INTRODUCTION

As in the past, we had no real trouble in assembling interesting cases for this seminar. In fact, I have received more than I can try to discuss and evaluate them. I encountered most difficulties which, in some instances, I found insuperable. How hard and long is the road to the understanding of minor growth! It seems to me that with the constant increase in the world's population, the number and variety of tumors increases faster than we can keep up with it. In this small group of eleven cases the some that are unique in my experience for one reason or another and at least one that has completely baffled me, I shall hope that when we discuss these cases together, your comments will eliminate some of the features of these cases which I have found so baffling.

Discussions by:

Dr. Arthur Purdy Stout
INTRODUCTION:

As in the past, we had no real trouble in assembling interesting cases for this Seminar, but when I settled down to try to discuss and evaluate them, I encountered great difficulties which, in some instances, I found insuperable. How hard and long is the road to the understanding of tumor growth! It seems to me that with the constant increase in the world's population, the number and variety of tumors increases faster than we can keep up with it. In this small group of eleven cases are some that are unique in my experience for one reason or another and at least one that has completely baffled me. I shall hope that when we discuss these cases together, your combined experience will eliminate some of the features of these cases which I have found so baffling.
Case 1 - P&S 66999: Thymoma - (Malignant ?)

Case 2 - P&S 66401: Benign localized mesenchymoma (hamartoma) of Mediastinum

Case 3 - P&S 66675: Granulomatous Thymoma (malignant ?)

Case 4 - P&S 66400: Undiagnosed condition of mediastinal lymph node

Case 5 - P&S 65439: Neurofibroma (bizarre) of mediastinum

Case 6 - P&S 67439: Partly Undifferentiated ganglioneuroma (Ganglioneuroblastoma) of the mediastinum

Case 7 - P&S 66998: Undiagnosed tumor of mediastinum (Malignant granular cell myoblastoma (?) )

Case 8 - P&S 66918: Fibromatosis of retroperitoneum and mediastinum

Case 9 - P&S 67549: Benign diffuse mesenchymoma of mediastinum and retroperitoneum

Case 10 - P&S 67215: Malignant diffuse tubular mesothelioma of the pleura

Case 11 - P&S 66075: Primary Chorionepithelioma of the mediastinum with widespread metastases
A 52 year old white woman was referred to the Henry Ford Hospital because of a mass in the mediastinum which was discovered on an x-ray of the cervical spine taken because of pain in that area. The physical examination and past history were not contributory. Hemoglobin was 12.2 grams, hematocrit 40, serum lipid 536 mg.%, total cholesterol 195 mg.%, BUN 13, and blood sugar 100 mg.%. Peripheral blood smear showed 45% segmented neutrophils, 2 eosinophils, 41% lymphocytes, 3 leukocytoid lymphocytes and 9 monocytes. Chest x-ray revealed a right superior mediastinal mass which appeared attached to or was part of the ascending aorta. An I.V. angiogram ruled out the possibility of an aortic aneurysm. Photofluorograms of the chest taken at the place of employment revealed a negative film on 10-10-56 and the presence of a mediastinal shadow on 6-16-59 which was 15 months prior to the present admission.

Exploration of the mediastinum revealed a mass on the pericardium adjacent to the ascending aorta. The pericardium was opened and the mass was removed by sharp dissection.

The 4.5 x 3 x 2.5 cm. specimen was tan, grey, moderately firm and well circumscribed, being separated from a small rim of fibrofatty tissue by thick fibrous tissue. Cut surface was divided into poorly defined irregular nodules by thin fibrous septa.
THYMOMA - (MALIGNANT?)

Case 1 - (P&S 66999)

Microscopic Observations: This lesion is composed of a mass of cells resembling reticuloblasts. They are enclosed within a capsule and, as noted in the gross description, they are divided vaguely into smaller masses by incomplete fibrous septa. They seem to be all of the same kind, without any intermingling of lymphocytes or spindle shaped cells. I counted 5 mitoses in 50 fields in two different slides. Three of these came in the last five fields counted, so I counted another 10 fields and found 9 more mitoses. Getting away from this nest of activity, I counted another 10 fields and found only one mitotic figure. Obviously growth in this nodule has not been at a uniform rate but has occurred chiefly in special zones of activity. The Laidlaw stain shows that very fine reticulin fibers pass out from the collagen septa and gradually disappear. This suggests that the fine fibers are more like a supportive framework than formed by the tumor cells. In the fibrous tissue outside of the main tumor mass are several foci of thymic tissue with Hassall's corpuscles.

Discussion: I do not see how it is possible to escape calling this tumor a thymoma in spite of the fact that it is largely a monocellular type of growth. The thymic tissue does not appear in the Seminar slides, but I could have made no other diagnosis even if I had not seen it. Thymomas that vary from the usual type are always interesting to discuss and speculate about. This one is encapsulated, therefore the problem of invasive growth can be dismissed. But this appears to be a monocellular growth while most thymomas are bicellular. Does this mean it is a reticulum cell sarcoma? Certainly a reticulum cell sarcoma can originate in or secondarily involve the thymus. As I recall malignant lymphomas of the thymus, I have the impression that the septal framework of the thymus was absent at least in part. I also have the impression that malignant reticuloblasts manufacture their own reticulin. In this tumor, the reticulin seems to come out from the fibrous framework and to be more supportive than neoplastic. I have also the impression that in a reticulum cell sarcoma, mitoses are evenly distributed throughout. Here the increased mitotic rate appears more to occur in focal areas. Incidentally, I strongly recommend counting mitoses in any tumor of uncertain nature and malignancy, using 50 or more high power fields scattered through several different areas. I wish I had started to do so years ago instead of only recently. If I had done so, I think I would know a lot more about growth and malignancy than I do now. But indescribable impressions also have some value in judging a tumor. I have the impression, the reason for which I cannot convey to you, that these cells look like thymoblasts and not like the reticuloblasts of a reticulum cell sarcoma.

