here, as in Case 10, we did an examination under ultraviolet light which again showed a faint autofluorescence. Grimelius stains show argyrophilic granules.

Dr. Lattes' Diagnosis:

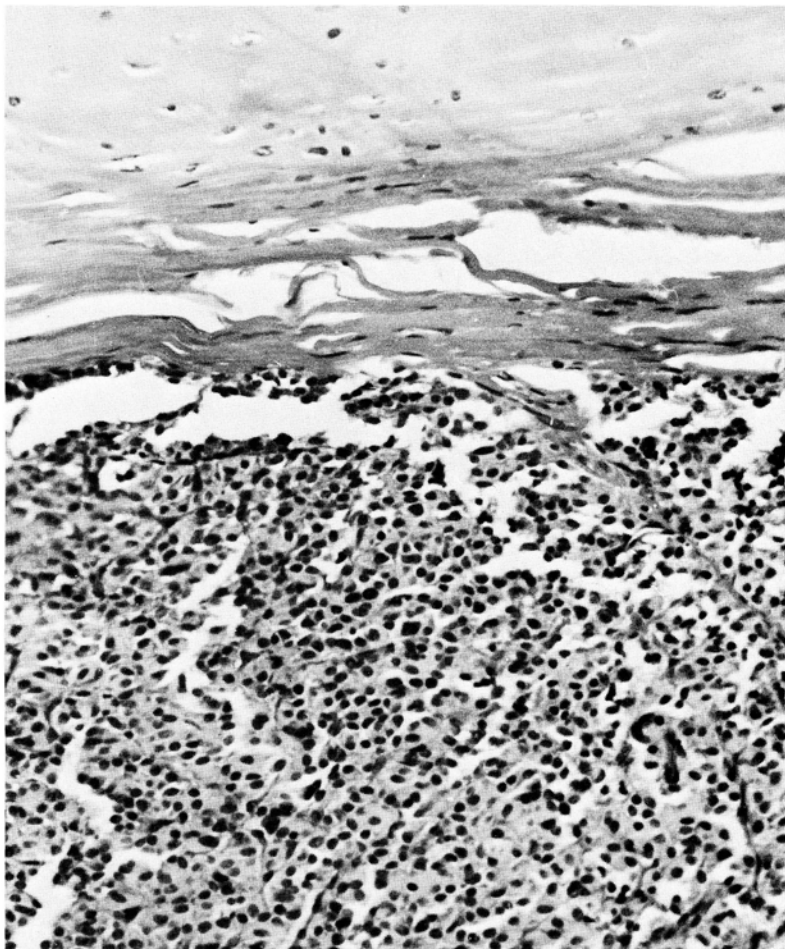
CARCINOID TUMOR

Histopathologic diagnoses submitted:

Carcinoid tumor (adenoma)	68
Paraganglioma	13
Others	21

Dr. Lattes: It is not a true paraganglioma. Again, I would like to make a plea to drop the term "bronchial adenoma" for these tumors; it implies that they are benign lesions, and that is really not true.

Fig. 3—Carcinoid tumor, disrupted by shrinkage artifact and a portion of bronchial cartilage (H + E, × 270).



Dr. del Regato: There was no dissent among our correspondents in the diagnosis of this case as carcinoid, but suggestions were made of parathyroid adenoma and paraganglioma.

Subsequent History: On February 9, 1978 the patient was examined by Dr. Saul Rakoff and was reported well.

Dr. Ferguson: In our experience, an endophytic tumor entirely within the lumen of the bronchus is unusual for a carcinoid tumor. In the trachea and main stem bronchi, totally endophytic tumors would be of the cylindromatous type. Had I seen this patient and the tomogram, I would have thought of a fibroma or lipoma of the bronchus, although the density of this is probably a bit heavy for a lipoma. The management of this case was superb, in my view; sleave resections or wedge excisions ought to be used more often with carcinoid tumors. One must be very careful not to leave any of the bronchus behind that might be involved. If one can get around the tumor by several millimeters in all directions, then a cure can have been affected. A sleave resection or wedge excision can be done if the tumor arises from the spur at the bifurcation between the right upper lobe and the right bronchus intermedius. The alternative is a sleave resection, reanastomosing the bronchus intermedius to the right main stem bronchus after removal of the right upper lobe, with that small tubular section of the bronchus.

References

Bonikos, D. S., Bensch, K. G., and Jamplis, R. W.: Peripheral pulmonary carcinoid tumors. Cancer 37:1977-1998, 1976.

13. INTRAPULMONARY HETEROTOPIC LIVER

Contributed by **Y. LeGal, M.D.**, Strasbourg, France

The patient was a 9-year-old boy in July 1977; he appeared physicially retarded. The roentgenograms of the chest showed a lobulated mass near the diaphragm and posterior mediastinum.

Dr. Viamonte: In all of the films, one sees a well circumscribed, slightly lobulated mass in the right paraspinal region which silhouettes the lower portion of the right paraspinal line. Its superior margin is well circumscribed; its inferior border blends with the density of the right hemidiaphragm and the underlying liver. There may be an adenopathy in the right hilus.

The differential diagnosis would include a pleural, mediastinal, diaphragmatic, or subdiaphragmatic process. In this age group, it would be unlikely to deal with a mesothelioma and with metastatic disease. Bronchopulmonary sequestration is a possibility. However, usually it does not have a lobulated outline and most often presents in the region of the posterior segment of the right lower lobe. A diaphragmatic tumor is also a rare condition and infrequent in this age group. Exceptions are diaphragmatic lipomas. A subdiaphragmatic process would include herniation of the liver into the chest secondary to a congenital diaphragmatic defect, traumatic rupture of the diaphragm, or focal diaphragmatic hypoplasia. A CT study would rule out the possibility of a lipoma. A liver scan would define the position of the liver and may rule out the possibility of an intrathoracic liver (supra-

Fig. 1—Well circumscribed mass in the right hemithorax with suggestion of right hilar adenopathy.

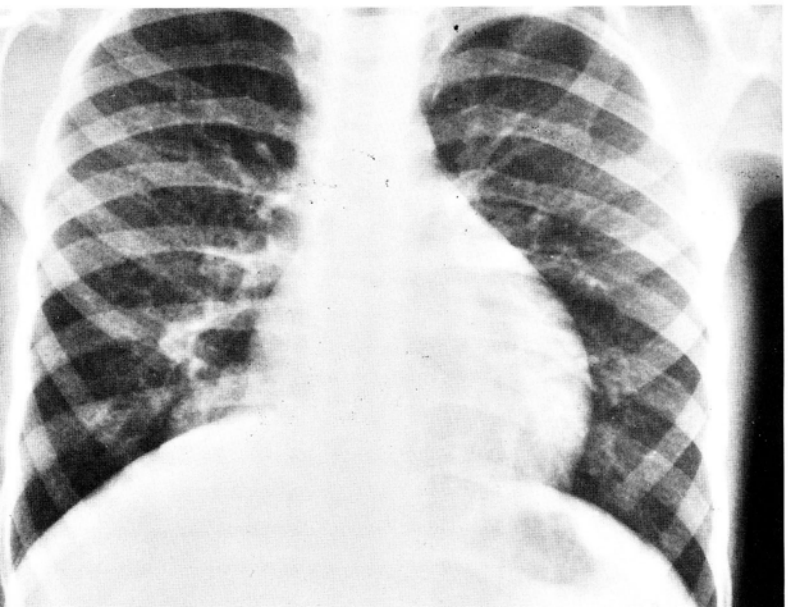
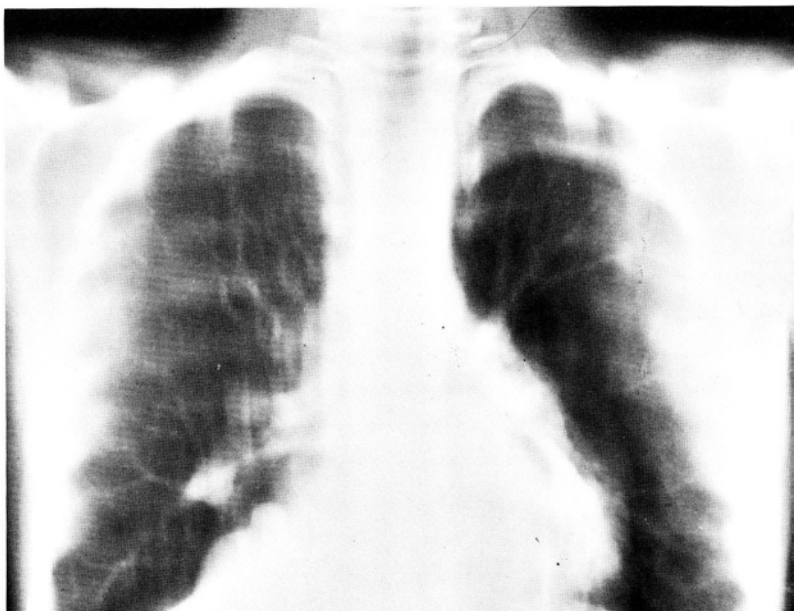


