A MALIGNANT HEMANGIOMA OF THE LUNG WITH MULTIPLE METASTASES *

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Malignant hemangiomas with metastases by way of the blood stream are extremely rare. Wright,[1] in 1928, described such a case and stated that less than a dozen reports of proved cases of this group could be found in the literature. The same statement is true today. He reviewed briefly the reports of the following authors: Borrmann,[2] Ewing,[3] Shennan,[4] Homans,[5] Langhans,[6] Theile,[7] and Jores.[8] Attention was called to the fact, however, that of these seven reports only the last three qualified as regards malignancy of the primary tumor. Wright's case should be classed with those of Langhans, Theile and Jores. Dassel's [9] case should also be included in the latter group.

Schlopsnies,[10] in 1930, gave a fairly complete summary of the reported cases of multiple angiomatous tumors. The summary includes multiple benign angiomas, angiosarcomas, multiple "system" tumors and *malignant metastasizing hemangiomas*. He classified his own case as an angiosarcoma of the spleen with multiple foci confined apparently to the hemopoietic system. In addition to this case, the reports of Grabowski,[11] Shennan,[4] and Wollstein[12] should be included among the hemangiomas with multiple foci but histologically benign. It is somewhat doubtful whether or not the angiosarcomas should be included in the group of malignant hemangiomas, since many of these may be only vascular sarcomas and not true tumors of the vascular system.

REPORT OF CASE

Clinical History: L. P., a married, white female, aged 40 years, was seen by a physician on Nov. 28, 1933, at which time she complained of severe pain, of 6 weeks duration, in the right hip; backache, the onset of which was concurrent with the last menstrual period 6 weeks previously; weakness, insomnia, mental

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depression and nausea of 1 weeks duration, with some vomiting. She had had influenza in 1918, "heart trouble" and rheumatic fever at 16 years of age.

Her father had hypertension, and her mother had a manic depressive psychosis. Her brothers and her husband are living and well. During the past 18 months the husband had lost his business and at the time of the patient's illness necessities were being provided by other members of the family. Three pregnancies had resulted in three normal deliveries. The children, aged 16, 9 and 6 years, are normal.

Physical Examination: This revealed a pale, but well developed, well nourished woman of about 40 years. The positive findings were mitral stenosis and regurgitation, pulse 136, blood pressure 105/88. There was a tiny cervical polyp protruding slightly from the cervical canal.

Examination of the blood showed a hemoglobin of 40 per cent, red blood cells 3,100,000, white blood cells 5600, with the following differential count: polymorphonuclears 60, lymphocytes 31, monocytes 4, eosinophils 2, and basophils 2.

The patient was exhausted by the examination and wept most of the time. Her physician advised rest in bed, preferably in a rest home or sanitarium with supportive treatment. Bromides were prescribed as a sedative.

Course of Illness: On Dec. 2, 1933, the patient was cheerful, was eating well and nausea had disappeared. The pain in her hip was relieved. The blood pressure was 120/84, the pulse 90. Improvement continued until December 17th. At that time the hemoglobin had risen to 48 per cent and the red blood cells were 3,900,000. The pulse had dropped to 88.

From Dec. 17, 1933 to Jan. 7, 1934, there was recurrent pain in the right hip, for which it was necessary to use codein, as salicylates failed to relieve the pain. On January 7th, at 2 A.M., the patient complained of a severe sharp pain in the right chest. She was sent to a private hospital where she remained for a week. Examination revealed a small area of consolidation at the base of the right lung. There were râles over this area and increased density of the mediastinum. The patient was dyspneic. The temperature was 100.4° F., the white blood count 5800. It was believed by the physician in charge that the patient had developed pneumonia, possibly tuberculous in origin. While in the hospital the patient's temperature fluctuated from 101.8° F. to normal.