Thymomas are such peculiar tumors that I could not feel sure this is not malignant, but I will guess that the patient may have been cured by the removal of this tumor. The follow-up will be most interesting.

Arthur Purdy Stout, M. D.
As a result of a chest roentgenogram in a mobile unit, this 44 year old white man was referred to a thoracic surgeon and admitted to Presbyterian Hospital in November 1955. The history and general physical examination revealed no significant findings except that he had suffered from "rheumatic fever" at age 12 which required bed rest for several months. No sequellae of this were evident. Laboratory studies including complete blood count, sternal marrow aspiration, serum electrophoretic pattern and electrocardiogram revealed no abnormalities. A chest roentgenogram showed a smooth nodular protuberance in the right hilar area. Thoracotomy revealed filmy fibrous adhesions over the right lung. A soft, lobulated mass, approximately 5 cm. in diameter, was dissected from the hilar aspect of the lung just cephalad to the main bronchus. The 5.4 x 3.8 x 3.5 cm. bosselated mass was covered by a thin capsule containing fibrous adhesions. The finely lobulated yellowish-orange sectioned surface bulged slightly. Small deposits of anthracotic pigment were present peripherally.
Case 2. (P&$ 66401)

BENIGN LOCALIZED MESENCHYMOMA (HAMARTOMA) OF MEDIASTINUM

Microscopic Observations:

This large mass is composed of a good deal of differentiated lymphoid tissue that seemingly has germinal centers and is encapsulated. There are several striking features which make it differ from any ordinary lymph node. One is the complete absence of any lymph sinuses. The second is the presence of a great many capillaries which, inspite of their very thick collagenous walls are presumably blood capillaries since some of them contain red blood cells. Occasionally, one can observe that one of these capillaries will pass through the lymphoid cells that are circumferentially disposed about a central area which one might assume is the germinal center of a follicle and seem to end there. These pseudogerminal centers often show no reticulum cells and are hard to accept as true germinal centers. Another peculiar feature of this nodule is the presence in it of a number of large veins; some of the largest appear to be passing through it with the nodular components surrounding the veins but a number of the smaller veins appear to be a definite part of the growth. Some anthracotic pigment is contained in the lymphatic tissue.

Discussion:

A number of suggestions have been advanced to explain these peculiar structures which have been found not only in this situation at the hilus of the lung but further out in the mediastinum, in the neck and in the retroperitoneum. The suggestion that they are thymomas is certainly improbable, first because they do not have the characteristics of thymomas, and second because they have appeared in places where the thymomas could not be. It has also been suggested that they are hemolymph nodes, but this is probably not true, first because it is claimed that hemolymph nodes are not found in humans. The ones so-called in the abdominal cavity are simply accessory spleens. An even better reason is that the hemolymph nodes in animals are simply ordinary lymph nodes with their sinuses packed with red blood cells. The favored idea is to consider them hyperplastic lymph nodes resembling thymomas as expressed by Castleman, Iverson and Menendez. But as Rafe Lattes has pointed out to me, none of these interpretations are valid, because they are not lymph nodes. His suggestion is that they be considered hamartomatous proliferations. Abell expressed the thought that lesions such as these are hamartomas in 1957, but he did not realize that the growths are not in lymph nodes. I do not have any important objection to this except to the fact that hamartoma is an extremely vague term and does not call to mind any definite picture. Since this is a benign lesion and composed altogether of differentiated mesenchymal derivatives, I might suggest it be called a benign mesenchymoma.

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(See next page for references).
References:


This 14-year-old boy was well until he was sent home from school for a mild indisposition, probably a respiratory ailment. Fluoroscopic examination in the physician's office revealed a mediastinal mass which was then x-rayed and clearly demonstrated.

At operation, a large mass was found, I would judge 15 - 20 cm. in maximum dimension, in the upper thoracic region, extending over to the left. It encroached on the great veins and the aorta, and could not be removed. Generous fragments were taken for biopsy.

Discussion

This seems to me to fulfill the criteria of a lymphoma. The questions to be debated concern the nature of the large and sometimes multinucleate cells. Can they be Reed cells and is this, therefore, an example of Hodgkin's disease of the thymus? The most diverse opinions have been published concerning this question. For example, Thomas says "yes" in a big way, for he would have us believe that Hodgkin's disease is always thymic in origin. The only paper I have seen that investigated this contention was by Marshall and Wood who studied the autopsies of 56 patients dying of Hodgkin's disease. In 85 cases, the thymus was not macroscopically involved and in the other 21, it was involved. They concluded that while the thymus might be secondarily involved in 15 percent, there was no justification for supposing all Hodgkin's disease started in the thymus. Whether or not the cases in which lesions such as the present one are examples of Hodgkin's disease limited to a single organ is of course almost inevitable. Effer and McCormick discuss this question and arrive at no conclusion but say they personally think they are probably malignant lymphomas. Andritsakis and Sumner using PAS-aldehyde fuchsin-light green say that the large and giant cells in a granulomatous thymic focus will show cytoplasmic granulations while Reed cells from real Hodgkin's disease will show no cytoplasmic granulations. Of course, I can only have an opinion about it, but I feel very strongly that unless one has an entirely satisfactory histological picture of Hodgkin's disease, it is a mistake to classify it as such. I learned very many years ago that one could often see pseudolymphoma lesions in the spleen which were limited to that organ and did not appear anywhere else. Another lesion which has to be discussed in some cases...
GRANULOMATOUS THYMOMA (MALIGNANT?)

