PRIMARY FIBROMYXOSARCOMAS OF THE HEART AND PULMONARY ARTERY *

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Primary myxomas, fibromyxomas and fibromyxosarcomas of the heart have been recognized for many years, but they are still very rare. According to Diebold,[1] the first case was reported by von Albers in 1835, a citation which we were unable to verify. In the postmortem service of the Allegheny General Hospital we recently had a case of primary fibromyxosarcoma originating in the first portion of the pulmonary artery, extending along the pulmonary tree and producing multiple metastases in the left lung and bronchi and in the vessels of the right lung. We believe the case to be of general interest not only because it is unusual, but because the site of origin and the manner of extension appear to throw some light on the histogenesis of tumors of this type.

Fibromyxosarcomas of the heart are far less common than the myxomas from which they apparently develop. The literature dealing with cardiac myxomas contains numerous discussions concerning their true nature.

Thorel, in a series of articles on tumors of the heart published in 1903,[2] 1907,[3] 1910[4] and 1915,[5] assembled reports of 24 cases that had been reported as fibromyxomas of the heart chambers. He maintained that they were organized thrombi and stated in his final report that, with the single exception of the case of Horneffer and Gautier,[6] which had metastasized, all of the tumors were explainable on the basis of the organization of a thrombus. Among the cases cited by Thorel was that of Kesserling,[7] who advocated the theory that fibromyxomas of the heart valves arose in embryonic rests associated with the anlagen of the heart valves, admitted to be of myxomatous tissue, and that of Bacmeister,[8]

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who seems to have been the first to postulate that the tumors began as organizing thrombi and underwent metaplasia into true neoplastic growths. Thorel quoted Czapek [9] in support of the organizing-thrombus theory and concluded finally that, if the structures were true tumors, there were two possibilities for their explanation: (1) they arose from myxomatous metaplasia of a thrombus; and (2) they came from the myxomatous anlagen of the valves, rests of which either might persist in accordance with Ribbert's theory or revert in later life to an embryonic myxomatous state.

Brenner [10] in 1907 collected 32 myxomas of the heart and added 1. Of these, 19 were in the left auricle, 10 on heart valves, 2 in the right ventricle and 1 beneath the epicardium at the apex. Of the 19 in the left auricle, 8 were on the septum, 6 above the mitral valve and 5 at various other points on the wall. Two of those which occurred on valves were on the mitral, 6 on the tricuspid and 2 on the pulmonic. Brenner believed the tumors to be true neoplasms, although he said they could not all be differentiated in the gross but had to be diagnosed microscopically; this could be done on their arrangement and cytology, and sometimes microchemically by the use of the mucicarmine reaction. Husten [11] in 1922 collected 71 polypoid tumors of the endocardium of the right heart and 17 of the left. He divided and classified them into organized thrombi, pseudotumors and true myxomas. He accepted only 9 from the right heart and 2 from the left as true myxomas. He cited six authors who had reported sarcomas but did not discuss them, since they were definitely malignant. Kirch [12] in 1927 added 12 myxomas, including 2 hemangiomyxomas, and concluded that the older views of Thorel and Czapek could no longer be held but that the growths were true neoplasms.

Other cases of polypoid tumors of the heart which we were able to review and which resembled ours in the gross included those of Binder,[13] 1913 (sarcoma); Binder,[14] 1927 (myxoma); Barnes and Yater,[15] 1929; Jaleski,[16] 1934; Fossel,[17] 1936, 2 cases; and Müller,[18] 1932, who reported 3 myxomas and 1 sarcoma.