On January 13th the patient returned home. Her condition continued steadily downward. Three days before death, the physician was permitted to call a cardiologist and a surgeon in consultation. A diagnosis of acute cardiac decompensation, internal hemorrhage and shock was made. The patient's physician had previously made a tentative diagnosis of a malignant pelvic tumor with pulmonary metastases.

The patient was admitted to the Los Angeles County Hospital where examination revealed a pale, slightly yellowish, dyspneic and extremely weak, white female. There was flatness over the chest from the right base to the second rib. Breath sounds were distant or absent. The left lung field was resonant. The heart was displaced to the right, the rate rapid but regular. Blood pressure at this time was 80/40. Examination of the abdomen showed that the liver was displaced downward about 1 inch below the costal border. No masses and no tenderness were found.

It was thought that hemorrhage had taken place into the right pleural cavity, probably from pulmonary metastases. A thoracentesis yielded 200 cc. of bloody fluid, and 150 cc. of air was replaced.

A blood examination showed 30 per cent hemoglobin, 2,380,000 red blood cells and 14,700 white blood cells. The urine was essentially normal.

While preparations were being made for a transfusion the patient died suddenly.

Autopsy Report

The autopsy was performed $3\frac{1}{2}$ hours postmortem. The body is that of a well developed, well nourished white female about 40 years of age. The skin and mucous membranes are pale. The superficial lymph nodes are not palpable and there is no edema. The diaphragm level is at the fifth rib on the right, the sixth rib on the left.

On removing the sternum about 3000 cc. of bloody fluid is found in the right pleural cavity and about a liter of somewhat bloody fluid is found in the left pleural cavity.

The pericardium is normal. The heart weighs 240 gm. and is normal, except for the right coronary which has no opening into the aorta, although the artery, which is smaller than normal, is found in the epicardial fat about 1 cm. from the aorta. There is a small dimple in the aorta opposite the right aortic cusp at the usual site of the coronary orifice.

The right lung is almost completely collapsed; the left lung is partially collapsed. The right lung weighs 330 gm. and forms a mass a little larger than a man's fist (Fig. 1). All three lobes are quite firm, except a small portion of the upper lobe which contains air. In the pleura of the interlobar and posterior surfaces of the upper lobe, and throughout the middle and lower lobes, are a number of raised, reddish black tumor nodules which appear to contain blood. These vary from 0.2 to about 1 cm. in diameter. In places, several of these nodules are more or less confluent. At the lower border of the lower lobe there are several larger, granular red areas covered more or less with a buffy coat of fibrin. The largest of these measures 5 by 1.5 cm. These are angiomatous tumor masses with some hemorrhage into the pulmonary tissue surrounding them. There are approximately 50 hemorrhagic nodules scattered throughout the pleura. On the cut surface an occasional similar nodule is seen deep in the lung tissue, but the greater number are pleural and subpleural.

The left lung is slightly larger than the right, but weighs only 290 gm. About one-third of the upper lobe and a small portion of

the upper part of the lower lobe are air-containing. Hemorrhagic nodules similar to those described are found throughout the surface of the lung but they are not so numerous as in the right lung. In the diaphragmatic surface of the lower lobe there is a larger tumor measuring 2 by 1.5 by 1.5 cm. Occasional hemorrhagic areas are found on the cut surface. Some 20 to 25 pea-sized, hemorrhagic tumors are found scattered over the parietal pleura of the right side and 12 to 15 similar ones on the left. These are localized over the intercostal muscles.

The spleen weighs 120 gm. The capsule is smooth, the pulp pale red with distinct markings. Two small accessory spleens are found near the hilum which measure 0.6 and 1.2 cm. respectively.

The adrenal glands and kidneys are normal.

The uterus is slighly enlarged. The tip of the cervix is rather large with a smooth surface. There is a tiny polyp projecting from the cervical canal. The uterine cavity is normal. The ovaries are slightly cystic. The tubes are normal.

The duodenum, bile ducts, stomach and pancreas are normal except for marked pallor.