Microscopic Observations:

It is quite obvious that this tumor is in direct continuity with a fragment of normal thymus. It can be seen with low magnification that groups of tumor cells are separated one from the other by thick septa of fibrous tissue. The tumor cells consist of two principal varieties: first, relatively normal-appearing lymphocytes and second, much larger cells that are very variable in appearance. The smallest suggest the appearance of neoplastic reticulum cells. From this base, some of them are much larger, a number multinucleate, and several are of giant proportions with very bizarre nuclei. Mitoses vary in the larger cells up to 20-25 per 50 high power fields. One calcospherite is observed. Many cells have vacuolated cytoplasms. So far as I have observed, none of the multinucleate cells has the characteristics of Reed cells. I have not observed any eosinophiles. The reticulin stain shows many fine reticulin fibers among the tumor cells, but some cells are in small groups free from fibers. There is a considerable amount of necrosis in isolated areas.

Discussion:

This seems to me to fulfill the criteria of a thymoma. The questions to be debated concern the nature of the large and sometimes multinucleate cells. Can they be Reed cells and is this, therefore, an example of Hodgkin's disease of the thymus? The most diverse opinions have been published concerning this question. For example, Thomson says "yes" in a big way, for he would have us believe that Hodgkin's disease is always thymic in origin. The only paper I have seen that investigated this contention was by Marshall and Wood who studied the autopsies of 86 patients dying of Hodgkin's disease. In 64 cases, the thymus was not macroscopically involved and in the other 22, it was involved. They concluded that while the thymus might be secondarily involved in 25 percent, there was no justification for supposing all Hodgkin's disease started in the thymus. Whether or not the cases in which lesions such as the present one are examples of Hodgkin's disease limited to a single organ is of course almost insoluble. Effler and McCormack discuss this question and arrive at no conclusion but say they personally think they are probably malignant lymphomas. Andritsakis and Sommers using PAS-aldehyde fuchsin-light green say that the large and giant cells in a granulomatous thymoma focus will show cytoplasmic granulations while Reed cells from real Hodgkin's disease will show no cytoplasmic granulations. Of course, I can only have an opinion about it, but I feel very strongly that unless one has an entirely satisfactory histological picture of Hodgkin's disease, it is a mistake to classify it as such. I learned very many years ago that one could often see pseudoHodgkin's lesions in the spleen which were limited to that organ and did not appear anywhere else. Another lesion which has to be discussed in some cases
Case 3. (P&S 66675)
Continued,
of thymic tumor is seminoma. I do not seriously consider it in this case because of the bizarre giant cells, but the question arises when there are groups of the larger mononuclear cells without giant cells. There are two ways in which true seminomas can appear in the anterior mediastinum - metastasis from a primary tumor in the testis and proliferation of seminoma cells from a teratoma. Unless I have proof of either of these two possibilities and the growth is in the thymus, I favor the interpretation of such collections of large cells in the thymus as part of a granulomatous thymoma.

While we have this particular tumor under consideration, we might touch upon the malignancy of thymic tumors. There is no question about local spread directly into lymph nodes, lungs, over the pericardial and pleural surfaces and, after extension through the diaphragm, extensive involvement of the liver and peritoneum. It is very hard in recent years to find proof of embolic metastasis which is satisfactory. Ericsson and Höök have described one case with isolated metastases in the kidney which they believed were embolic. But in many other case reports, proof that thymomas can produce embolic metastases is not convincing.

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References:


This 82-year old white man was in good health until December of 1955, when in Florida, he developed symptoms of a peptic ulcer and was placed on a medical regimen. About one month later, he developed acute urinary retention and was subsequently admitted for a TUR which revealed nodular hyperplasia of the prostate and carcinoma. Gastrointestinal roentgenogram revealed deformity of the first and second portions of the duodenum consistent with ulcer. During the next 9 months, he had 3 admissions for recurrent upper abdominal pain and obstructive symptoms. These gradually became more suggestive of esophageal obstruction and for several months were relieved by passage of a bougie. In September 1956, he became rapidly dysphagic to the point where even liquids were poorly tolerated. The bougie passed with some resistance and the barium-filled esophagus showed a smooth funnel-shaped deformity just above the diaphragm. Thoracotomy revealed a thickened lower esophagus which was resected. During the operation, an ovoid mass was found in the posterior mediastinum just above the diaphragm which was easily dissected from the surrounding structures. It was 3.8 cm. long and averaged 1.5 cm. in diameter. The lobulated cut surface was smooth, yellowish-tan and finely granular. Even in the "retrospectoscope", this mass was not detected in any of the many roentgenograms.

Discussion:

This seems to me to be an incredible growth, and I can think of no good explanation for it. Originally, I thought it might be a thymoma, but the presence of anthracotic pigmentation and its partial encroachment within a cost of smooth muscle makes that diagnosis very hard to accept. I thought of lymphangioma or a lymph node but actually this does not have the architecture of a lymph node and how can you account for the surrounding smooth muscle coat? Can this growth lie within a venous aneurysmal dilatation? But if so, how could it get there? Has this growth actually developed in the wall of a large vein? It seems very difficult to believe so. I have never seen anything like this, and I don't know what to make of it. I hope Bob Totten or someone will be able to enlighten me.
UNDIAGNOSED CONDITION OF MEDIASTINAL LYMPH NODE

Microscopic Observations:

When one first looks at this section with the H&E stain, one observes toward the central part several foci of lymphoid cells and since one focus has several cells filled with anthracotic pigment, it is natural to wonder if it could be a lymph node. But very quickly it is realized that if this is a lymph node, it has an incredible number of sinuses, so many that it appears as if there were more sinuses than lymphocytes. Further, these apparent sinuses as shown by the reticulin stain have definite walls and are more suggestive of actual lymphatic vessels than of simple lymph node sinuses. But this is not the most remarkable feature of this section.

