SOLID TERATOID TUMORS OF THE ANTERIOR MEDIASTINUM

REPORT OF TWO CASES

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Because of the comparative rarity of tumors of the mediastinum, and the incompleteness of the data in many of the published cases, Haagensen (1) has recently emphasized the desirability of adequately reporting additional instances. The gravity of exploratory procedures in this region makes necessary a basis upon which to arrive at a reasonable preoperative clinical evaluation of such cases. In this paper, two teratoid tumors are reported in some detail, both from the clinical and the pathological standpoint.

The term "teratoma" is commonly used to describe tumors including derivatives from all three germ layers. There is, however, a large group of tumors of presumably the same etiology but which include demonstrable multiple elements derived from but two or even a single germ layer. In many of these instances the failure to demonstrate additional elements is attributable (1) to the taking of insufficient sections for microscopic study, (2) to extensive necrosis of tissue, the actual nature of which is obviously impossible to determine, or (3) to an early overgrowth of a single germ layer. In order to include these essentially similar tumors, whether complete or incomplete, under a single heading, the term "teratoid" has been used.

Although not the most common of the mediastinal tumors, these teratoid growths are among the most interesting from the pathological standpoint, since they apparently arise from totipotential cells, and may exhibit any combination of tissues, benign or malignant.

Teratoid tumors, in general, arise most commonly in relation to the gonads, but are seen not rarely retroperitoneally, in the mediastinum, and intracranially.\(^1\) As Willis (2) has indicated, these tumors may be of a relatively mature type, or quite undifferentiated. In the first instance, the reported examples are made up largely of dermoid or dermoid-like tumors containing a wide variety of additional elements which are usually mature and often organoid. Malignancy is not frequent in this group and usually represents the degeneration of a single element, most often epithelial. The more immature forms are frequently found in the testis, but occasionally arise elsewhere. The cells are rarely differentiated into recognizable tissue and may all show evidence of malignancy, although a single malignant element usually dominates the picture.

Mediastinal teratoids almost invariably arise in the anterior mediastinum. A single report was found of a posterior location, and in this instance the

\(^{1}\) A more comprehensive review of the general question of teratomata with particular reference to mediastinal location may be found in the very recent article of Houghton (37).
origin was presumed to be pulmonary (3). Because of the inaccessibility of many of the older reports, and the inadequacy of some of those found, it has proved impossible to arrive at an accurate statistical representation of the incidence of teratoids in the mediastinum. From a correlation of the periodically appearing reviews and the available individual case reports we have estimated the numerical incidence of such tumors at about 200 (1-28). Of these, about 55 per cent appear to have been single dermoids, 25 per cent complex benign dermoids, and 20 per cent malignant tumors. This incidence of malignancy is somewhat higher than reported by other reviewers because of the inclusion of 5 cases reported as tumors of the thymus (23-28) but described as containing multiple elements. The variety of the types of malignant change reported is particularly interesting and is indicated in the following table, in which are included the two cases to be reported here.

Malignant degeneration of dermoids
- Squamous-cell or adenocarcinoma ........................................... 7 cases
- Sarcoma .................................................................................. 1 “

Primary malignant tumors
- Chorionepithelioma .................................................................. 5 “
- Sarcoma (all types) .................................................................... 9 “
- Adenocarcinoma ........................................................................ 6 “
- Sarcoma and carcinoma ........................................................... 6 “
- Cystosarcoma (?) ....................................................................... 1 “
- Lipo-rhabdomyosarcoma ............................................................ 1 “
- Undetermined 3 ........................................................................ 2 “

Total ............................................................................................ 38 “

Some interest attaches to the age and sex incidence of these tumors. The impression gained by reviewers (2, 9a) seems to be that, while malignant degeneration of the mature types occurs more commonly about the cancer age, the incidence of primary malignant teratoids is highest in the third decade. Our own data indicate that the great majority of primary malignant tumors occur in males (a relative incidence of 8:1), and in the ages between eighteen and twenty-five years. Hedblom (18) tabulated all cases found by him on the basis of age alone, irrespective of type, malignancy, etc., and found a strikingly higher incidence in the second and third decades.

The two following cases are reported as sarcoma (possibly of marrow cells) plus adenocarcinoma in the first instance, and lipo-rhabdomyosarcoma in the second.

**Case I:** Clinical History: W. R., a white male twenty-one years old at death, was first seen at Billings Hospital in 1929, at the age of fourteen, because of obesity, feminine configuration, and retardation of secondary sexual development. He had had pneumonia, frequent sore throats, severe glandular fever at the age of two, and mumps at seven. The obesity was first observed soon after a right herniotomy at seven years of age. There was no family history of neoplasm. At this time, roentgen examination of the sella turcica was

2 Houghton (37), accepting Hedblom’s figure of 191, found 25 subsequent cases, arriving at a total of 216 cases of mediastinal teratomata. Of these, however, he considered only 25 to be malignant.