Fig. 2—Paraspinal mass with well circumscribed border.



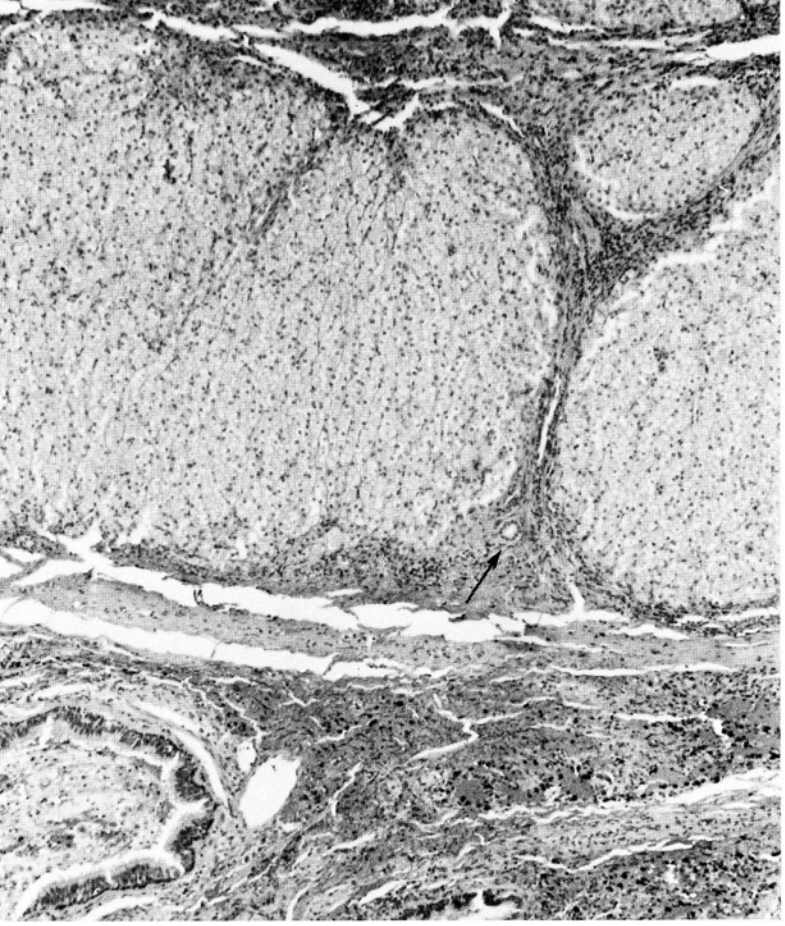


Fig. 3—Note the lobules of liver tissue, separated by fibrous trabeculae containing a small biliary duct (arrow), and associated with compressed pulmonary tissue at left of the picture (H + E, × 84).

diaphragmatic accessory liver). A pneumoperitoneum would reveal the presence of a diaphragmatic defect.

If the patient has a true adenopathy, one might deal with an intralobar bronchopulmonary sequestration with possible infection and enlargement of draining nodes.

Dr. Viamonte's Impression:

1) DIAPHRAGMATIC HERNIA
2) LIPOMA
3) SEQUESTRATION

Radiologic impressions submitted:

Sequestration	43
Lymphoma	33
Tuberous sclerosis	10
Various tumors	50
Others	31

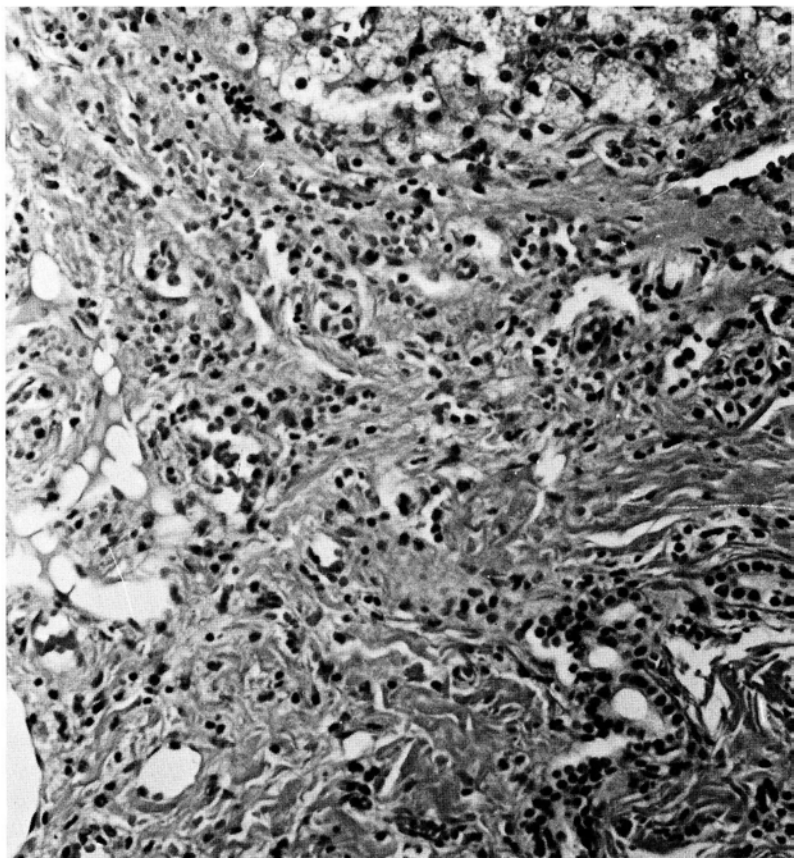
Dr. Viamonte: Sequestration is among the three entities that I mentioned. Lymphoma could be suspected, but there is no clinical evidence that this child had any systemic lymphoma. The lesion is lobulated and has an associated abnormality of the right hemidiaphragm, so I would think that the mass is developmental in origin. Also, this child is mentioned to be physically retarded; it might be that he has other anomalies as well. Tuberous sclerosis goes along with mental retardation, but the pulmonary lesions of tuberous sclerosis are cystic areas resembling scleroderma. Reticular pattern in the lower lobes is the hallmark of tuberous sclerosis. Occassionally in tuberous sclerosis, lymphomatosis of the lung has been described, and most of these bilateral lesions present with nodulation and reticulation, which are not present in this case. This is a solitary lesion. I would add to sequestration the other two diagnoses of diaphragmatic hernia and the possibility of a lipoma of the diaphragm.