With the trichrome stain, it is very apparent that this peculiar lesion has a very considerable coat of smooth muscle which surrounds the outer part of the lesion in its capsule and sometimes dips into it. This can be seen in the H&E sections, but it might be easily overlooked because one would not be looking for smooth muscle about a nodule in this situation. I studied the muscle cells with oil immersion to make sure there are no cross striations, and I could find none. If this smooth muscle belongs to the aorta, a considerable amount of the vessel wall must have been dissected away. But this looks to me much more like the smooth muscle belonging to a large vein rather than the aorta.

Discussion:

This seems to me to be an incredible growth, and I can think of no good explanation for it. Originally, I thought it might be a thymoma, but the presence of anthracotic pigment and its partial enclosure within a coat of smooth muscle makes that diagnosis very hard to accept. I thought of lymphangioma of a lymph node but actually this does not have the architecture of a lymph node and how can you account for the surrounding smooth muscle coat? Can this growth lie within a venous aneurysmal dilatation? But if so, how could it get there? Has this growth actually developed in the wall of a large vein? It seems very difficult to believe so. I have never seen anything like this, and I don't know what to make of it. I hope Bob Totten or someone will be able to enlighten me.

Arthur Purdy Stout, M.D.
A 59-year old white male was admitted 3/19/60 for evaluation of a coin lesion in the upper lobe of the left lung. This was found on a routine physical examination at New York Memorial Hospital 2 months prior to admission. There had been no symptoms, and physical and laboratory examination were entirely normal. A planigram of the left chest showed a solid density, thought to be in the left upper lobe and peripheral. It was well rounded and about 2 cm. in diameter. A bronchoscopy showed no abnormal findings. On the fifth hospital day, a left thoracotomy was performed. No lung lesion was found. Instead there was a mass on the posterior chest wall between the 4th and 5th ribs. Portions of these ribs including the lesion were resected.

Pathologic findings: The specimen consisted of 2 segments of rib with intercostal muscles attached. A 2.2 x 1.8 x 1.5 cm. firm, circumscribed, rubbery tumor was present over the concave surface of one rib at about its middle third. The tumor was covered by intact parietal pleura, and was tightly adherent to the underlying fibromuscular tissue. The cut surface showed homogeneous, bulging, greyish-tan tissue. On the external surface, a small segment of nerve trunk was identified.
Case 5. (P&S 65439)

NEUROFIBROMA (BIZARRE) OF MEDIASTINUM

Microscopic Observations:

This tumor obviously has the features of a neurofibroma in which remarkably large facsimiles of Wagner-Meissner tactile corpuscles have been formed. Almost all of the cells in this strange tumor are on a big scale, and many of them seem to have assumed extremely bizarre shapes. Instead of the straight elongated Schwann cells, many are contorted and distorted with markedly acidophile cytoplasms and with the nucleus at one end. Because of the acidophile cytoplasms, a special search was made using the trichrome stain but no cross striations or evidence of myofibrils was detected. There are some cells of giant size with a huge nucleus. In other areas, the cells are much smaller, often stellate and set in a slightly myxoid stroma. At its periphery, there is a slender layer of adipose tissue into which the tumor sends short finger-like prolongations. After considerable search, only one mitosis has been encountered.

Discussion:

Because this is such a bizarre neurofibroma, I thought we should include it in this Seminar. It is certainly unlike any I have ever seen before. Only occasionally can one find the ordinary appearance of neurofibroma. Even the facsimiles of the Wagner-Meissner tactile corpuscles are on a grandiose scale. What has happened to the rest of the tissue I do not understand. I am familiar with the fact that various differentiated tissues of a mesenchymal type can appear in neurofibromas including bone, cartilage, fat, striated muscle, etc., and it is customary to blame the mesectoderm for this but none of the tissues in this tumor are recognizably differentiated. I simply do not know what to make of them. I wondered if any of them could be interpreted as neuroepithelial and be evidence of malignancy. But when neuroepithelial elements appear in a neurofibroma, they consist of small rounded cells which have few connective tissues associated with them whereas in this tumor the cells all seem surrounded by reticulin. I presume, therefore, this must be a benign neurofibroma of a type I have not before encountered.

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Female, age 2-1/2 months, who in January 1951, was found to have a huge mediastinal tumor, with marked displacement and compression of the trachea to the left. The mass was located in the posterior mediastinum and the sulcus. Breathing was becoming increasingly more difficult, and the child had to be held in her mother's arms for a considerable part of each twenty-four hours.

She was carried to the operating room and after intubation, a right anterior thoracotomy incision was made carrying it well round to the axilla, lifting the breast upward. The mass was dissected free from all its moorings and as nearly as one could visualize, it was completely removed. Prophylactic radiation to the area was also given. The patient had an uneventful recovery.
Case 6. (P&S 67439)

PARTLY UNDIFFERENTIATED GANGLIONEUROMA (GANGLIONEUROBLASTOMA) OF THE MEDIASTINUM

Microscopic Observations:

Sections of this tumor show a tumor that is composed of many isolated tumor cells that vary from small rounded cells about the size of reticulum cells with but little cytoplasm to much larger ones with single, double, or triple nuclei eccentrically placed with a homogeneous faintly acidophile cytoplasm. These cells show no mitoses and are set in a very fine meshwork of twisting fibrils. This is stained pink with eosin and fuchsin and is not blackened by the Laidlaw stain. None of the cells shows a big nucleolus and there are no satellite cells. The cells and the meshwork in which they are found are gathered into small masses separated one from the other by fibrovascular septa.