3 The case reported by Houghton, while exhibiting the phenomenon of metastasis, was not considered histologically malignant.
reported negative; the basal metabolism rate was — 26 per cent. Administration of thyroid extract resulted in but little weight loss. A diagnosis of eunuchism was made.

By 1932 the patient weighed 245 pounds. An unconfirmed report states that about this period he received some form of glandular medication. From this time on his obesity gradually decreased, the weight falling to 180 pounds, and he developed normally sexually and physically.

He next came to the hospital in April 1935 as a patient on Dr. Alexander Brunschwig's service, because of attacks of pain in the right anterior chest, intermittent since July 1934, continuous for the past month, and pain in the right central portion of the abdomen for two months. He had had a dry hacking cough for several weeks, usually induced by lying on his back, and occasional elevations of temperature. In six weeks he had lost 30 pounds. There had been no hemoptysis or bleeding of any sort.

Physical examination showed a well developed young man of twenty-one, weighing about 150 pounds. An area of increased dullness was found to the right of the sternum. Tactile fremitus and breath sounds were decreased in the right axilla. The liver edge was 2 cm. below the right costal border. There was one discrete node in the left axilla. X-ray examination on April 30, 1935, showed an enormous mediastinal mass believed to be due to lymphosarcoma or Hodgkin's disease (Fig. 1). The laboratory reports were essentially negative: white cells 7300, with 73 per cent polymorphonuclears, 23 per cent lymphocytes, 1 per cent monocytes, 2 per cent eosinophils, and 1 per cent basophils; hemoglobin 88 per cent; red cells 4,880,000; urine negative; temperature normal. An unsuccessful attempt was made on May 2, 1935, to secure for biopsy the lymph node in the left axilla, but no enlarged node was found.

The patient was given 5058 r units of x-ray over anterior and posterior thoracic portals, and subsequent roentgenograms, July 17, showed a moderate regression in the size of the mediastinal mass (Fig. 2). He was discharged on July 30, 1935, his condition not much changed.

The patient returned on Sept. 3, 1935, because of vomiting and upper thoracic pain and tenderness. The temperature was 101°. X-ray examination (Fig. 3) showed the mass to be almost twice as large as on July 17, and also revealed a small collection of fluid in the right costophrenic angle. The hematologist reported at that time: hemoglobin 54 per cent; red cells 3,080,000; white cells 6300, with 82 per cent polymorphonuclears, 3 per cent small lymphocytes, 8 per cent monocytes, 3 per cent eosinophils, 4 per cent metamyelocytes, 1 per
cent myelocytes, 1 per cent reticulocytes, the neutrophils and monocytes appearing very toxic. The patient began to bleed from the nose and gums. He weakened steadily, developing a temperature of 104.4°, pulse 140, and died on Sept. 12, 1935.

Post-mortem Examination: Autopsy was performed one hour and fifteen minutes after death. The important findings are summarized in the following anatomical diagnosis: Large cystic and hemorrhagic mediastinal teratoma with marked displacement of the heart and pulmonary artery; local adenocarcinomatous and generalized (marrow cell-like) sarcomatous changes, with metastases to regional and abdominal lymph nodes, spleen, liver, lung, and bone marrow; obliteratorive fibrous pericarditis; bilateral bloody hydrothorax; hyperemia, edema, and hemorrhagic bronchopneumonia of the left lung; atelectasis of the right lung; multiple subcutaneous, subpleural, subepicardial, subendocardial, and submucosal hemorrhages; dilatation of the right heart; fatty infiltration of the liver with cloudy swelling; hypoplasia of the testicles; bile duct adenoma; marked necrosis of rib bone marrow (irradiation effect?).

The skin and mucous membranes were pale, and there was slight icterus of the sclerae.

FIG. 3. CASE I: X-RAY OF CHEST TAKEN SEPT. 4, 1935, AFTER RECURRENCE OF SYMPTOMS
The mediastinal mass is even larger than in Fig. 1.

A bloody crusting was seen in the nose and mouth. Areas of brown pigmentation were evident over the anterior and posterior chest walls, and there were multiple subcutaneous hemorrhages associated with needle puncture marks. The secondary sex characteristics, including beard, axillary and pubic hair, were normal, but the testes appeared small.

The peritoneal surfaces and cavity were essentially normal. The mesenteric lymph nodes and those about the abdominal aorta were somewhat enlarged and firm.

Each pleural cavity contained about 200 c.c. of bloody fluid and there were fibrous adhesions over each lung apex. The right cavity was greatly encroached upon by a large mass bulging in from the upper mediastinum, and the lung, adherent medially to the mass, was markedly compressed. The left cavity was also slightly encroached upon by the mass, and the left lung, more completely expanded, was adherent medially. The visceral pleurae of both lungs contained many small subpleural hemorrhages.