Dr. del Regato: Dr. J. F. Wilson of Milwaukee suggested neurofibrosarcoma. Dr. J. E. Crymes of Miami preferred "lymphoma" of the right lower pulmonary lobe with hilar adenopathy. Dr. R. Thurer of Miami suggested Hodgkin's disease.

Operative Findings: On October 18, 1977 a thoracotomy was done. A paranephric mass 4 x 1 cm in diameter was found almost entirely within the lung. Two arterial pedicles and a large vein crossed the diaphragm and were connected with the mass. The patient had a horseshoe kidney and anomalies of the ribs.

Dr. Lattes: This "tumor" is not a true neoplasm but rather a nodular mass of liver tissue complete with portal spaces. The usual lobular architecture has been distorted somewhat by dense fibrous trabeculae, some of which contain biliary ducts and blood vessels. In other

Fig. 4—Bile ducts and inflammatory cells in one of the fibrous trabeculae which separate the nodules of hepatic tissue (H + E, × 270).



words, it has a vague "cirrhotic" pattern. It also resembles the so-called nodular hyperplasia of liver. That the "tumor" was in the thoracic cavity is proven by the fact that there is adherent lung tissue without any intervening diaphragmatic muscle. The bile canaliculi probably drained into the larger bile ducts through the diaphragm, or into the esophagus.

This is obviously a malformation. Even though we are not given any additional information, it would not be surprising if it were associated with other broncho-pulmonary foregut malformations or other congenital anomalies. Occasional similar cases can be found in the literature. The lung bud and the liver bud are very close to each other in the five weeks embryo. It is probable that this ectopia has occurred when the septum transversum, in closing, entrapped a lobule of the developing liver in the forming thoracic cavity.

Dr. Lattes' Diagnosis:

Liver tissue HAMARTOMA
(congenital foregut malformation)

Histopathologic diagnoses submitted:

Heterotopic liver	69
Various tumors	27

Dr. del Regato: Whether ectopic or heterotopic, our correspondents recognized the malformation implied in the finding of liver tissue in the lung.

Dr. Ferguson: I have never seen a case of entirely heterotopic liver. I had a patient with a congenital defect in the diaphragm, a perfectly round hole about 2 cm in diameter; it looked like a punched hole through which a huge mushroom of liver tissue had herniated without trauma. At the time of the thoracotomy, a paranephric mass was found almost entirely within the lung. I gather that paranephric means there was no hole in the diaphragm through which the kidney was actually herniated. However, it would not be large enough to really account for the entire mass seen on the roentgenogram.

I wonder if this is, after all, some sort of malformation related to sequestration because two arterial pedicules and a vein crossed the diaphragm and were connected with the mass. That is a highly suspicious finding, and I think that whenever one finds a systemic arterial blood supply coming from anywhere outside the thorax into the thorax, sequestration has to be considered.

Dr. Viamonte: I indicated that there was a nodule which I thought could represent an adenopathy. If a patient has a true adenopathy, one might deal with an intralobar bronchopulmonary sequestration with possible infection and enlargement of draining nodes. That was my second diagnosis. However, in true bronchopulmonary sequestration, the tissue is of a pulmonary nature, but this was liver. Bronchopulmonary sequestration should not be a consideration. Hamartoma is excessive proliferation of tissue that normally is present in an organ; a nevus is the most common hamartoma. If there was intact diaphragm, then this could be a choriostoma in the lung.

Dr. Lattes: I think I made it seem too simple about the closing of the septum transversus because I did not keep in mind the fact that the lesion is apparently intrapulmonary. Therefore, it is much more complex, and it might very well be a variation of sequestration, including foregut elements other than the liver tissue.

References

Hansbrough, E.T. and Lipin, R.J.: Intrathoracic accessory lobe of the liver. Ann. Surg. 145:564-567, 1957.

Hudson, T.R. and Brown, H.N.: Ectopic (supradiaphragmatic) liver. J. Thor. Cardiov. Surg. 43:552-555, 1962.

Lasser, A. and Wilson, G.L.: Ectopic liver tissue mass in the thoracic cavity. Cancer 36:1823-1826, 1975.

14. PULMONARY GASTROENTERIC CYST WITH ADENO(CARCINOMA?)TOUS CHANGES

Contributed by **E. R. Jennings, M.D.**, Long Beach, California

The patient was a 59-year-old man in April 1965 when he complained of intermittent hemoptysis of many years duration; there had been no dyspnea, pain or loss of weight. In 1941 a rounded paratracheal mass had been noted; through the years, other masses had appeared, but the patient had been successful in avoiding surgery. The patient was in good physical condition; bronchoscopy revealed blood in the right posterior basal segment.

Dr. Viamonte: The chest roentgenogram of July 7, 1958 shows several large pulmonary nodules in the lung bases. There are three that are well recognized in the right lower lobe and at least two small ones that are seen in the left

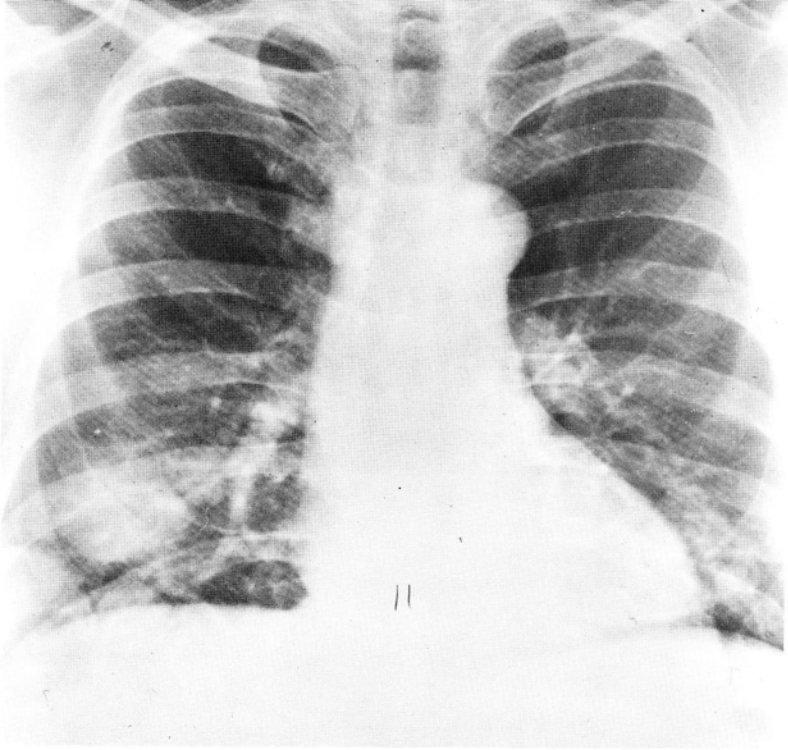
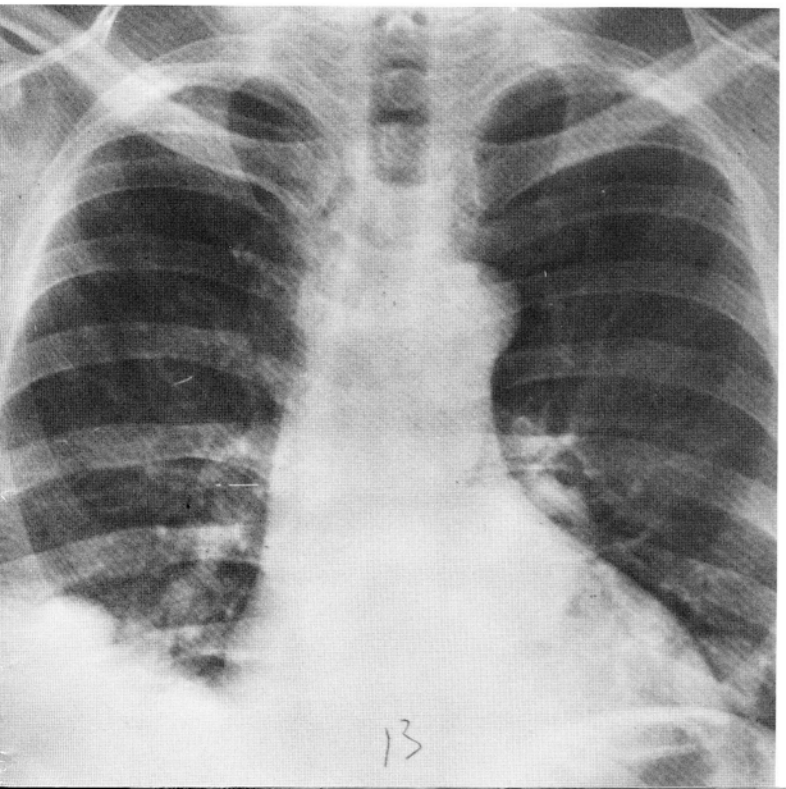