Discussion:

This is a tumor composed of a mixture of undifferentiated and partly differentiated sympathicoblasts set in a stroma of glial fibers. I became acquainted with tumors of this sort quite early and as far as I am aware published the first description of such a case in the United States in 1918, although it had been known abroad ever since Loretz reported such a case in 1870. In those early days, it took a long time for information concerning unusual cases to be recognized in this country largely I suppose because pathology was so far behind Europe in development in the last century and early part of the present century. This posterior mediastinal tumor developed in the posterior mediastinum, grew to a large size, extended through an intervertebral foramen, compressed the cord, and the child died following an operation attempting to remove the extradural extension. Later in 1924, this case was republished together with one that developed in the cervical sympathetic chain of a 2-1/2 year old girl. This was successfully excised. The child had a Horner's syndrome following operation. This gradually cleared up and 6 years after operation, there was no evidence of recurrence. In a later paper, I made a much more extended study of cases of this partly differentiated group of ganglioneuromas and found that of 33 cases, 6 (18.2%) were known to have metastasized. It is, therefore, not a completely benign growth like the differentiated ganglioneuromas nor nearly as malignant as the pure sympathicoblastoma or the tumors that have some fully differentiated areas and also completely undifferentiated sympathicoblastomas. Sixty-five percent of such compound tumors will metastasize. Ackerman and Taylor like to call tumors made up of partially differentiated sympathicoblasts "ganglioneuroblastomas." That seems to me to be a reasonable term, and I have no objections to it. They found that among 7 such tumors in the posterior mediastinum, only 3 were living and well and 4 had died. But only 2 of the 4 that died were known to have metastases.
When studying neurogenous tumors from a biopsy alone, it is well to remember that the biopsy may not tell the whole story because other parts of the tumor may show that the tumor has other areas showing a different degree of differentiation.

Arthur Purdy Stout, M. D.

References:


2.) Loretz, W., "Ein Fall von gangliosem Neurom (Gangliom)", VIRCH. ARCH. f. PATH. ANAT., 49:435, 1870.


An 18-year old white girl was first seen in early February of 1957 because of chest pain and some difficulty with breathing. A routine chest film revealed a marked widening of the superior mediastinum due to a soft tissue mass which extended to the left and inferiorly to the level of T-10. The esophagus and trachea were deviated to the right and somewhat anteriorly and the lower portion of the trachea was narrowed due to extrinsic pressure. The lungs were clear. A small left pleural effusion was noted. The entire physical examination with the exception of the chest was normal. The white count was 13,800 and 8,050 with a normal differential, hemoglobin was 12.1 gms.%, red blood cells 4.2 million per cm., NPN 29 and fasting blood sugar 108. Thoracic exploration revealed 500 cc. of serosanguinous fluid in the left pleural cavity with numerous small fleshy, tan-colored, soft pleural nodules over the visceral and parietal pleura. The mediastinum was distorted by a large lobulated tumor which extended from the apex of the thorax to the diaphragmatic orifice of the aorta. The tumor was intimately associated with the aorta and was believed to extend into the abdomen. It was the surgeon's impression that the anterior mediastinum was not involved by tumor.

The tissue removed was moderately firm, grey-red and coarsely lobulated, representing a small portion of the tumor.

Following exploration, the patient received 3600 r via 4 ports to the chest using the Cobalt machine. In addition, 75 millicuries of radioactive gold were instilled into the left pleural cavity. She continued to have considerable chest pain with accumulation of pleural fluid and increasing dyspnea. Bronchoscopic examination revealed extrinsic pressure on the trachea with marked narrowing. She expired 2 months after exploration and 3 months after the discovery of the mediastinal mass.

Permission for autopsy could not be obtained.
UNDIAGNOSED TUMOR OF MEDIASTINUM (MALIGNANT GRANULAR CELL MYOBLASTOMA (?))

Microscopic Observations:

This appears to be a tumor made up of rounded cells. They are relatively uniform in size although an occasional one is somewhat larger, and there is often a distinct cell membrane. The nucleus is centrally placed and mitoses average 7 in 50 high power fields. The cytoplasm seems to be granular as shown by the trichrome stain and the fine granules are slightly pink. It is difficult to see any granules in other stains. The cells lie in an inconspicuous fibrovascular meshwork. They are collected into groups without any reticulin fibers among them. Mucicarmine stain is negative.

Discussion:

We are faced with a very difficult problem in this case, because we cannot be certain whether the tumor is primary or metastatic. From the description, it appears probable that it did not involve the anterior mediastinum which seems to permit us to exclude an origin from a teratoma or the thymus. If it comes from the posterior mediastinum, we must consider a possible origin in neurogenous or lymphoid tissue. It does not look to me like any variety of malignant neurogenous tumor including neuroepithelioma and sympathicoblastoma nor does it remind me of any variety of malignant lymphoma. This narrows the field considerably and the only three tumor types that come to my mind are embryonal round cell rhabdomyosarcoma, organoid granular cell myoblastoma, and dysgerminoma.

There was a tumor somewhat resembling this reported in the Penrose Seminar of 1959. But that tumor was in the lung and at autopsy the 27 year old woman had a large pelvic mass. This was interpreted as an ovarian dysgerminoma that had metastasized to the lung and pleura. The other tumors that have occurred to me are embryonal rhabdomyosarcoma and organoid granular cell myoblastoma. The H&E section did not remind me at all of an organoid granular cell myoblastoma because it does not look organoid. But the trichrome stain does bring out a vaguely organoid pattern, and it does not show that the cells are granular. If one rejects this diagnosis, however, one is left with embryonal rhabdomyosarcoma, and that does not make me any happier than the myoblastoma suggestion. I can only say it might be either of the last two but at the moment I favor malignant granular cell myoblastoma.