The pericardial cavity was obliterated by dense but somewhat edematous fibrous adhesions.

The thyroid was small and not nodular. No recognizable thymus was seen. At the site of the thymus was a large circumscribed, lobulated tumor measuring 14 cm. vertically, 10 cm. transversely, and about 6 cm. anteroposteriorly. The mass was situated in the anterior superior mediastinum, bulging considerably into the right pleural cavity, densely adherent to the overlying sternum, bulging slightly into the left pleural cavity, and riding di-
rectly over the heart, which was displaced somewhat downward and to the left. Because of its presence the pulmonary artery was deviated widely to the left, and the right branch coursed through the peripheral portions of the tumor. Posteriorly the trachea, large bronchi, and esophagus were only slightly, if at all, deviated from their normal positions. The mass was entirely free from the vertebral column. When sectioned, it was seen to consist of large cystic spaces filled with necrotic tissue and clotted blood, and separated by dense fibrous trabeculae in which ran peculiar cartilage-like cords of tissue ranging from 0.2 to 0.5 cm. in diameter (Fig. 4). The peripheral mediastinal and tumor tissues had been stretched by the expanding tumor to form what appeared to be a pseudo-encapsulation. No evidence of gross extension of tumor tissue into surrounding structures was seen. Adjacent vessels, though displaced, were not appreciably narrowed, nor grossly infiltrated. At the bifurcation of the trachea an enlarged gray-white node was quite adherent to the mass.

The heart was not enlarged and was anatomically normal. The myocardium, however, was flabby and pale, and there were frequent subepicardial and subendocardial hemorrhages. The vascular system throughout was in good condition.

![Fig. 4. Case I: Frontal Section through Anterior Mediastinal Tumor, Showing the Massive Hemorrhagic and Necrotic Portions, the Pseudo-encapsulation, and the Peculiar Cartilage-like Trabeculation, as Well as the Relationship of the Heart and Lungs](image)

The right lung was largely compressed and rubbery. The left showed an extensive hemorrhagic bronchopneumonia posteriorly. The lymph nodes at the tracheal bifurcation, except for the one large node already mentioned, were discrete, slightly enlarged, and firm.

The liver weighed 2150 grams. The cut surfaces bulged and were greasy yellow. The spleen weighed 460 grams. The pulp could not be scraped from the cut surface and the follicles were prominent. The pancreas was normal. The peripancreatic nodes were somewhat enlarged, firm, and white. The gastro-intestinal tract, except for a few small submucosal hemorrhages in the colon, was normal. Peyer's patches were not prominent.

The adrenals were normal. The right kidney weighed 160 grams, was somewhat cyanotic, but presented a normal cortex, pelvis, and ureter. The left weighed 220 grams, and was somewhat paler. The cut edges bulged slightly, but the organ was otherwise not remarkable. The urinary bladder, prostate, and seminal vesicles were normal. The testes were small and white and the tubules could not be teased. No gross nodules were seen.

The bone marrow was pale. The skeletal system was otherwise normal. The brain and spinal cord were not examined.

**Histology:** The bulk of the tumor was necrotic with evidences of old and recent hemorrhage, scar formation, and partial calcification of the larger necrotic areas. Where not
necrotic, the tumor presented varied structures. There were numerous small and large tubules with a lining of vacuolated tall to low columnar epithelium, and frequent cystic spaces lined by flat epithelium. In other portions were structures resembling erectile tissue, being of angiomatous nature. Both the tubular and angiomatous tissue are illustrated in Fig. 5. Occasional islands of large clear cells resembled stratified squamous epithelium, and in a few instances were associated with actual keratinization. In other places irregular tubules suggested adenocarcinoma (Fig. 6). Some tubules contained mucin. No definitely neural elements were seen. There were many large blood-filled spaces, often lined by extremely hyperchromatic immature cells which constituted the metastasizing elements, and will be described later. No bone or cartilage was seen. Intermingling with these more differentiated elements, and infiltrating the stroma widely, were extremely undifferentiated and malignant appearing pleomorphic cells. These cells were the sole metastasizing element and were more clearly definable when seen as such. While these cells in the tumor con-

![Image](image.png)

**Fig. 5. Case I: Microscopic Appearance of Tumor, Showing both Epithelial and Angiomatous Structures. X 45**

...tained many odd mitoses, pyknosis and karyorrhexis were prominent, presumably from the effects of the radiation. Where least degenerated many of these tumor cells recalled in appearance the megakaryocytes of bone marrow.