Fig. 1—Roentgenogram taken in July 1958 showing large pulmonary nodules.

lower lobe. The heart is not involved. The hilar shadows appear radiographically normal. There are no signs of excavation or calcification in the pulmonary nodules. A second chest roentgenogram of April 27, 1965 shows increase in the size of the nodules in the left base. A large left retrocardiac nodule is now observed. The nodules at the right base have become confluent. There is obliteration of the right costodiaphragmatic sulcus, suggesting associated subpulmonic fluid. The high position of the diaphragm probably accounts for the prominent cardiac transverse diameter. The hilar and mediastinal shadows remain uninvolved radiographically.

Fig. 2—Roentgenogram taken in April 1965 showing increasing size of pulmonary nodules.



In a patient, age 59, showing slow growth of pulmonary lesions over a twenty-four-year period, one should diagnose a slow-growing neoplasm or a granulomatous process. There is nothing in the history to suggest rheumatoid arthritis or Wegener's granulomatosis. Papillomatosis of the tracheobronchial tree usually shows multiple pulmonary nodules, but often they excavate. This would be unlikely to represent metastatic disease to the lungs. Pulmonary angiomatosis would not have such a slow indolent course.

Pseudolymphoma of the lung, alveolar sarcoid, pulmonary adenomatosis, and bronchoalveolar carcinoma are other possibilities.

Dr. Viamonte's Impression:

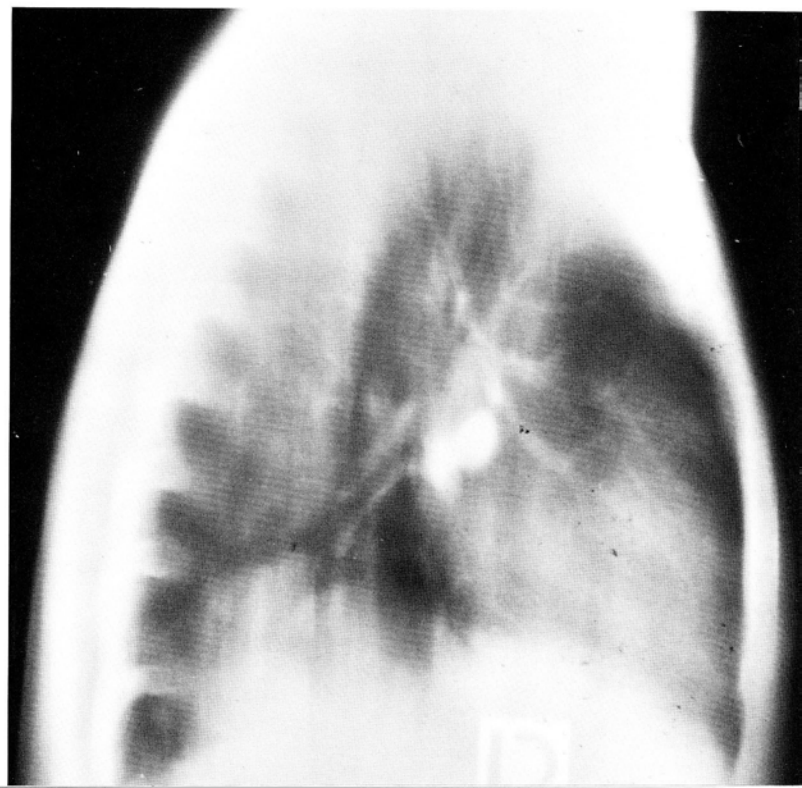
1) **ADENOMATOSIS**
2) **PSEUDOLYMPHOMA**
3) **SARCOID**
4) **GRANULOMATOSIS**

Radiologic impressions submitted:

Wegener's granulomatosis	55
Multiple leiomyomas	18
Rheumatoid nodules	13
Metastatic tumor	18
Your guess is better than mine!	01
16 others	60

Dr. Viamonte: With Wegener's, the nodules excavate, and very often there are associated upper respiratory symptoms. This patient did not have a history of arthralgia, and pulmonary fibrosis was not present; with the masses limited to the lower lobes, I would rule out that as a possibility. Pulmonary leiomyoma is seen more in

Fig. 3—Large retrocardiac nodule and obliteration of costal diaphragmatic sulcus.



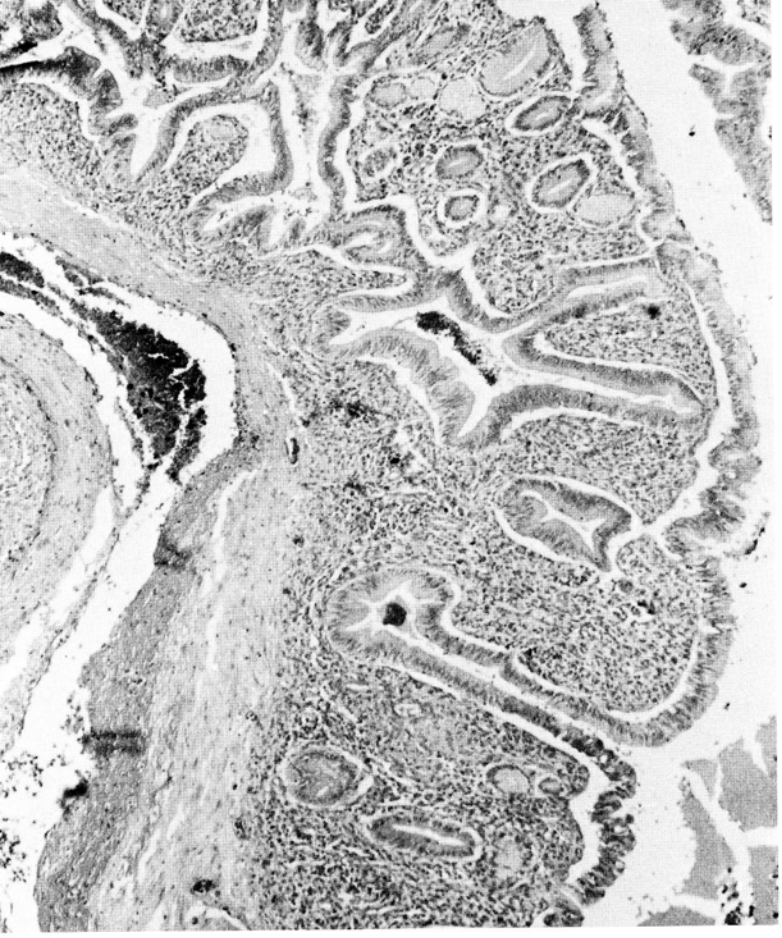


Fig. 4—Cystic space lined by mucosa of antral type (H + E, × 84).

women than men; if seen in men, it would represent a hamartomatous condition that has been labeled leiomyomatosis. That is a possibility, but it would be disseminated, bilateral, and not limited to the lower lobes. A metastatic tumor lasting twenty years would be unlikely. I think the main possibilities are a granulomatous process, lymphoid granuloma of the lung, pseudotumor, or a malformation of some sort.