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Reference:

A 75-year-old man entered the hospital with a picture suggesting a cerebrovascular accident. He became comatose, and died a few days after admission.

Autopsy revealed that the retroperitoneal area was occupied diffusely by dense greyish-white tissue surrounding kidneys and adrenals, without evidence of ureteral or aortic compression. In addition, similar tissue was found in the auriculo-ventricular groove, almost completely encircling the heart and forming a nodular mass over the right atrium and apparently extending into it.
Case 8. (P&S 66918)

FIBROMATOSIS OF RETROPERITONEUM AND MEDIASTINUM

Microscopic Observations:

This is an example of a disease process that seems to have attracted a good deal of attention recently. It consists of a proliferation of dense fibroblastic tissue in the retroperitoneum with relatively few vessels and varying numbers of inflammatory cells, that has encased the kidneys and adrenals without evidence of aortic or ureteral compression and a similar proliferation in the mediastinum surrounding the heart. The fibrous tissue is of the most ordinary appearance. The two areas apparently were not in continuity.

Discussion:

Although this case bears some resemblance to the 64 cases of idiopathic retroperitoneal fibrosis that have been reported, there is at least one variation that seems to make it unique. In none of the previously reported cases has there been any separate involvement of the tissues above the diaphragm. In one case reported recently by Dineen et al, the diaphragm was traversed and the heart invaded. But in this case, there was continuity between the two areas of involvement. In the other cases, the fibrosis started at the promontory of the sacrum, extended upward to encase both ureters and both kidneys but scarcely ever extended above the upper pole of the kidney. Further, the fibrosis was frequently but not always associated with inflammatory cells, fat and sometimes areas of abscess formation so that the suggestion was strong that it was some kind of inflammatory process. In this case, there is some evidence of inflammation. In a majority of the other cases, the new-formed fibrous tissue has squeezed the tubular structures producing varying degrees of obstruction. In this case, there does not appear to have been any squeezing effect. Efforts to find an etiological factor for the fibrosis have had some success. Salyer et al found histoplasmosis associated with the four retroperitoneal cases they reported, and Popham et al stated that their case was associated with a coagulation defect which was a Factor VII Deficiency. It has also been likened to sclerosing lipogranuloma and to Weber-Christian's disease (Dineen et al).

It is a remarkable fact that most of those who have reported retroperitoneal idiopathic fibrosis are seemingly unaware that a similar process can occur in the mediastinum without any involvement below the diaphragm. The papers of Salyer et al and Barrett indicate this very clearly. These authors are well aware of the process that occurs in the retroperitoneum and believe that the fibrosis is secondary to some kind of infection such as tuberculosis, syphilitic, histoplasmosis, etc. This seems to me to be a tenable hypothesis for many mediastinal cases also because the usual case of mediastinal fibrosis results in contraction of the scar-like tissue with pressure on the great vessels or other mediastinal structures producing symptoms of obstruction.
I would guess, therefore, that a majority of the cases both in the mediastinum and the retroperitoneum are diffuse scar-like formations of fibrous tissue and can properly be classified as fibroses. This case and perhaps one or two of the others that caused no pressure symptoms are more like the fibromatoses that occur singly or in multiple form in children and adults.

Arthur Purdy Stout, M. D.

References:


This 17 year old white male was followed at Presbyterian Hospital since November 1955 for mediastinal widening, dyspnea, questionable pulmonary fibrosis and recurrent pulmonary infections. A history of bronchospastic episodes and allergy dates back to the age of three months. Terminally, he developed hypofibrinogenemia and bilateral bloody effusions.

At autopsy, a diffuse tumor-like infiltration was present involving the structures in the anterior, middle and posterior mediastinum. This process involved the pericardium, the hilum of both lungs, surrounded the thoracic aorta, trachea, esophagus and extended beneath the pleural reflection over the thoracic vertebrae. This process was also present within the lungs and diaphragm and extended into the abdomen enclosing the aorta to the origin of the renal arteries. A small area of involvement was also found in a lumbar vertebra.

[Handwritten notes]
Microscopic Observations:

The sections made at autopsy show that the tissue composing the infiltrating mass is composed of many blood vessels of capillary or venous type, probably some lymphatics, occasional unattached smooth muscle and plenty of adipose tissue. A striking feature of the fat is the presence of many normal marrow cells both isolated and in groups. There are also occasional groups of lymphocytes. The fibrous tissue that binds all of these different tissues together is very variable in amount but shows no unusual features. Occasionally, one can find isolated areas that suggest the appearance of vascular mesenchyme preceding the formation of differentiated blood vessels. Wherever this tissue grows, it engulfs all the normal structures it encounters but without distorting or invading them with the exception of the diaphragm which is penetrated by all of the elements but most prominently by the vessels and one lumbar vertebra.