Diebold [1] in 1930 was the first to separate the sarcomas of the heart from the myxomas. He collected 45 cases and prepared a table giving the authors, sites of the primaries and metastases, microscopic diagnoses and clinical notes. Of 34 cases upon which

the data were complete, 25 were males, 9 were females and all were between the ages of 20 and 70 years. The primaries occurred in the right auricle 14 times; right ventricle, 3; pulmonary artery, 1; left auricle, 8; left ventricle, 1; auricular septum, 1; and ventricular septum, 1. Twelve cases produced metastases which occurred in the lungs 6 times; kidney, 3; lymph nodes, 3; and once each in the heart itself, pericardium, pleura, liver, pancreas and brain. The microscopic diagnoses included 15 spindle cell sarcomas, 12 round cell sarcomas, 4 giant cell sarcomas, 4 myosarcomas and 3 mixed cell sarcomas. Diebold's own case was diagnosed a "mixed cell" sarcoma, but both his description and his pictures resemble our own case closely and we believe it could have been interpreted as a fibromyxosarcoma. The only case beside our own in which the primary site was given in the pulmonary artery was that of Esbach, quoted by Diebold.

Since Diebold's [1] report we have found 2 additional cases with metastases. Müller [18] in 1932 described a case of primary "fibrosarcoma" of the left auricular wall with secondary nodules of the lungs and pleura. Both his pictures and his microscopic description lead us to believe that his neoplasm was a fibromyxosarcoma similar to ours. Fenster [19] in 1933 reported a "malignant myxoma" of the right auricle with multiple metastases to the liver, retroperitoneal lymph nodes, kidneys, adrenals and brain.

Yater [20] in 1931, in a review of all tumors of the heart and pericardium, found a total of 49 primary sarcomas of the heart. Of these, 15 had produced metastases and the diagnosis of myxosarcoma had been made in only 3 instances. Pollia and Gogol [21] in 1936 reviewed the incidence of heart tumors in 46,072 autopsies and found 154 primary and 220 secondary neoplasms.

As far as we have been able to ascertain, our case is the second fibromyxosarcoma occurring in the pulmonary artery.

Report of Case

Diagnoses. Primary fibromyxosarcoma at root of pulmonary artery, extensive metastases to left lung and to pulmonary arteries of right lung, pulmonary arteritis, multiple hemorrhagic infarcts of right lung, hydrothorax, edema of ankles, benign leiomyoma of uterus, and thrombosis of uterine venous plexus.

Clinical History

The patient,* A. K., was a white housewife, age 51.

Eight months before admission to the hospital the patient noticed pain about the heart and shortness of breath. She was placed at rest in bed with a diagnosis of pleuritis and, after 1 month, was apparently cured. Later the shortness of breath recurred and gradually increased. About 2 months before admission the patient suffered an attack of hemoptysis, which was not repeated. There were several gastro-intestinal upsets not accompanied by bloody stools. The patient had lost weight, although she was still rather stout. Her past history, as well as the family history, was irrelevant.

Physical Examination. The patient was well nourished and well developed. She exhibited severe respiratory distress. The skin was of normal color, and there were no palpable nodes. Eyes, ears, nose and mouth appeared normal. The chest was symmetrical, although there was limited motion on the left side, especially in the upper portion. Breath sounds, vocal fremitus and tactile fremitus were decreased over the upper, anterior portion of the chest, and no râles or rhonchi were present. There was a healed cholecystectomy scar in the right upper quadrant. Temperature, 100° F.; pulse, 98; respirations, 24; blood pressure, 110/72 on admission.

Laboratory Examinations. Laboratory findings showed the urine negative; a slight anemia; r. b. c., 4,040,000; w. b. c., 11,500; Hb., 69 per cent. Differential counts gave an excess of polymorphonuclear leukocytes up to 93 per cent. An autopsy was performed on December 2, 1939, 4 hours after death.