Sections taken from mesenteric, peripancreatic, peri-aortic, and peritracheal lymph nodes showed an interesting progression of tumor invasion. The peripheral sinuses of the mesenteric nodes were the site of invasion by very hyperchromatic, frequently multinucleated cells with acidophilic cytoplasm similar in appearance to the megakaryocyte-like cells seen in the main tumor (Fig. 7). Where not multinucleate, these cells were round or spindle-shaped, and occasionally were seen in dense clusters. In some instances, cells belonging to this group were found to contain engulfed red cells and other débris. Accompanying these cells were frequent eosinophilic myelocytes, and other cells suggesting normoblasts, nucleated reds, and other elements of bone marrow. A peripancreatic node showed more extensive invasion, but still retained its architecture. In a pair of peri-aortic abdominal nodes the tumor had so dilated the sinuses, which were still distinguishable, that the lymphoid tissue was almost entirely crowded out. Nearby lymphatics could be found containing similar hyperchromatic large cells. A large peritracheal node related to the main tumor mass pre-
FIG. 6. CASE I: PORTION OF MEDIASTINAL TUMOR SHOWING IRREGULAR TUBULES SUGGESTING ADENOCARCINOMA
Some of the tubules contain mucin. × 90.

FIG. 7. CASE I: MESENTERIC LYMPH NODE SHOWING BEGINNING INVASION OF PERIPHERAL SINUSES BY PLEOMORPHIC, OFTEN MEGAKARYOCYTE-LIKE CELLS. × 90
presented a more advanced picture. the architecture being entirely obliterated, although the outline was preserved. In this node, in addition to the cells seen elsewhere, rather large mononuclear cells with vesicular nuclei and pale cytoplasm were prominent, resembling the stem cell of Maximow. More abundant also were cells apparently belonging to the myelo- and erythropoietic system. Common to the tumor cells seen in all the nodes were the extreme pleomorphism and the frequent bizarre mitoses.

In the liver there was a diffuse accumulation of cells in the sinusoids, the most prominent cell type being the large hyperchromatic cell already described. These occurred singly or in pairs, and in a few instances in tiny foci of proliferation about portal triads, along with eosinophilic myelocytes. The spleen and lung exhibited a similar picture of blood-

FIG. 8. CASE 1: VERTEBRAL BONE MARROW

The normal marrow elements are largely replaced by a diffuse growth of large cells suggesting particularly somewhat atypical megakaryocytes. X 215.

borne cells trapped in the finer circulation, with very occasional small foci of tumor proliferation. The splenic enlargement appeared to be due chiefly to hyperplasia of the lymphoid follicles, and to unusual engorgement with blood.

The most extensive metastatic growth was seen in the bone marrow. A section of squeezed rib marrow was almost entirely necrotic, the few living cells being almost all similar to those seen in the tumor. Marrow from a lumbar vertebra contained the normal elements, but these were largely crowded by a diffuse proliferation of giant cells similar to those seen elsewhere, and suggesting again, more than anything else, somewhat atypical megakaryocytes (Fig. 8).

Microscopic examination of other tissues showed little of interest. Sections of both testes were examined and showed only an absence of spermatogenesis. No hyperplasia of interstitial cells was evident. The prostate was normal for the age.

Various portions of the tumor and the involved organs were subjected to special staining procedures. Silver impregnation indicated an independence of tumor cells and reticulum, no increased amount of which was noted in the nodes stained. Mallory's connective-tissue stain revealed no tendency to fibrous tissue production. Phosphotungstic acid and hematoxylin served to bring out a few immature smooth muscle elements in the main tumor. Maximow's hematoxylin-eosin-azure stain emphasized the number of myeloid and erythroid
elements associated with the large tumor cells in the various tissues. Mucicarmine stains of the tumor mass demonstrated the true mucous nature of most of the differentiated epithelium.

Case II: Clinical History: W. K., a white male forty-eight years old at death, was never hospitalized, and the history is pieced together from several sources. He was apparently well until late in 1933. That autumn he developed a dry, non-productive hacking cough which persisted. Physical examination revealed nothing. In February 1934 he consulted a doctor in his home town because of the persistent cough and some loss of weight. He was told he had cancer. He came to Chicago as a patient of Dr. C. F. Weir, who on physical examination found almost the entire right anterior chest dull, and the heart

markedly displaced to the left. X-ray examination revealed the esophagus and mediastinal structures displaced also to the left. The heart was found to be approximately normal in size. Occupying the proximal three-fourths of the right lung field was a dense mass with a sharply circumscribed lower border suggestive of a large cyst, although malignancy could not be ruled out. Bronchoscopy revealed paralysis of the right vocal cord and compression of the right main bronchus. Further x-ray examination showed the tumor to have gradually increased in size. Because of its location and contour, it was diagnosed as a dermoid cyst, although no calcification was evident.