Dr. del Regato: A diagnostic impression of multiple leiomyomas was offered by Drs. B. Felson of Cincinnati and J. E. Crymes of Miami as well as by Dr. Stuart Frenchman of Tampa.

Operative Findings: A first surgical attempt had to be postponed due to hemorrhage. On a second intervention for lower lobectomy, the hemorrhage required clamping of the corresponding pulmonary vein. There were palpable nodules in the middle lobe that were not removed. The tumor nodules were friable white-tan, and the largest measured 5 cm in diameter.

Dr. Lattes: The findings here are surprising. In fact, there is in some places, I am sure, non-neoplastic mucous membrane of the gastrointestinal type, occasionally with pyloric-like glands and frequent enterochromaffin cells. In addition, there is what appears to be a well differentiated glandular and papillary tumor, in which the tumor cells are generally columnar with mucous secreting features, as proven by the differential stains (mucicarmine and PAS).

This appears to be a gastroenteric cyst which by history has been there since 1941. The problem is whether or not a neoplasm has taken place in association with the cyst. On the basis of the histology seen in the sections sent to me, there appears to be a benign neoplasm of the adenomatous polyp type. However, I cannot explain the multiple pulmonary masses that we are told about, and I would like to know whether they have been explored. Possibly, a more definite adenocarcinomatous change, not seen in these sections, has taken place. However, I am not aware of any similar reported case.

Dr. del Regato has informed me that this case was published in 1966 by Dr. Bauermeister et al as an example of pulmonary blastoma. On the basis of the sections sent to me and my interpretation of them, I cannot agree. As I have already said, I would like to learn what the nature is of the multiple bilateral pulmonary masses, which apparently were not present in 1941.

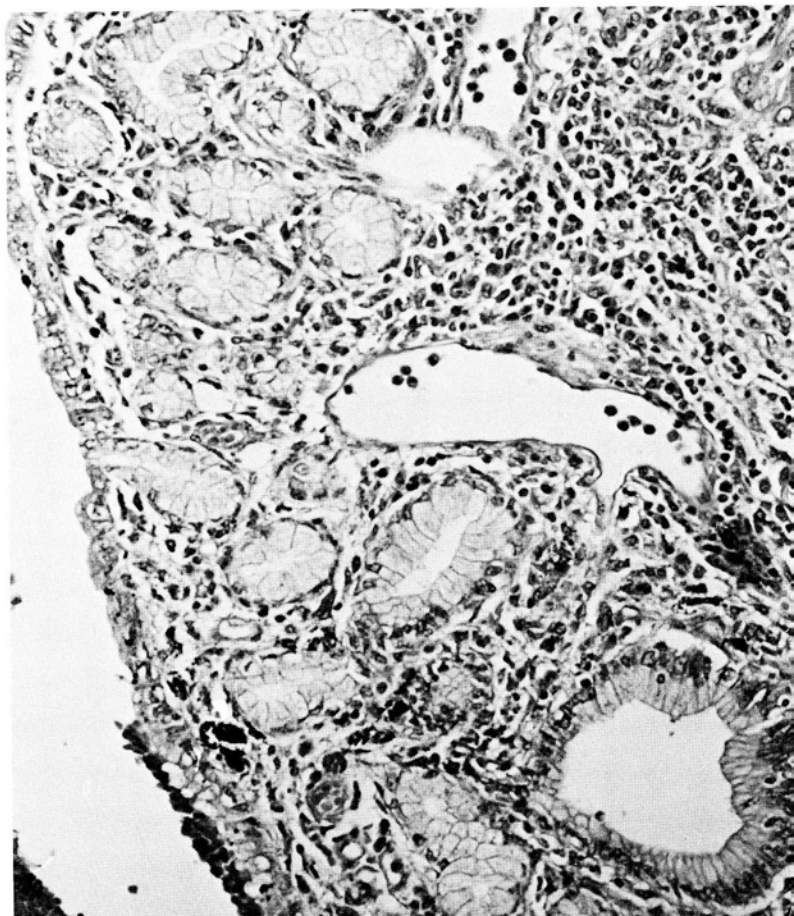
Dr. Lattes' Diagnosis:

GASTROENTERIC CYST
with adenomatous changes

Histopathologic diagnoses submitted:

Adenoma in enteric cyst	15
Adenomatoid malformation	14

Fig. 5—Details of preceding figure, showing glands of pyloric type and lamina propria (H + E, × 270).



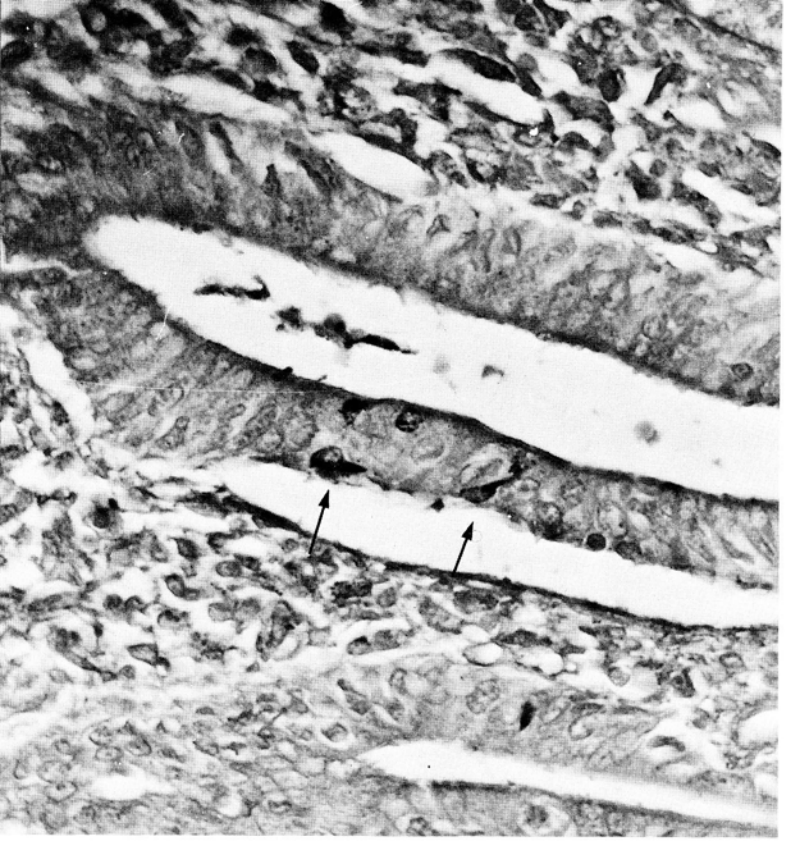


Fig. 6—Gastric crypts containing argyrophilic cells (arrows) (grimelius stain, × 530).

Hamartoma	18
Grade I adenocarcinoma	18
Blastoma	07
Don't know!	01
Others	17

Dr. Lattes: I believe that this is adenoma in an enteric cyst. Adenomatoid malformation is fine if qualified by gastroenteric cyst, but my concept of adenomatoid malformation does not include the presence of displaced normal mucosa. Hamartoma should be used in a very broad sense because there is normal tissue here and not as found in hamartoma. Grade I adenocarcinoma is probably the correct interpretation of the adenomatous changes in the enteric cyst. That is, probably there was a very low grade adenocarcinoma which I interpreted as adenoma originating in a preexisting enteric cyst. I do not agree with the diagnosis of blastoma.