Roentgenologic Report. The first films were made on March 17, 1939. At that time there was a rather dense shadow at the base of the left lung and evidence of an enlarged gland in the root of the left lung. Films, made on August 9, revealed cloudiness in the lower two thirds of the left lung. There were three large tumor shadows. Those made September 26 showed that the tumor shadows had enlarged so that they were probably twice the size found at the preceding examination. On October 3 a probable diagnosis of carcinoma of the left lung was made and the patient referred for X-ray treatment. The Department of Roentgenology considered the case one of Hodgkin's disease and treated the patient on that basis. There was rapid symptomatic improvement but films made on October 19 failed to show any decrease in the size of the tumor shadows. If anything, they were slightly larger. Treatment was continued until November 8, during which time 6090 r. were given, with about 2000 r. over each of the three shadows. Following the treatment on November 8, the chest filled rapidly with fluid. On November 10 a part of the fluid was removed and air was introduced. The tumor shadows at that time had not changed in size or appearance.

Synopsis of Postmortem Findings

The body was that of a middle-aged, white female with extensive edema of the subcutaneous tissues of the chest and of both ankles.

The left pleural cavity contained about 1000 cc. of clear, straw-

* On the service of Dr. W. B. Ray and referred by Dr. William Marshall, of Aspinwall, Pa.

colored fluid and the right about 500 cc. The left lung was attached by dense, fibrous bands covering all of the pleural surfaces except the diaphragmatic. The right lung was adherent at the apex and over the posterior portion of the heart.

Heart. The pericardial sac contained 200 cc. of clear fluid. *In situ* the heart was distended. The right auricle was greatly dilated. The apex was situated beneath the fifth interspace in the axillary line and the base extended to the right beyond the sternal margin. When empty the heart weighed 400 gm. and measured 14 by 11 by 5 cm. The epicardium was smooth and glistening. The subepicardial fat was excessive, and watery in appearance. The myocardium was flabby and dark red. The auricular and ventricular cavities were normal. The pulmonary valve orifice was enlarged and the pulmonary artery was increased in diameter. All other valvular orifices were of average size and all valve cusps were pliable and apparently in good condition. The left ventricular wall was 1.3 cm. in thickness.

In the pulmonary artery three myxomatous polyps were attached to the posterior wall at a point about 3 cm. above the corpus arantii of the middle semilunar cusp. The polyps hung downward in the pulmonary artery and almost occluded it. They were grayish in color and were of aspic-gelatin appearance and consistency. Their pedicles were united in a common, broad base. The largest polyp was roughly pear shaped and measured 3 cm. in length and 2.5 cm. in its greatest diameter. It was pendulous and hung freely over the other two polyps and slightly to the right of the next smaller one. This one was egg shaped and had a very short pedicle. It measured about 2.5 cm. in all diameters. The smallest polyp measured 1.5 cm. in length by 0.6 cm. in diameter and was completely obscured until the largest polyp was lifted. The surfaces of all the polyps were smooth, glistening and semitransparent. For at least 2 cm. to the left, 1 cm. above and below and 3 cm. to the right of the base of the polyp the arterial wall was thickened, reddened, appeared ulcerated and was covered with a layer of fibrin of varying thickness. Directly over the center of the right semilunar cusp there was a thickened nodule about 8 mm. in diameter which protruded for a distance of 4 mm. into the lumen. It was hemorrhagic but appeared to be solid throughout. About 1 cm. above the right semilunar valve

there was a second smaller nodule, not more than 3 mm. in diameter, which was red in color.

Aorta. The aorta showed slight yellowish streaking. Small atheromatous plaques and ulcerations were present in the thoracic and abdominal portions. None was calcified.

Left Lung. The left lung weighed 750 gm. and measured 20 by 11 by 6 cm. The pleura was covered with broken adhesive bands. When placed in water the lung sank except for a portion of the lower lobe. A soft, tenacious, gelatinous, tan-colored polyp protruded from the main bronchus. On section the central portion of the lung was replaced by new growths made up of nodular, gelatinous masses. At least two thirds of the lung was involved. The nodules varied from 1 to 8 cm. in diameter. Some were cystic and others contained hemorrhagic zones. Some were located in veins which they distended, some were in bronchi and others were nonencapsulated and grew freely in the parenchyma. The intravascular extensions grew as elongated polyps or resembled obturating thrombi undergoing white softening. Beneath the pleura the remaining lung was in part air-containing and in part collapsed from pressure of the tumor and the pleural effusion. Moderate anthracotic pigmentation was present.