In December 1934 the patient returned home. He felt well and gained weight. He worked for five months. In May 1935 he returned to Chicago complaining of dyspnea and showing some cyanosis. His activity became more and more restricted. About June 1 he

Dr. N. C. Gilbert, consultant.
began to have edema of the feet. About July 1 he was forced to remain in bed. Edema of the feet and ankles increased. There was no evidence of ascites. Cyanosis and dyspnea became marked, with increasing evidence of heart failure. Death occurred Aug. 1, 1935.

Post-mortem Examination: Autopsy was performed five hours after death. The following anatomical diagnosis was made: Massive solid tumor (liporhabdomyosarcoma) of the anterior mediastinum with metastases to the right cervical lymph nodes; complete pressure atelectasis of the right lung; partial atelectasis of the left lung; marked posterior dis-

FIG. 10. CASE II: FRONTAL SECTION OF TUMOR

A portion of the left lung is seen above the mass. In the lower right quadrant of the tumor lies the fleshy nodule of rhabdomyosarcoma, partially necrotic. All other nodules of the tumor are fatty despite the varied appearance. Some are largely adult fat, others fetal and malignant in type. The tissue between the nodules is edematous. It does not take the mucin stains.

placement of the heart with partial compression of the great vessels; dependent edema; peripheral cyanosis; passive congestion of the abdominal viscera.

Gross Description: Externally only cyanosis, fulness of the right side of the neck, edema, and a definitely barrel-shaped chest were noted. No emaciation was evident. The abdominal viscera were severely congested. The entire liver lay below the costal margin. The diaphragm was convex downward on the right, and extended 3 cm. below the costal margin. On the left it was at the level of the 7th intercostal space.

On removing the breast plate a huge mass bulged out of the chest markedly, as if under great pressure. This mass was more on the right than on the left, but filled the anterior portion of the chest, displacing the thoracic organs posteriorly. The tumor was not adherent to the parietal pleura but the left lung was extensively adherent to the lateral
chest wall by old fibrous adhesions. The heart was pushed posteriorly and to the left so that its right border lay in line with the left sternoclavicular joint. The left border was within 3 cm. of the left lateral chest wall. The lungs lay entirely posterior to the tumor. The left contained a little air, but the right consisted of a small atelectatic roll along the vertebral column (Fig. 9). The major vessels of the heart extended through the tumor mass and were compressed by it. The aorta showed the least compression. A cross-section of the vena cava can be seen near the center of the tumor in Fig. 10.

![Image](image_url)

**Fig. 11. Case II: Microscopic Picture of Typical Fatty Nodule**

In the right half of the field is seen the irregular spread of liposarcoma with occasional giant cells. $\times 90$.

The tumor was lemon yellow and externally uniform in appearance. The tissue was much like adipose tissue but considerably more solid than normal fat. Some lobules were firmer than others. There was a completely enclosing capsule about the mass, but superior to the main tumor were about a dozen nodules of similarly appearing tumor extending up into the right side of the neck. Each of these masses was smoothly encapsulated. The thyroid appeared normal, and bore no relation to the tumor. No gross thymic tissue could be seen. The main tumor mass measured in its fresh state $32 \times 27 \times 15$ cm. Together with the heart, which was of average size, and the compressed lungs it weighed 10 kg.

On cutting through the tumor, it was found to consist of numerous encapsulated nodules of various size and differing considerably in consistency. Some were rather soft but most of them were surprisingly firm, since they looked like adipose tissue. Except for one large nodule, all of them were lemon yellow. The intervening tissue was pale and edematous. Grossly it appeared to be myxomatous. The one nodule differing from the rest measured about 12 cm. in diameter, was encapsulated, and had the fleshy appearance of muscle. Large portions of it were soft and necrotic.

**Histology:** Numerous sections of the various fatty nodules exhibited a very similar picture. Fig. 11 is representative. Large areas consisted of adult adipose tissue, but scattered diffusely through the fat were areas as shown in the right half of the illustrated field. This tissue was malignant in cellular characteristics with frequent mitoses, and was made up of lipoblasts. Giant cells were relatively frequent. Some of the softer nodules had much
adult fat and little malignant tissue while the firmer ones showed the liposarcoma predominating.

Sections from the nodules in the neck showed this same type of fatty tumor invading the cervical lymph nodes. No other metastases were found.

The tissue between the gross nodules proved not to be true myxomatous tissue, but merely edematous fat and fibrous stroma.