Dr. del Regato: Dr. H. A. Azar of Tampa also made a diagnosis of papillary adenoma arising in an enteric cyst. Dr. C. Maso of Chicago called it a mucous adenoma. Dr. Stephen E. Vernon of Los Angeles offered pulmonary blastoma. Dr. R. R. Pascal of New York and Dr. E. L. Lee of Tampa diagnosed metastatic intestinal adenocarcinoma.

Subsequent History: In January 1971 a cervical nodule was biopsied and interpreted as metastatic adenocarcinoma. In May 1971 the patient died. Autopsy showed tumor in both lungs, in the mesentery, in the rectum, in the bone marrow of the vertebral column; in all places, the tumor was reported to appear as a mucous secreting adenocarcinoma.

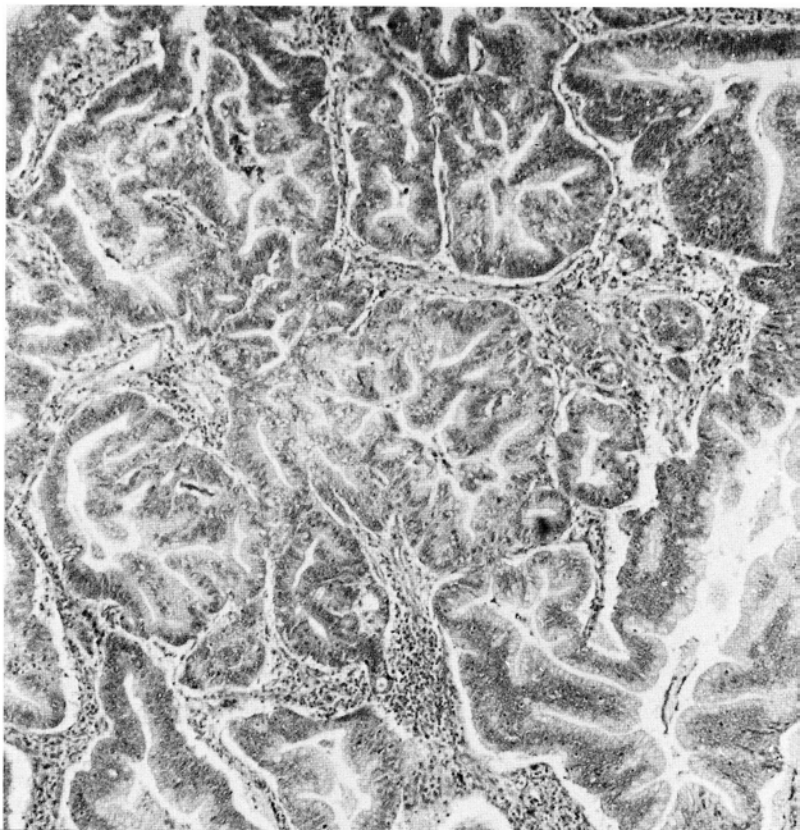
Dr. Ferguson: Looking at the films and long history, we would lean very heavily towards a diagnosis of infectious granuloma. We have a number of cases that followed patterns like this over years and years, with slowly reappearing masses getting larger. None of the things classically related to Wegener's have to be present. There does not even have to be excavation, as Dr. Viamonte indicated. The other type of lesion one might have thought about in this case is multiple hamartomas, but clinically I could not make much of a case for that. I was somewhat concerned about the patient's repeated episodes of hemoptysis for a number of years, particularly taking into account what Dr. Lattes found; to my knowledge, gastroenteric cyst, single or multiple, would not cause hemoptysis.

Dr. Mario J. Saldana, Miami, FL: It was not clear to me whether or not cyst was found. Could you explain the pulmonary findings? Were there any masses in the mediastinum?

Dr. del Regato: At autopsy, there was tumor found in the lungs, in the mesentery, in the rectum, bone marrow and the vertebral column. In all places, the tumor reported was a mucous secreting adenocarcinoma.

Dr. James C. Wilson, Miami, FL: I was interested in Dr. Lattes' finding of neuroid-like tissue; in some of the sections, I thought I noticed

Fig. 7—Adenomatous, perhaps adenocarcinomatous, area (H + E, × 84).



something similar. Dr. Valdes-Dapena, who is a pediatric pathologist, told us that neuroenteric canal remnant cysts can be widespread. I wonder if that would be a possible consideration.

Dr. Lattes: It is a possibility. I do not know if neuroenteric cysts can occur within the lung. There is another thing: at autopsy, there was a carcinoma reported in the rectum. It is very unusual to have metastasis to the rectum. I wonder if this patient might have had two lesions, a benign adenomatous change, gastroenteric or neuroenteric cyst, plus a carcinoma of the rectum, which killed him.

Dr. Frank J. Menendez, St. Petersburg, FL: In 1941 a rounded paratracheal mass was noted. What happened to that mass?

Dr. del Regato: Actually, this man had the lesions for a number of years. All I know is that they did not succeed in bringing him to surgery; he finally had to have chest surgery and eventually came to autopsy. I have given you all of the information given to me. I have no other information. I agree that cancer in the rectum is more likely to be primary.

Dr. Viamonte: It is interesting that the chest film did not show the paratracheal mass, and yet there was no evidence of a thoracotomy. The classic neuroenteric cyst, as seen radiologically, is an anomaly, presenting more on the right than the left as a large mass, sometimes occupying the entire hemithorax. There are coincidental vertebral anomalies, and there is often a defect of vertebral bodies because the classic neuroenteric cyst connects with the spinal canal.

References

Abell, M.R.: Mediastinal cysts. Arch. Pathol. 61:260-279, 1956.

Bauermeister, D. E., Jennings, E. R., Beland, A. H., and Judson, H. A.: Pulmonary blastoma, a form of carcinosarcoma. J. Clin. Pathol. 60:322-329, 1966.

Chitale, A. R.: Gastric cysts of the mediastinum. J. Pediatr. 75:104-110, 1969.

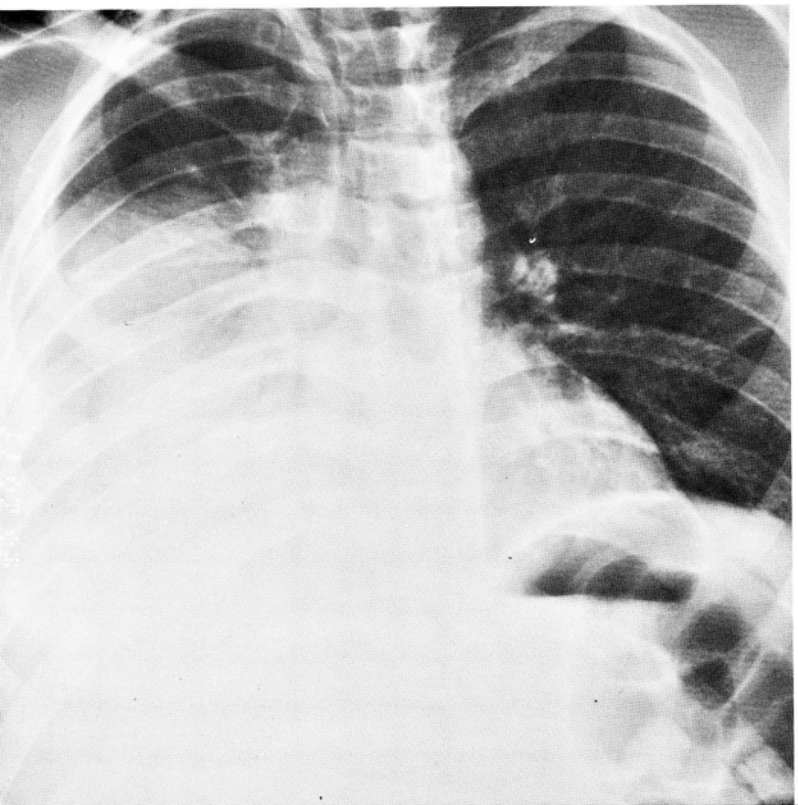
Gray, S.W. and Skandalakis, J.E.: Embryology for Surgeons. Philadelphia, W. B. Saunders Co., 1972.