The liver weighs 1800 gm. In the anterior portion of the liver a number of grayish red, poorly defined, metastatic nodules may be seen through the capsule. On the under surface, just to the right of the gall-bladder, there is an elevated nodule 2 cm. in diameter, which is dull red with a few pale grayish areas showing through the red background. On the cut surface the nodules vary from 0.3 to 1 cm. in diameter, and show the same mottled reddish gray color. The remaining portion of the liver is pale and the markings are rather indistinct. The gall-bladder and contents are normal.

There are a number of small, hemorrhagic tumors in the fat surrounding the pancreas. None is found, however, within the body of the gland itself. Immediately below the head of the pancreas there is a firm, rounded mass measuring 8 cm. in diameter and consisting of a group of 12 to 15 enlarged hemorrhagic lymph nodes surrounded by fibrous fatty tissue. The largest of these nodes measures nearly 2 cm. in diameter. Most of them are reddish black, due to the large amount of blood present. Several, however, show small grayish spots scattered through them, while the more cellular ones contain considerable grayish tissue. Similar enlarged nodes are found on either side of the aorta almost to the

bifurcation. The aorta is somewhat smaller than normal. Occasional yellowish streaks are seen in the intima.

The bone marrow of the sternum is pale red and of normal consistence.

The dura and leptomeninges are normal. The convolutions over the convexity of the brain appear slightly flattened. The brain tissue is exceedingly pale. The large vessels at the base of the brain are distinctly hypoplastic and show an occasional atheromatous spot.

A rapid frozen section through one of the nodules from the lung and also one from the liver revealed cellular angiomatous growths showing malignant characteristics.

Anatomical Diagnoses: Malignant hemangioma of right lung; malignant hemangioma, metastatic, left lung, parietal pleura, liver and retroperitoneal lymph nodes; fatal hemorrhage into right pleural cavity; anemia, secondary; congenital malformation of heart (imperforate right coronary); hypoplasia of aorta and cerebral vessels, and multiple accessory spleens.

Histological Examination

Retroperitoneal Lymph Node: The body of the gland is surrounded by a dense fibrous capsule. The lymphoid tissue is completely replaced by a vascular tumor consisting of a cavernous part and a more cellular part. In the cavernous part are many large spaces filled with red blood cells. These spaces are lined for the most part by the usual flattened endothelial cells. The partition walls are rather thin in most places, but occasionally spread out into fairly broad fibrous bands. An increased proportion of polymorphonuclear leukocytes is seen in the spaces among the red blood cells.

In the cellular part the blood spaces are small and partially or wholly collapsed. Only a few of the open ones contain red blood cells. The cells lining these spaces are very atypical. Some are more or less elongated, hypertrophied endothelial cells, while others are large polygonal cells with oval or spherical nuclei, many of which are hyperchromatic (Fig. 3). All gradations between these two extremes may be seen. Surrounding the spaces, or in the more cellular areas, the same kind of cell is predominant. Mitoses can be found in nearly every high power field. In many places the

stroma is loose and edematous with abundant fibrin present and considerable numbers of polymorphonuclear leukocytes.

In some of the lymph nodes the tumor tissue is arranged in whorls and papillary extensions (Fig. 2). The lymphoid tissue is almost wholly replaced by a turbulent-appearing tissue. There are numerous smaller and larger blood spaces, some of the latter forming long sinuous channels among islands and promontories of cellular tissue.

Many nucleated red cells, mostly normoblasts, are found in the vascular spaces. In one small space practically filled with normoblasts seven cells were counted. Many of these cells show the nuclear material broken up and scattered through the cell as dark staining fragments. Occasional megaloblasts are seen also. In addition to the above, many polymorphonuclear neutrophilic leukocytes are present, also moderate numbers of lymphocytes, a few eosinophils and occasional basophils.