The large fleshy nodule in the non-necrotic portions presented the appearance seen in Fig. 12. The tissue was a densely packed, wildly growing sarcoma with a suggestion of

![Fig. 12: Case II: Histological Appearance of the Fleshy Nodule](image)

Note the whorled bundle arrangement, the irregular large muscle cells, and the frequent mitotic figures. $\times 135$.

whorled bundle arrangement. The cells were extremely variable. Many multinucleated and some giant cells were found. The larger cells scattered through the tissue were frequently strung out in spindle shapes. In many, cross-striations could be made out, even with ordinary hematoxylin-eosin staining. Phosphotungstic acid and hematoxylin stain brought them out more clearly. One such cell, seen near the center of the field in Fig. 12, is shown under high magnification in Fig. 13. All the cells were of this immature appearance. No group of actual muscle fibers was found. The necrosed areas did not suggest the presence of any other type of tissue.

Sections taken from the anterior superior portion of the tumor showed remnants of thymic tissue with definite Hassall's corpuscles. No such picture was found elsewhere in the tumor.
COMMENT

The reason for the frequent location of teratoid tumors in the mediastinum has been the subject of considerable controversy, and it would perhaps be well to summarize briefly the conflicting views. Where complete teratomata, and particularly those giving rise to choriocarcinomas are concerned, it seems necessary to postulate the dissociation of totipotential cells in the blastomere stage before the development of the separate germ layers (29), and their quiescent inclusion in the developing embryo until some later stimulus incites the cells to activity. The high incidence of teratoid tumors in the late second and early third decade of life caused Pflanz (30) to suggest that this stimulus might be hormonal, related to puberty. Other somewhat less acceptable possibilities, as far as mediastinal tumors are concerned at least, have to do with persistent polar bodies, displaced primary sex cells, and fetal inclusions. A reasonable explanation for the eventual location of these tumors in the mediastinum, and one favored by several authors, is well stated by Jacobs (9), who makes the following comment: "It is now generally accepted that the anlage for these tumors is in the cervical region during the early embryonic period along with the lungs, heart, and thymus, before the closure of the blastodermic folds, and that they move into the thorax along with these organs. This is suggested rather strikingly in a number of cases, notably that of Collenburg, whose case was found to have a band-like connection that extended from the posterior part of a large tumor about the size of a child's head, in the right

Fig. 13. Case II: Detail of center of field illustrated in Fig. 12, demonstrating the striations in a malignant muscle cell. × 1350

stage before the development of the separate germ layers (29), and their quiescent inclusion in the developing embryo until some later stimulus incites the cells to activity. The high incidence of teratoid tumors in the late second and early third decade of life caused Pflanz (30) to suggest that this stimulus might be hormonal, related to puberty. Other somewhat less acceptable possibilities, as far as mediastinal tumors are concerned at least, have to do with persistent polar bodies, displaced primary sex cells, and fetal inclusions. A reasonable explanation for the eventual location of these tumors in the mediastinum, and one favored by several authors, is well stated by Jacobs (9), who makes the following comment: "It is now generally accepted that the anlage for these tumors is in the cervical region during the early embryonic period along with the lungs, heart, and thymus, before the closure of the blastodermic folds, and that they move into the thorax along with these organs. This is suggested rather strikingly in a number of cases, notably that of Collenburg, whose case was found to have a band-like connection that extended from the posterior part of a large tumor about the size of a child’s head, in the right
lower anterior mediastinum, upward to the lower edge of the right lobe of the thyroid. He was able also to trace a branch of the inferior thyroid artery into this band along with some fibers of the sternothyroid muscle. He was, thus, the first to suggest the cervical anlage of the mediastinal dermoid. He also assumed that it was the thymus which gave origin to it."

Imperfect teratomata are explained by Budde (29) on the basis of "hamartomes" or cellular inclusions, which obviously must arise after some of the completely totipotential character has been lost. The possible relationship of the thymus to many tumors of this type in particular is evident when one recalls the origin of the structure embryologically. Ewing (24) states that it arises from the third and fourth branchial clefts, and that its eventual constituents, the reticulum stroma and the Hassall corpuscles, are entodermal, while the remaining elements (31) represent mesenchymal invasion. He considers that the finding of congenital multiloculated cysts, lined with flat pavement cells or even ciliated or mucous epithelium, represents persistence and development of the epithelial canals of the embryonal thymus. He further suggests that the inclusion of ventral ectoderm may give rise to the ordinary dermoid.

In an attempt to explain the appearance of so many elements in tumors attributed to the thymus, Jacobson (27) cites Zotterman on the normal thymic structure in lower animals. It appears that in the mole the thymus is purely ectodermal, while in the pig it is mixed ectodermal and entodermal. In the fowl, in addition, isolated portions of striated muscle may be found, and also cysts lined by ciliated epithelium. It would seem, thus, that the thymus presents unusual opportunities for the development of teratoid growths.