Right Lung. The right lung weighed 450 gm. and measured 22 by 14 by 4 cm. Most of the lung was air-containing. Several of the smaller pulmonary arteries were filled with gelatinous growths. Near the apex there was a recent wedge-shaped, hemorrhagic infarct. In the lower lobe there was a grayish brown, infarcted area undergoing organization.

Uterus. The only abdominal organ that presented a gross pathologic lesion was the uterus. It was somewhat enlarged and the cavity was distorted by the presence of a fibroid tumor, 6 cm. in diameter, located in the posterior wall. At the margin of the growth there were several dilated veins of the uterine plexus, filled with thrombi. Most of these were deep red in color, although some appeared to be well organized and of a red-brown color.

Microscopic Examination

Heart. The cardiac muscle cells were of normal size and staining qualities.

Polyps of Pulmonary Artery. A striking feature about the polyps was the great excess of myxomatous stroma in comparison to the cellular elements. The external surfaces were smooth and probably had been covered with endothelium. There was a concentration of the stroma just beneath the surface and this zone was more cellular than the central part of the polyp. At the junction of the polyp with the pulmonary arterial wall there was an interchange of cells and vessels with those of the pulmonary artery. The most cellular part of the growth was near the attachment. Here the cells were very numerous and varied greatly in size and shape. Some of the cells were spindle shaped with long, stellate processes, and others were round or oval. Many of the cells were multinucleated and appeared to be true neoplastic forms. The multinucleated cells had from 2 to 30 or more nuclei. Some of them resembled striped muscle cells but could not be shown by special methods to have cross striae. In addition to the tumor cells there were numerous single and multinucleated phagocytes, occasional lymphocytes and numerous red cells. Mitoses were numerous in some zones. In the more cellular zones there was a fair amount of collagen in the stroma. As the central portions of the polyp were approached there were fewer tumor cells and many of those that were present were unstained. Near the central portion the stroma was very edematous; large, cystic spaces were present, and numerous hemorrhagic areas were seen. The number of vessels varied and most of them were capillaries or thin-walled arterioles. The sessile nodule of the pulmonary artery proved to be a deep-seated, hemorrhagic, atheromatous cyst.

Pulmonary Artery Near Attachment of Polyp. The intima was ulcerated and covered with adherent, hyalinized fibrin undergoing organization. This zone contained many mononuclear phagocytes and less numerous multinucleated giant cells. Beneath the ulcerated surface the intima and part of the media presented a myxomatous appearance and were infiltrated with typical neoplastic cells of the type already described.

Aorta. The aorta showed a moderate degree of intimal sclerosis.

Lungs. A section of the main bronchus showed a very active inflammatory process. The lumen was filled with a myxomatous polyp of exactly the same structure as that found in the pulmon-

ary artery except that it was unattached at the point where the section had been taken. Other sections containing large branches of the pulmonary artery showed them to be filled with neoplastic thrombi. Some of these completely closed the vessel and infiltrated the walls, while others were mural with finger-like polypi extending out of the main masses. One vessel showed several points at which the tumor was penetrating its walls and invading the lung. At the points of perforation the cells were growing at right angles to the vessel wall. The secondary nodules in the lung tissue showed concentration of the cellular and fibrous elements in their peripheries but appeared to displace and compress the surrounding lung tissue rather than to form definite capsules. In the right lung there were two areas of hemorrhagic infarction, one of which was partially organized. Vessels leading into these areas were filled with simple emboli without tumor cells. It was thought that these originated from the thrombi in the uterine plexus.

Uterus. The tumor of the uterus was a very dense leiomyoma of the fibroid type in which multiple sections failed to show any unusual growth activity.