Lung (Right): Sections through one of the vascular tumors at the base of the right lung show a number of large cavernous spaces in the pleura. Cellular, moderately malignant areas, similar to those described, border the larger spaces. The partition walls of the large sinuses are broken down in some instances and the blood is clotted. Over the surface is a layer of fibrin of irregular thickness. It was evidently from these large, coalesced blood sinuses that hemorrhage occurred into the pleural cavity.

Moving inward from the periphery one sees a peculiar arrangement. The blood spaces are relatively small, many of them collapsed. The open ones contain red blood cells and groups of extremely large phagocytic "dust cells," the latter containing either red cells in various stages of disintegration, or coarse clumps of brown pigment (hemosiderin). The septa are thick and quite vascular. Large, swollen polygonal cells line the spaces. The nuclei are large, oval or spherical, and some are hyperchromatic. These areas, no doubt, represent collapsed lung in which small hemorrhages have occurred because of the presence of metastatic tumor. In addition, there is active phagocytosis of red blood cells and all the alveolar lining cells appear to be hypertrophied.

The bronchi are nearly all large and irregular. The lining epithelial cells show hypertrophy and crowding. Many of the nuclei are pyknotic.

Liver: The nodules in the liver are roughly spherical and fairly well circumscribed growths having the characteristics of metastatic rather than primary tumors. These consist in part of angiomatous and cavernous spaces filled with blood and partly of very cellular areas similar to those described above. The angiomatous portion gradually merges into the cellular, more malignant areas. In some of the latter there is a tendency to form a papillary type of growth. In one place a medium sized vein (3 mm. greatest diameter) shows tumor growing completely through the wall at one side. Tumor is heaped up on the inside of the vessel and spreads along the wall for some distance on both sides. At one end of the same vessel a similar phenomenon has occurred. The liver cells are swollen, the cytoplasm is finely granular and pale staining. The Kupffer cells are normal.

Spleen: The capsule is of uniform thickness and the trabeculae are moderately thick in places. The reticulum is everywhere thickened and appears to be somewhat edematous. Large, early fibroblastic cells are also present. The littoral cells of the venous sinuses are large, with round or plump oval nuclei. Occasional, large, atypical tumor cells are found free in the sinuses. The lymphoid follicles are rather small. The malpighian arteries are moderately thickened and show some hyaline degeneration.

Kidney: Essentially normal.

Pancreas: Normal.

Bone Marrow (Sternum): Stained with Giemsa, many myelocytes, a moderate number of eosinophilic myelocytes and many normoblasts are seen. The red cells show moderate anisocytosis and poikilocytosis and tend to be small. Occasional megakaryocytes are seen, and now and then a large irregular cell with oval nucleus, which is probably an atypical endothelial cell from one of the malignant areas.

Comment

Wollstein,[12] in 1931, reported a malignant hemangioma of the lung in a female infant 4 months and 20 days old. She considers this the first case reported in which the principal tumor was found in the lung. Although the lung was the organ chiefly involved, it is not certain that this was the primary site. Shennan [4] presented an unusual case, a female, 23 years of age, who had a large angiomatous

tumor nodule near the root of the left lung. A larger mass involved the superior mediastinum. Because of the greater size of the mediastinal tumor and the peculiar barking cough suggesting mediastinal pressure, the author favored the mediastinum rather than the lung as the primary site. The spleen was enlarged by the tumor growth, and other tumors were found in the thymus, pleurae, mediastinal lymph nodes, liver and bone marrow. In Shennan's case the tumors were largely confined to the hemopoietic system, as in most of the "multiple foci" tumors. The tumors were histologically benign, further evidence in favor of a system disease neoplasm. The patient died of hemorrhage into one of the pleural cavities.

In the author's case a similar situation is seen in regard to the primary tumor as in the 2 cases referred to above. The marked dyspnea, the fatal hemorrhage and the more extensive growth of the tumor in the right lung point to this organ as the seat of the disease. On the other hand, the metastases in the lungs, pleurae and liver are more readily explained by assuming the primary growth to have been located in the retroperitoneal lymph nodes. The tumor-like mass found in the latter situation, together with the history of pain in the right hip for a period of 6 weeks, are further points in favor of this location. It is evident that no definite conclusion can be reached in regard to the primary site.