The first case may be summarized briefly from the pathological standpoint. A large hemorrhagic and necrotic anterior mediastinal tumor was found in a twenty-one-year-old male. Histologic study revealed a tumor containing mixed epithelial elements predominantly entodermal in nature, and in places undergoing carcinomatous degeneration. A small amount of keratinizing squamous epithelium was also seen. There was also definite angiomatosus tissue. A few immature smooth muscle cells were found. The predominant element, however, was an immature cell type with marked hyperchromatic tendencies, seen variously as round, spindle, or multinucleate forms with acidophile cytoplasm, the latter being most prominent, particularly in the metastatic growths, where its resemblance to the megakaryocyte of bone marrow was enhanced by its constant association with eosinophilic myelocytes in particular, but also with other elements or myelo- and erythropoiesis. Dissemination of the chief malignant element was by lymphatic spread to regional and abdominal lymph nodes, and presumably by the blood stream to lungs, spleen, liver, and bone marrow. In the latter site alone did the cells show marked signs of proliferation.

It is the identity of this chief malignant element which constitutes the main pathological question. The teratoid nature of the tumor permits of no restriction of the possibilities. The assumed origin in the thymus, however, offers certain considerations. Ewing (24) comments on mixed round-, spindle-, and giant-cell tumors, all of which, he says, may easily be derived from the reticulum, which, being of entodermal origin, would make these tumors car-
cinematous. He describes in particular, however, myeloid giant cells with opaque acidophile cytoplasm and many vesicular nuclei. The presence of eosinophilic myelocytes has been often noted in thymic tumors and indeed in normal thymus, where their significance is in dispute. If, as Maximow (31) concludes, myelopoiesis is an embryonic function of the thymus, and is carried on to less extent in post-embryonic life, the presence of eosinophilic myelocytes in the normal thymus is easily understood. Similarly, the origin in this region of a marrow-cell tumor, the chief malignant element of which resembles the megakaryocyte, is also more easily understood. Besides morphological and histogenetic reasons, one other factor favors the assumption that bone marrow cells have become malignant: namely, the peculiarly luxuriant growth of the tumor in the sites of normal bone marrow, as compared to its growth in other sites of metastases. Other possibilities which cannot be entirely ruled out include especially an atypical Hodgkin's disease or a reticulum-cell sarcoma, accompanied by a compensatory extramedullary myelopoiesis arising in the face of the developing anemia and replacement of the bone marrow. Silver impregnations would indicate that, if so, such reticulum cells were as yet too immature to elaborate additional reticulum fibrils.

No cases have been found in the literature which entirely resemble the above tumor. A few are suggestive. Shields Warren (32) reports a case of "malignant tumor simulating bone marrow" which from description and illustration much more nearly resembles true bone marrow tissue that has become peculiarly invasive. Shennan (28) (Case 29) reports a hard, white malignant thymic tumor composed microscopically of dense fibrous reticulum with a few cells, these being large abundantly cytoplasmic giant cells, occasionally multinucleate and associated with many clusters of eosinophils, and occasional small epithelial-lined cysts. Rose (13) reports an anterior mediastinal tumor showing histologically frequent Sternberg-like giant cells, several epithelial-lined cysts, and a few areas of cartilage. The tumor reported by Rolleston (23) as arising from the thymus was found to contain, in addition to a cystic epithelial portion of benign nature, a hemorrhagic portion containing basic large cells of sarcomatous nature, areas of lymphoid cells, and many small islands of cartilage.

Some interest attaches to our case from the clinical standpoint. First, the tumor proved relatively radioresistant, having regressed but slightly, according to x-ray pictures, under therapy, only to spring into extremely active new growth soon after therapy was discontinued. A more interesting point is the possible relationship of the tumor to the previous endocrinopathy. It may be recalled that the patient presented a typical Froehlich's syndrome when first seen at the age of fourteen, and that this condition spontaneously regressed at about eighteen years of age. Conceivably some functioning glandular element was included in the original tumor which was destroyed by the later malignant phase. As Willis (2) has pointed out, some evidence of function is associated with teratomata. Mucous glands are seen to have been obviously secreting. Positive Aschheim-Zondek tests are recorded with teratomatous chorionepitheliomata. Hematopoiesis and lymphopoiesis are seen. Arendt (14) has reported a case of gynecomastia in a twenty-year-old male associated with a mediastinal teratoma with chorionepitheliomatous degenera-
tion. Houghton (37) comments on the incidence of interstitial-cell hyperplasia of the testis with teratomata, suggesting the action of a hormone arising from such tumors. No such hyperplasia was found in our Case I.