Discussion

The neoplasm in this case was a malignant tumor originating at the root of the pulmonary artery and belonging in the category of myxomas, fibromyxomas and fibromyxosarcomas of the endocardium.

Microscopically it could have been called a spindle cell sarcoma, a mixed cell sarcoma or even a giant cell sarcoma if cellular morphology alone had been considered. The diagnosis of fibromyxosarcoma was made on the presence of large, spongy, round and spindle-shaped cells with stellate fibrils spreading in the loose meshes of the stroma, and on the nature of the stroma itself. The cells varied greatly in size and in the number of nuclei. Many were in mitosis. The stroma was typically myxomatous with peripheral zones of collagenous fibrils. It was watery in appearance and tended to undergo necrosis and form cysts. The type of stroma offered no support to the proliferating capillaries and areas of hemorrhage were common. The metastatic growths established the diagnosis of sarcoma.

As to the origin of polypoid tumors of the heart, the views of

Thorel, Czapek and others that they are organized thrombi could be excluded at once in our case. The location of the tumors on the wall of the pulmonary artery at some distance from any point at which myxomatous anlagen are known to exist makes it extremely unlikely that they arose in an embryonic rest. The interpretation of Bacmeister and others that these tumors are derived by myxomatous metaplasia within a thrombus could not be excluded. In view of the facts that there was an ulcerated area of the pulmonary arterial wall covered by a hyaline, mural thrombus in the immediate vicinity of the pedicle, that there was no line of separation between the arterial wall and the elements of the tumors, that the blood supply of the new growth was continuous with vasa vasorum and that fibroblasts, tumor cells and capillary endothelium were common to the growth and to the arterial wall and were generously intermingled, we feel that organization and metaplasia offer the most logical explanation. It is no more difficult to accept the possibility of neoplastic metaplasia in a zone undergoing reparative proliferation than it is to accept the abrupt establishment of a malignant growth in otherwise apparently normal tissues.

Conclusions

1. An example of fibromyxosarcoma of the pulmonary artery is described. This is probably the second tumor of its type to be reported in this location.

2. The primary growths resembled organized thrombi in the gross, yet presented all of the microscopic evidences of malignancy.

3. There were extensive metastases along the pulmonary arterial tree and in the lungs and bronchi.

4. There was a zone of pulmonary arteritis, about the pedicle of the tumor, covered with an organizing thrombus that showed no neoplastic changes.

5. The association of pulmonary arteritis with the base of the tumor suggests that a logical sequence in the tumor's development may have been: pulmonary arteritis with loss of endothelium, protective thrombosis, organization of the thrombus with myxomatous metaplasia, sarcomatous change in the myxoma and secondary extensions to the lungs by way of the branches of the pulmonary artery.

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DESCRIPTION OF PLATES

PLATE 51

FIG. 1. Gross photograph of the heart showing the attachment of one small and two large polyps to the wall of the pulmonary artery 3 cm. above the middle semilunar cusp. Note the thickening and roughening of the pulmonary artery.