Regardless of our inability to designate the original growth with any degree of certainty, it is quite evident that the greater number of angiomatous nodules found in the lungs, pleurae, liver and lymph nodes are true metastases. Let us consider the nodules in the liver in this respect. The tumor masses all tend to be spherical and the surrounding liver tissue is normal except for occasional small hemorrhages. The Kupffer cells particularly show no abnormal changes. In the liver metastases both cavernous and cellular angiomatous structures are found. The malignant character is evident, not only by the anaplasia of the tumor cells, but also by invasion of the wall of one of the veins.

From the foregoing, there would seem to be no escape from the conclusion that the multiple tumor foci in this case are true metastases. The characteristics that distinguish a system disease tumor are largely lacking. Although the liver and the retroperitoneal lymph nodes are involved, the spleen is not involved and, so far as we know, the bone marrow likewise is free. Furthermore, the

distinctly malignant appearance of the tumor growth wherever encountered is contrary to the usual benign histological character of the system disease tumors.

The presence of congenital anomalies of the circulatory system in this patient may have etiological significance. Cohnheim's theory of tumor growth in aberrant or misplaced portions of organs or systems, which is well established for certain kinds of tumor, suggests itself as a probable causative factor. A definite congenital anomaly was present in the right coronary artery which failed to arise from the aorta in the usual way. A small dimple was present at the usual site opposite the right leaflet of the aortic valve. Lack of any evidence of syphilitic changes and the presence of only very early atheromatous lesions in the aorta make it quite certain that the condition is congenital. The aorta was moderately hypoplastic and the large cerebral vessels at the base of the brain were distinctly smaller than normal. Two small accessory spleens were found at the hilum of the main organ.

SUMMARY

1. A case of malignant metastasizing hemangioma, of which there are less than a dozen true cases in the whole medical literature, is reported.

2. The largest tumor was found in the right lung and death was due to hemorrhage into the right pleural cavity.

3. True metastases consisting of both cavernous and malignant cellular areas were found in the lungs, pleurae, retroperitoneal lymph nodes and liver.

4. The type cell is the endothelial cell which forms blood-vascular spaces in all the tumor nodules. The cells vary from practically normal appearing cells lining the cavernous spaces to extremely large atypical cells that almost fill the blood spaces in the more cellular areas. In the latter the growth is rapid and apparently highly malignant.

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DESCRIPTION OF PLATES

PLATE 53

FIG. 1. The collapsed right lung (two-thirds normal size) showing the main tumor mass at the base of the lower lobe with hemorrhage into the surrounding tissue. A number of hemangiomatous nodules are seen in the pleura of the upper lobe, also along the lateral border of the lower lobe.