Discussion:

This tumor is unique so far as my experience and reading go. It has the usual make-up of a benign mesenchymoma with the addition of a marked content of extramedullary marrow formation and it is diffuse, spreading widely in the mediastinum, extending through the diaphragm into the retroperitoneum to engulf the aorta to the region of the renal arteries, the kidney and suprarenal gland and invading a vertebra, the pleura and superficially the lung. We have only two cases of benign mesothelioma of the mediastinum in our files: one was in a 7-year old girl. It was 8 cm. in diameter and involved the pericardium, thymus and superior vena cava but caused no symptoms. The other was in the upper part of the mediastinum of a 48-year old man. It measured 10 x 7 x 4 cm. and was firmly attached to the pleura. A localized case somewhat comparable to this has been reported by Renzetti et al. We have also had 5 malignant mesotheliomas of the mediastinum. Extramedullary hematopoiesis in the form of myelolipomas have been described in the mediastinum. Litwer described two cases, both of which were associated with congenital hemolytic anemia. Knoblich reported a case with multiple myelolipomas in the mediastinum and pleura of a 63-year old man born in Greece who had Thalassemia Minor. All of these were solitary masses. Litwer refers to two cases in the literature with mediastinal myelolipomas without any type of bone marrow disease. Apparently this case is without any associated diseases.
In other cases of benign mesenchymoma in our files, all have had the combination of fat, blood vessels and smooth muscle in their composition. Elements that are much less commonly found are bone, cartilage and in one instance striated muscle fibers. This was in a unique benign mesenchymoma of the ovary. The majority of benign mesenchymomas have been found in the soft tissues of the body. But we have also found them in the kidney, liver and small intestine, uterus, ovary, prostate, testis, female breast, labium majus, scrotum, larynx and bones. While ordinarily the tumors are solitary and localized, there have been a few examples of multiple tumors, but no other examples of diffuse benign spreading mesenchymoma beside this one.

Arthur Purdy Stout, M.D.

References:


This is the case of a 37-year old white adult male who was admitted to Fitzsimons Army Hospital on 8 October 1952, with severe pain in the left anterior chest. The patient was perfectly well until 18 September 1952, when he experienced a sudden aching pain in the left anterior chest. The onset was sudden and disappeared within 24 hours. On 22 September, the pain reappeared and was markedly aggravated by breathing. The pain persisted intermittently until the patient reported into Fort Monmouth, New Jersey Hospital. The patient was treated symptomatically and investigated for various diseases. The patient was finally transferred to Fitzsimons Army Hospital on 7 October 1952, with a diagnosis of suspected neoplasm of the lung. After admission, a left thoracentesis was performed on 10 October 1952, and only 2 cc of grossly bloody fluid were obtained. It was felt that a massive effusion on the left was loculated. An enlarged supraclavicular lymph node was removed in October 1952, on 15th of the month. This was negative for any evidence of malignancy. An exploratory thoracotomy was performed on 7 November 1952. At operation, the left pleural cavity was obliterated and the entire left chest filled with necrotic tumor tissue and old clotted blood. It was felt at time of surgery that the tumor mass arose from the pleura. A pneumonectomy was impossible because of extensive adhesions. Due to the constant oozing of blood, the patient was packed with several yards of iodoform gauze. Post-operatively, the patient did surprisingly well. On 25 November 1952, the iodoform gauze packs were completely removed and there was a minimal amount of subsequent drainage. The pain in the patient's right lower chest and left chest persisted. X-ray revealed a slight infiltration in the right base. It was felt that this represented minimal atelectasis or malignant change in the right base. The patient was presented to the Tumor Board on 28 November 1952, and it was recommended that palliative x-ray therapy be given to the left chest. X-ray therapy was begun on 1 December and continued daily until the time of death. During early morning of 18 December 1952, the patient developed sudden pain in the right chest and respiratory distress. He was given oxygen but suddenly expired. It was felt that he probably had a massive hemorrhage into the right chest, causing sudden death. The clinical diagnosis was malignant tumor of the left parietal pleura with extension into the right lung and massive hemothorax.

Postmortem examination performed on 18 December 1952, 3 hours after the patient's death, revealed a "left chronic fibrous pleuritis" and a tumor of the pleura with massive involvement of the left lung. There was also metastases to the right middle lobe with massive right hemothorax. There was bilateral atelectasis. Tumor metastases were also found in the left hilar nodes. There was congestion of the mediastinal and abdominal lymph nodes. A small agonal ulcer was found on the anterior wall of the
duodenum. The liver showed moderate congestion and cholangiolitis, and there was a cholecystitis with cholelithiasis. Scattered petechiae were found in the region of the right dentate nucleus and internal capsule. A small area of hemorrhage was found in the right frontal lobe.

Discussion:

The diagnosis in this case seems to be relatively simple but there are a few features that deserve discussion. In the first place, the question of whether this is a mesothelioma or a malignant hematogenotum has been raised. If there had been any evidence of mesoplastic secretion, there would have been no doubt but as far as I can see, there is no evidence of this. On the other hand, if red blood cells in the lumen had been found, one would have to consider seriously the possibility of malignant hematogenotum, but I did not find any red blood cells in the lumen. Lymphangioadenosarcoma might be suggested, but this seems to be a variety of malignant tumor almost exclusively limited to lymphadenotum areas. We have to be influenced, therefore, by the fact that this is a tumor that very definitely has primarily involved the pleura which is overwhelmingly in favor of mesothelioma.

The second question concerns whether the fibroblastic elements in this tumor is to be considered simply a supportive framework for the mesothelial tubules or an integral part of the tumor for it is found in all sections showing the tumor. This is a difficult decision but in my opinion, since the fibroblastic elements have no features suggesting neoplastic change, I do not think they are an integral tumor element but suggest only a desmoplastic induced by the proliferation of the mesothelial tubules. A comparison of the histology of this tumor with the malignant mixed mesotheliomas of the pleura reported by Cassella and Spear will show that the spindle-shaped tumor cells filling the spaces between the mesothelial tubules is a tumor with a definite desmoplastic-like appearance. Despite this appearance, they were able to prove they were really mesothelial cells. I believe, therefore, that this present case is simply a malignant diffuse nodular mesothelioma of the pleura with metastasis to the hilar lymph nodes and to the opposite lung.

Arthur Purdy Stout, M.D.
Case 10. (P&S 67215)

MALIGNANT DIFFUSE TUBULAR MESOTHELIOMA OF THE PLEURA.