15. FIBROUS MESOTHELIOMA OF THE PLEURA

Contributed by **R. Thurer, M.D., J. E. Crymes, M.D.** and **M. J. Saldana, M.D.,** Miami, Florida

The patient was a 30-year-old man in March 1977 when he complained of right-sided chest pain. On examination there were decreased breath sounds of the right lung base and tenderness to palpation of the right upper abdominal quadrant. The pulmonary function tests revealed marked restriction.

Fig. 1—Opacity of the base of the right lung suggesting a pleural lesion.



Dr. Viamonte: A frontal view of the chest shows a large density occupying the lower two-thirds of the right hemithorax. The outer aspects of this density show no air shadows. The lung appears to be compressed by this process. The upper margin of the lesion appears indistinct and rises along the lateral chest wall. The radiographic findings suggest a pleural lesion. Due to rotation of the patient, it is not possible to establish if the mediastinal shadow is in the midline or if it is displaced. The left lung appears radiographically normal. An angiogram from a selective right pulmonary artery injection with the patient in the left posterior oblique position shows hypervascularity of the right hemithorax with large, tortuous vessels irregularly distributed. There is evidence of pleural effusion due to the separation of the periphery of the right lung (well demarcated by the angiographic study) and the lateral chest wall.

The vessels observed are unlikely to represent branches of the pulmonary artery. As the pulmonary artery supplies the lateral visceral pleura, we suspect that this is an example of a

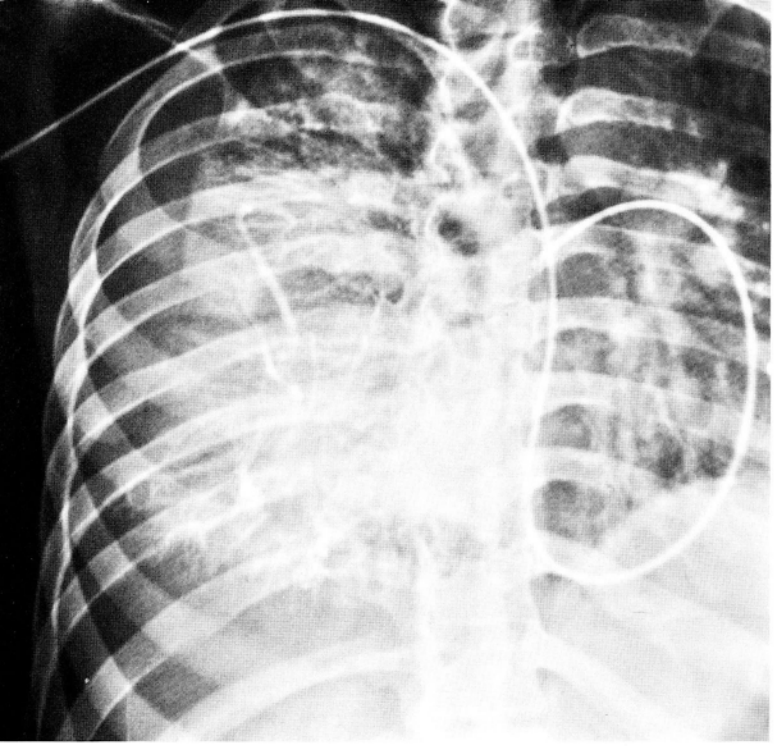


Fig. 2—Angiogram showing hypervascularity and tortuous vessels.

primary pleural tumor and therefore a mesothelioma. Pulmonary arterial supply to a neoplasm of the lung has been demonstrated only (to the best of our knowledge) in metastatic choriocarcinoma. Mesotheliomas usually arise from the visceral pleura. The presence of pleural effusion might suggest the possibility of a malignant mesothelioma.

Dr. Viamonte's Impression:

MESOTHELIOMA
(probably malignant)

Radiologic impressions submitted:

Mesothelioma	33
Pulmonary dysplasia	31
Sarcoma (angio-?)	21
Various benign lesions	45
Other malignant	20

Dr. Viamonte: Mesothelioma is certainly a possibility. I would disagree with pulmonary dysplasia, whatever is being considered there; the lesion is a peripheral one and is supplied by pleural vessels. The primary blood supply of any benign or malignant pulmonary lesion of the lung is the bronchial artery, not the pulmonary artery. A sarcoma, perhaps arising from the pleura, is a possibility.

Dr. del Regato: Dr. J. E. Crymes of Miami suggested a fibrous mesothelioma; Dr. John L. Pool of Connecticut preferred to call it diffuse mesothelioma.

Operative Findings: On April 11, 1977 a thoracotomy was done. A specimen weighing 1000 grams, measuring 11 x 13 x 7 cm was removed; it was solidly attached to the posterior basal segment of the right lung. An entire rib was also removed. There was an area of tumor 8 x 7 x 5 cm, well circumscribed, soft, friable and apparently necrotic.

Dr. Lattes: In my opinion, there is some superficial resemblance between the histological findings in this case and those of Case 4. In fact, there are interlacing bundles of elongated cells with occasional suggestion of palisading, areas of increased cellularity, but generally without definite anaplasia and without obvious mitotic activity. The reticulin stains show abundant reticulin fibers, but here and there are nests of epithelioid appearance, giving the tumor a biphasic pattern.

On microscopic grounds alone, this tumor is not definitely malignant. In this case, I favor a diagnosis of fibrous mesothelioma. If the information that it involved primarily the basal segment of the lung is correct, it is at least locally aggressive.

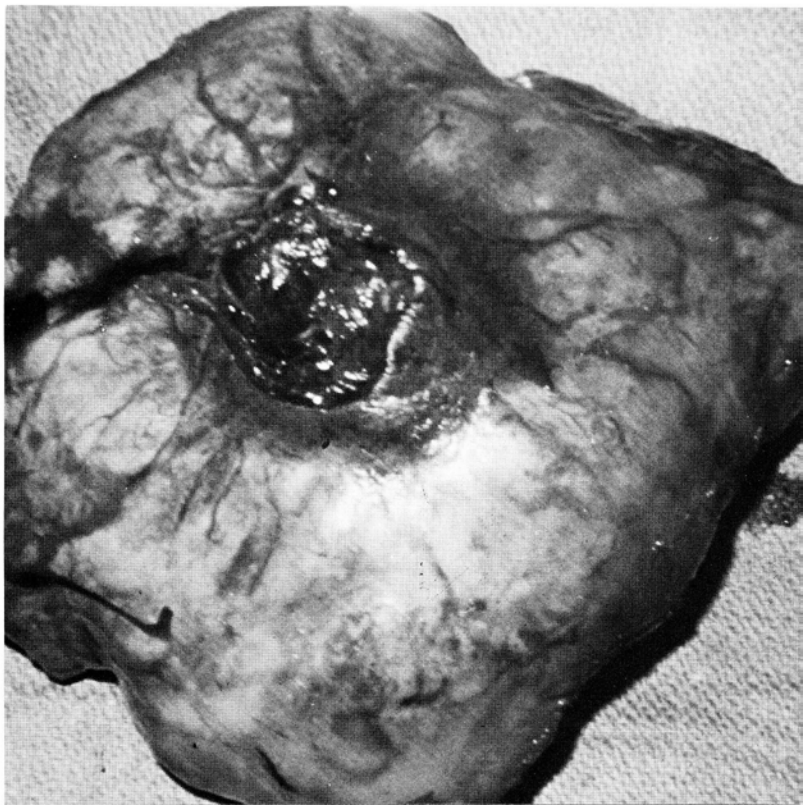
Dr. Lattes' Diagnosis:

FIBROUS MESOTHELIOMA

Radiologic impressions submitted:

Fibrous mesothelioma	45
Leiomyoma	16
Fibroleiomyoma	33
Others	09

Fig. 3—Surgical specimen showing friable well circumscribed tumor.