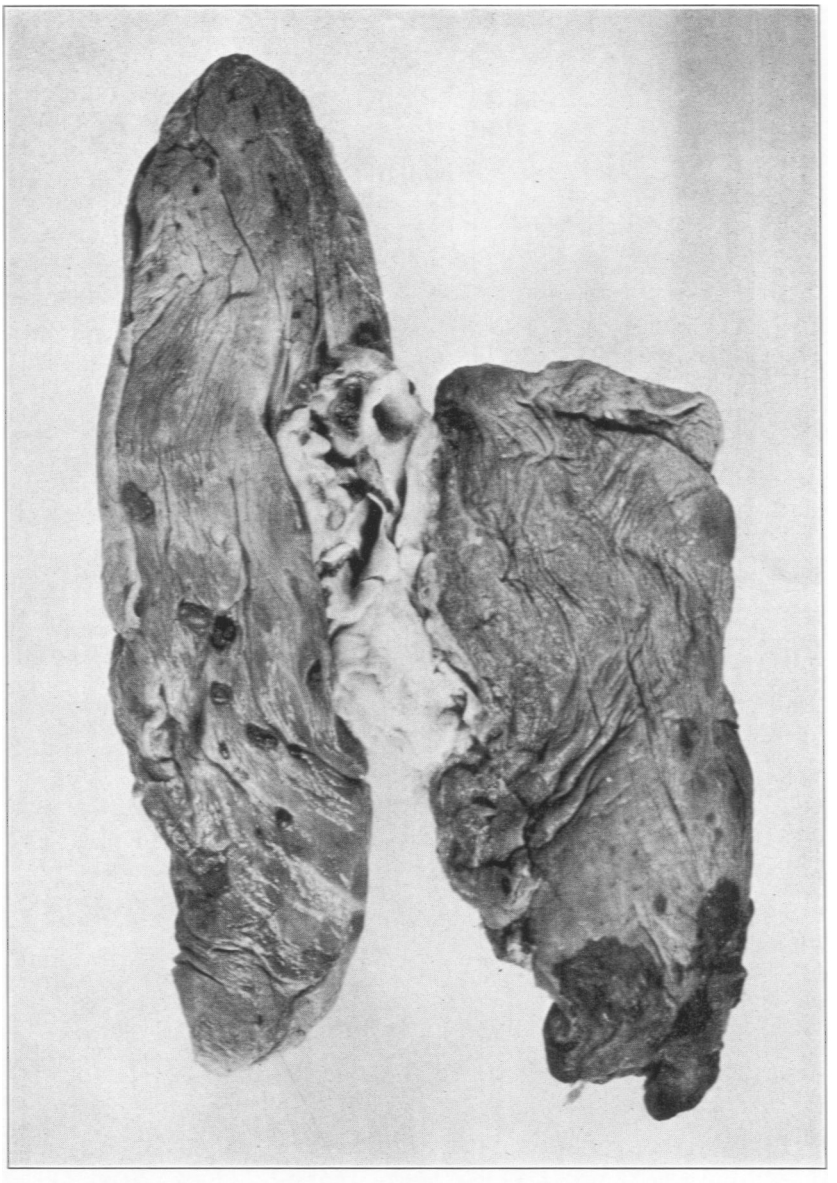

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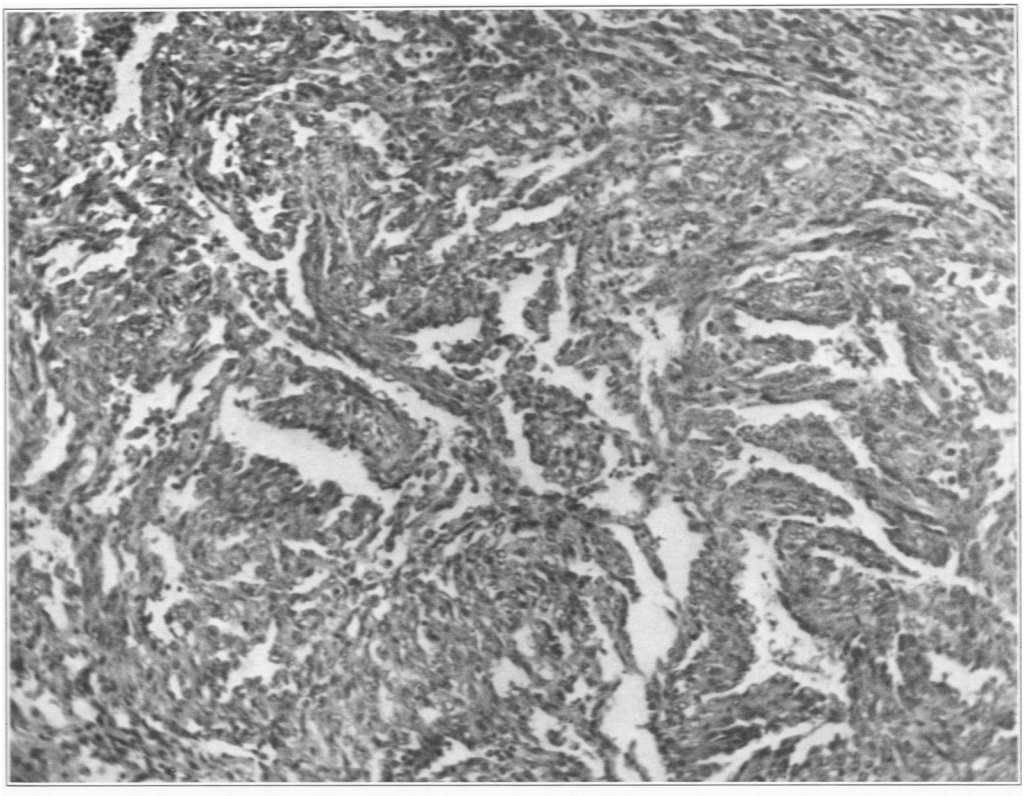
PLATE 54