Microscopic Observations:

Both the primary tumor involving the pleura and the metastasis in the right lung show a comparable picture although the histology of the tumor is much more easily recognized in some slides than in others. The basic formation consists of many tubes lined by prominent cells which sometimes completely fill the lumen. They turn and twist in a haphazard fashion. The lumens contain no red blood cells and apparently no recognizable secretion. The mucicarmine stain is negative so far as the tube lumens and their lining cells are concerned. The lining cells are obviously anaplastic and show mitoses. These tubes are set in a fibrous stroma which is found everywhere the neoplastic tubes are found. It appears to be ordinary fibroblastic tissue and does not have a neoplastic aspect.

Discussion:

The diagnosis in this case seems to be relatively simple but there are a few features that deserve discussion. In the first place, the question of whether this is a mesothelioma or a malignant hemangioendothelioma has been raised. If there had been any evidence of mucopolysaccharide secretion, there would have been no doubt but as far as I can see, there is no evidence of this. On the other hand, if red blood cells in any numbers had been found, one would have to consider seriously the possibility of malignant hemangioendothelioma, but I did not find any red blood cells in the lumens. Lymphangioendothelioma might be suggested, but this seems to be a variety of malignant tumor almost exclusively limited to lymphedematous areas. We have to be influenced, therefore, by the fact that this is a tumor that very definitely has primarily involved the pleura which is overwhelmingly in favor of mesothelioma.

The second question concerns whether the fibroblastic element in this tumor is to be considered simply a supportive framework for the mesothelial tubes or an integral part of the tumor for it is found in all sections showing the tumor. This is a difficult decision but in my opinion, since the fibroblastic elements have no features suggesting neoplastic change, I do not think they are an integral tumor element but suggest only a desmoplasia induced by the proliferation of the mesothelial tubes. A comparison of the histology of this tumor with the malignant mixed mesothelioma of the pleura reported by Ozzello and Speer will show that the spindle-shaped tumor cells filling in the spaces between the neoplastic tubes in their tumor have a definite sarcoma-like appearance. Inspite of this appearance, they were able to prove they were really mesothelial cells. I believe, therefore, that this present case is a malignant diffuse tubular mesothelioma of the pleura with metastasis to the hilar lymph nodes and to the opposite lung.

Arthur Purdy Stout, M. D.
Reference:

A 49-year old white male first seen in 1957 with complaints of waning potency and tender breast enlargements. This was soon followed by cough and hemoptysis. There was gynecomastia, rounded densities in both lung fields, and a widened upper mediastinum, the latter present in a chest film taken 6 months previously and originally considered normal. The condition went on deteriorating, signs of intracranial metastases appeared, and he died on April 3, 1958.

Autopsy revealed a large, soft, hemorrhagic mass in the mediastinum, principally in the anterior portion adherent to aorta, trachea and apex of left lung. Similar nodules were found in all lobes of the lungs, pericardium, esophagus, liver, right kidney, left adrenal, mediastinal, periaortic, hepatic and peripancreatic lymph nodes, occipital and frontal cortex. Breasts were twice the normal size. Testes and epididymides were apparently normal (650 sections).
Case 11. (P&S 66075)

PRIMARY CHORIONEPITHELIOMA OF THE MEDIASTINUM WITH WIDE-SPREAD METASTASES.

Microscopic Observations:

The diagnosis in this case needs no discussion because this is an obvious chorionepithelioma (choriocarcinoma if you prefer) composed of trophoblasts and syncytial cells. Our section comes from the lung metastasis but Jerry Fine informs me that all of the primary tumor as well as all of the metastases showed the same picture. Before death, there was a positive pregnancy test, and there is the further evidence of the demasculinizing effect.

Discussion:

Since almost serial sections of both testes have revealed no scars or any other evidence of primary tumor, it seems proper to accept this as a primary mediastinal neoplasm. If Yurick and Ottoman are to be believed, their case was the 12th recorded example of primary chorionepithelioma of the mediastinum. In most instances, there was no evidence of a preceding teratoma but occasionally the malignant growth developed in a known preceding teratoma. There have been a number of attempts to explain the development of a primary tumor of this sort in the mediastinum. The favored explanation suggests that there can be germinal rests along the urogenital anlagen. Since the plica urogenitale extends from the sixth thoracic to the second sacral element in the embryo, this might account for mediastinal chorionepitheliomas. This hypothesis is advanced to account for primary retroperitoneal chorionepitheliomas but it would seem to me that if it is also the source of mediastinal tumors, they should be found in the posterior rather than the anterior mediastinum. As a matter of fact, most authors read their predecessors' papers and give summaries of other people's theories just as I have done. I confess I have no original information about primary extragenital chorionepitheliomas. I think the evidence is good that this is a primary chorionepithelioma of the mediastinum but I have no original thoughts to explain its presence in this area.

Arthur Purdy Stout, M. D.

(See references on next page).
Case 11. P&S 66075
Continued.

References:

Kay, S., and Reed, W. G., "Chorioepithelioma of the Lung in a Female Infant Seven Months Old", AM. J. PATH. 29:555-567, 1953 (Discussion of origins.)


Lymphoma. Can't identify thymus.

2. Hyperplastic lymph node (Castleman-Iversen disease)


4. Benign Thymoma. This has been well described by Hubbell, Am. J. Path., 28:321, 1952.

5. Benign Neurogenous tumor. (It would be easy to dream up a fancy name for this.)

6. Ganglioneuroblastoma

7. Malignant Thymoma

8. Chronic Fibrosing Mediastinitis, Etiology Undetermined.


11. Choriocarcinoma probably primary in the testes, regardless of the 650 sections.