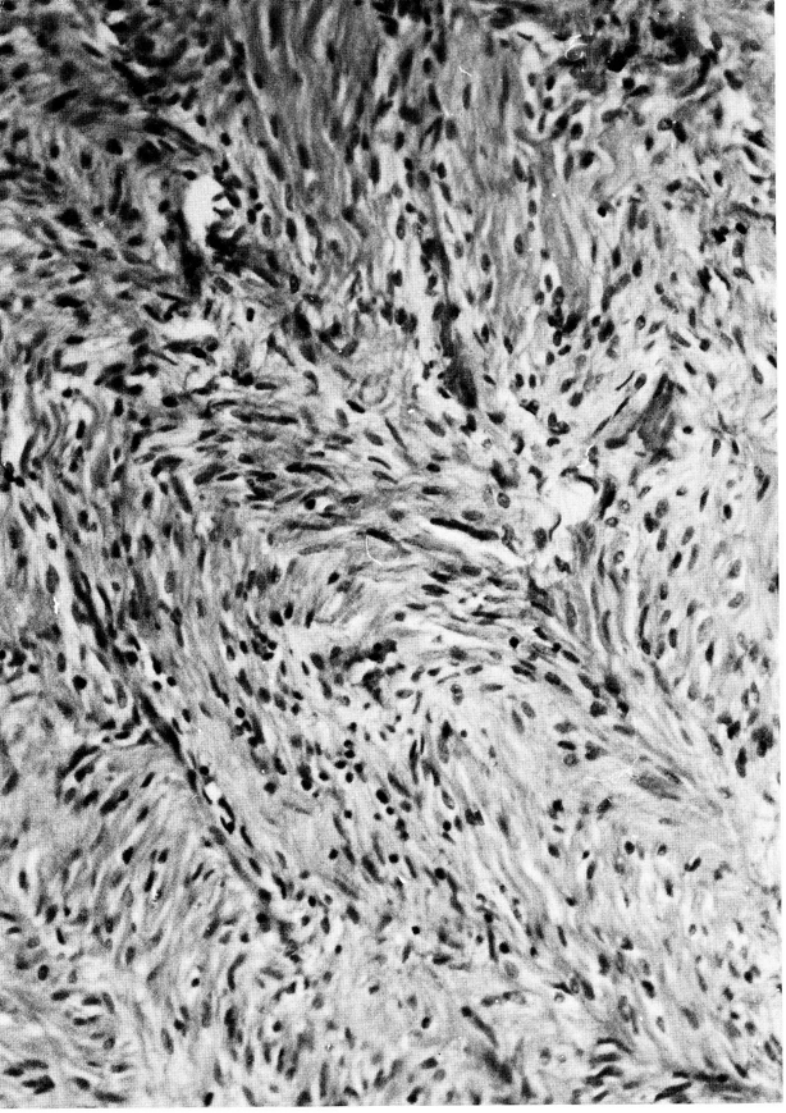


Fig. 4—Interlacing bundles of fibroblast-like cells (H + E, × 270).

Dr. del Regato: Sister Ignatius Owyang of Cincinnati submitted fibroleiomyoma. Drs. H. A. Azar of Tampa and Richard Johnson of Columbia, Missouri preferred fibrous histiocytoma.

Subsequent History: In February 1978 the patient was reported well.

Dr. Ferguson: Dr. Viamonte said one would have difficulty in pre-operatively calling this a benign or malignant tumor, particularly since there was a fair amount of fluid present. Even if mesothelial cells are found in that fluid, it is difficult to tell whether those cells are reactive cells, which probably they would be in this case, or whether they are malignant mesothelial cells. Our pathologists, Dr. Lattes and his group have difficulty in telling malignant mesothelial cells when taken from a specimen of fluid in the pleural cavity. When the chest is opened, the diagnosis in this case, benign or malignant, would be made immediately. Of course, everyone is aware of malignant mesothelioma's dismal prognosis. A faint ray of hope has been given by the group at Presbyterian St. Luke's in Chicago, where they reported a fairly large series of cases of malignant mesothelioma. Years ago, a number of these patients were operated on in order to remove in continuity the empyema and the destroyed lung by means of a pleuropneumonectomy. This was a procedure known to the first generation of thoracic surgeons; they had several cases into the third year without apparent recurrence, so this may be a way to manage some of these cases.

References

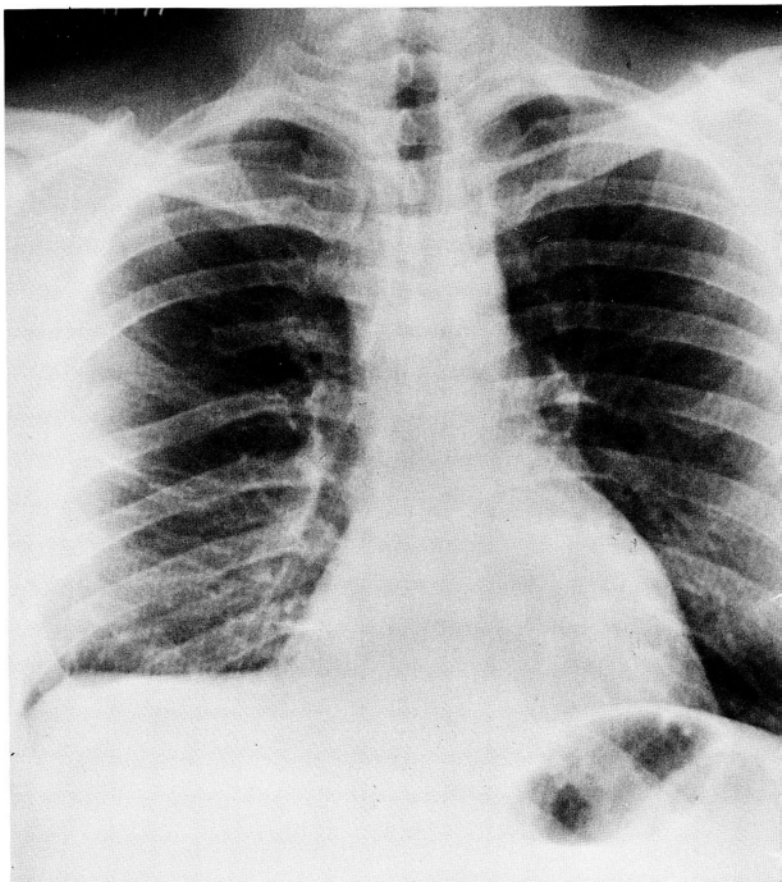
Green, J.D., Carden, T.S., Jr., Hammond, C.B., and Johnsrude, I.S.: Angiographic demonstration of arteriovenous shunts in pulmonary metastatic choriocarcinoma. Radiology 108:67-70, 1973.

Heller, R.M., Janower, M.L., and Weber, A.L.: The radiological manifestations of malignant pleural mesotheliomas. Am. J. Roentgenol. 108:53-59, 1970.

Klima, M., Spjut, H.J., and Seybold, W.D.: Diffuse malignant mesothelioma. Am. J. Clin. Pathol. 65:583-600, 1976.

Stout, A.P. and Murray, M.R.: Localized pleural mesothelioma. Arch. Pathol. 34:951, 1942.

Fig. 5—Follow-up post-operative roentgenogram of the chest showing missing fragment of right sixth rib.




UNIVERSITY of SOUTH FLORIDA
COLLEGE OF MEDICINE
1956
STATE OF FLORIDA