FIG. 2. Photomicrograph from section of retroperitoneal lymph node showing turbulent papillary type of growth completely replacing the lymphoid tissue. × 160.

FIG. 3. Photomicrograph from section of retroperitoneal lymph node showing marked anaplasia of the endothelial cells. Several mitotic figures are present in this field, but not all are in true focus. × 700.



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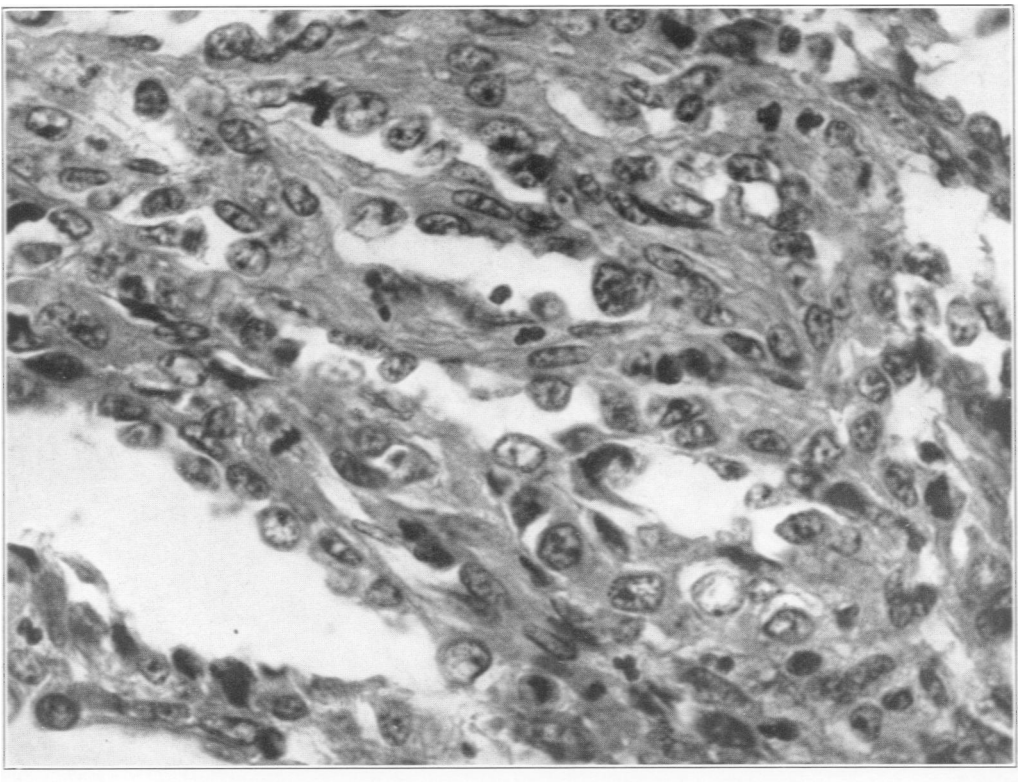

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Hall Malignant Hemangioma of Lung