The second case, pathologically speaking, is somewhat less complex. A massive tumor, weighing 9 kg. and apparently arising in the anterior mediastinum, was found occupying most of the thorax in a forty-eight-year-old man. By virtue of its size, the tumor had caused almost complete pulmonary collapse and marked posterior displacement of the mediastinal organs. The tumor externally resembled an encapsulated lipoma, but was unusually firm. On section, it was found to consist of many fatty lobules and one large fleshy mass, with myxomatous-like septa. Microscopically, the bulk of the tumor was found to be made up of adult adipose tissue intermingled with immature fat varying from fetal type to liposarcoma. The grossly myxomatous tissue was found to be only edematous fat and fibrous tissue. The fleshy nodule was largely necrotic, but contained sarcomatous elements of rhabdomyomatous nature. Incorporated in the upper anterior portion of the tumor was recognizable thymus. Several cervical lymph nodes containing liposarcoma were the only sites of metastases.

The derivation of this tumor is the chief point in question. The initial gross appearance suggests classification with the ordinary lipomas of the mediastinum. The contour, encapsulation, and structure of large parts of the tumor conform with such a diagnosis. Lipomas, in addition, not infrequently undergo malignant degeneration (33). The incorporation of the thymic tissue might be merely incidental to its location. However, the presence of rhabdomyosarcoma is not so readily explained.

This coincidental development of malignancy of two relatively unrelated types of tissue in one tumor makes it more or less mandatory that any common origin be from some initially undifferentiated tissue. While the persisting elements of this tumor can all be derived from the mesoderm, it is not possible to rule out the earlier presence of epithelial elements, especially in view of the considerable extent of necrotic tissue found. The inclusion of the thymus in this tumor further suggests its teratoid nature. While, on the basis of the findings of Maximow and Zotterman, discussed earlier, all the elements demonstrated here could be ascribed to a thymic origin, this need not be the case. As we have already seen, the rôle of the thymus may be purely mechanical, serving only to bear the primordia of the tumors from the cervical region down into the thorax.

Because of its gross appearance, this tumor could be classified after Virchow (4) as a teratoma myxomatodes mediastini. However, as we have seen, the supposedly myxomatous areas failed to take the mucin stain.

A rather extensive review of the literature fails to reveal a tumor of the mediastinum equal in size to this one. Cochrane and Nowak (15) reported a teratoma measuring $12 \times 10 \times 8$ cm. and stated that the largest to be found by them in the literature was that of Smith and Stone (7), measuring $15 \times 11 \times 9$ cm. Harrington (19) reported, as the largest intrathoracic tumor he had seen, a multilocular cystic squamous-cell epithelioma, probably a degeneration of a teratoma, measuring $20 \times 18 \times 15$ cm. The largest mediastinal tu-

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5 The largest found by Houghton (37) was that of Jores, which, including a large cyst ($19 \times 6$ cm.), was said to measure $31 \times 20 \times 16$ cm.
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mors described are the benign lipomas. These were quite adequately reviewed by Heuer (34) in 1933. No larger ones have been reported more recently. In agreement with Heuer we find the largest mediastinal lipoma to be one reported by Leopold (35) in 1920. This tumor measured $31 \times 30 \times 15$ cm. and weighed 17.5 pounds (8 kg.).

In 1920 Hirsch and Wells (36) reported the largest abdominal tumor found on record to that time, a liposarcoma weighing 69 pounds. Herewith we report what appears to be the largest mediastinal tumor yet recorded, weighing approximately 9 kg. (allowing for attached heart and lungs), and measuring $33 \times 30 \times 16$ cm. in its various diameters.

**Summary**

The clinical and pathological features of two cases of mediastinal tumor are presented. The first patient was a twenty-one-year-old white male who was first seen at the age of fourteen because of a marked Froehlich's syndrome which underwent spontaneous regression. After a period of normal health, he developed symptoms related to a roentgenologically demonstrable tumor mass which grew rapidly in spite of x-ray therapy. Post-mortem examination revealed a large hemorrhagic and necrotic tumor in the anterior mediastinum. Microscopically, this proved to contain elements derived from at least two germ layers. In addition, there were local adenocarcinomatous degeneration and extensive sarcomatous change which had metastasized to lymph nodes, lung, liver, spleen, and bone marrow. Because of its morphology, the constant association of myeloid and erythroid forms with the tumor, and its luxuriant growth in bone marrow, this sarcomatous portion has been regarded as arising from marrow cells. The possibility that the previous endocrinopathy was related to the tumor has been considered.

The second case was of a forty-eight-year-old white male whose clinical symptoms referable to a chest tumor began some three years before death. At autopsy, a huge lipoma-like mass, weighing about 9 kg., almost filled the thorax, but was presumed to have arisen in the mediastinum. Several enlarged cervical nodes constituted the only metastases. Histologic examination revealed liposarcoma predominant, but in one portion of the tumor definite rhabdomyosarcoma was observed. No epithelial elements were found except remnants of normal thymus in the upper pole of the tumor. This tumor is believed to be the largest intrathoracic tumor ever reported.

**Bibliography**