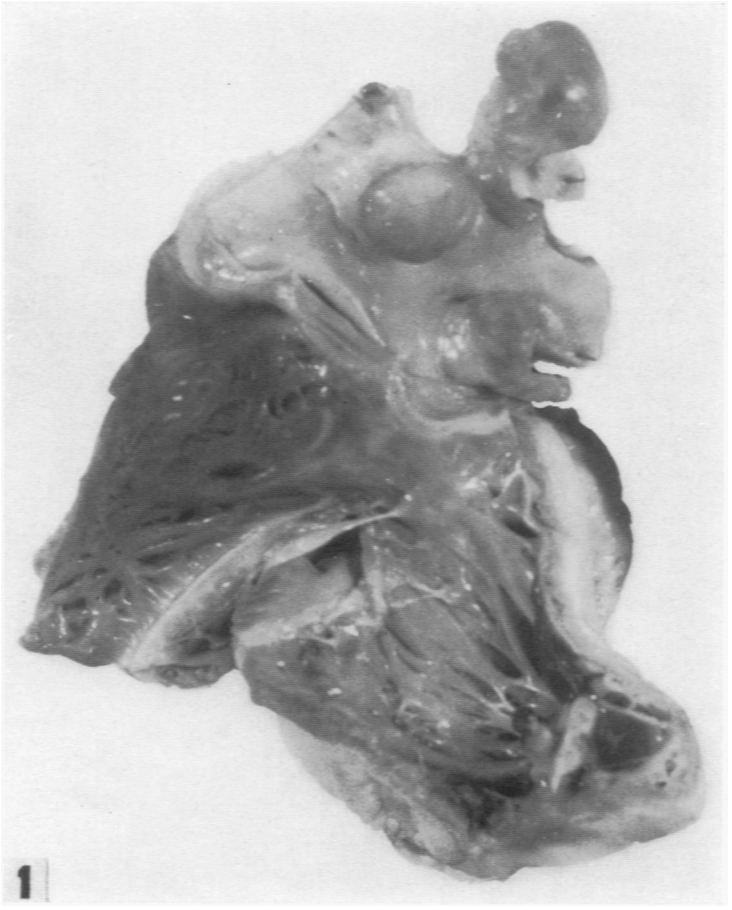

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PLATE 52

FIG. 2. Gross photograph of left lung showing extensive secondary myxomatous tumors. In the center a polypoid mass may be seen protruding from the main bronchus. The large, bulbous structure in the lower right-hand corner was a cystic, polypoid mass which was squeezed out of the lung when it was sectioned.

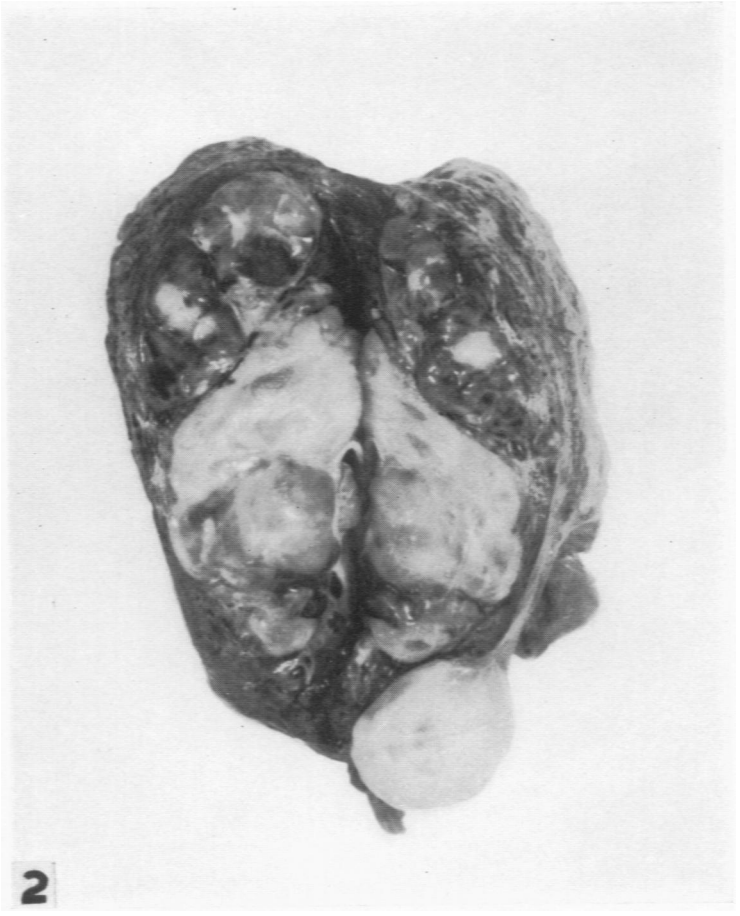

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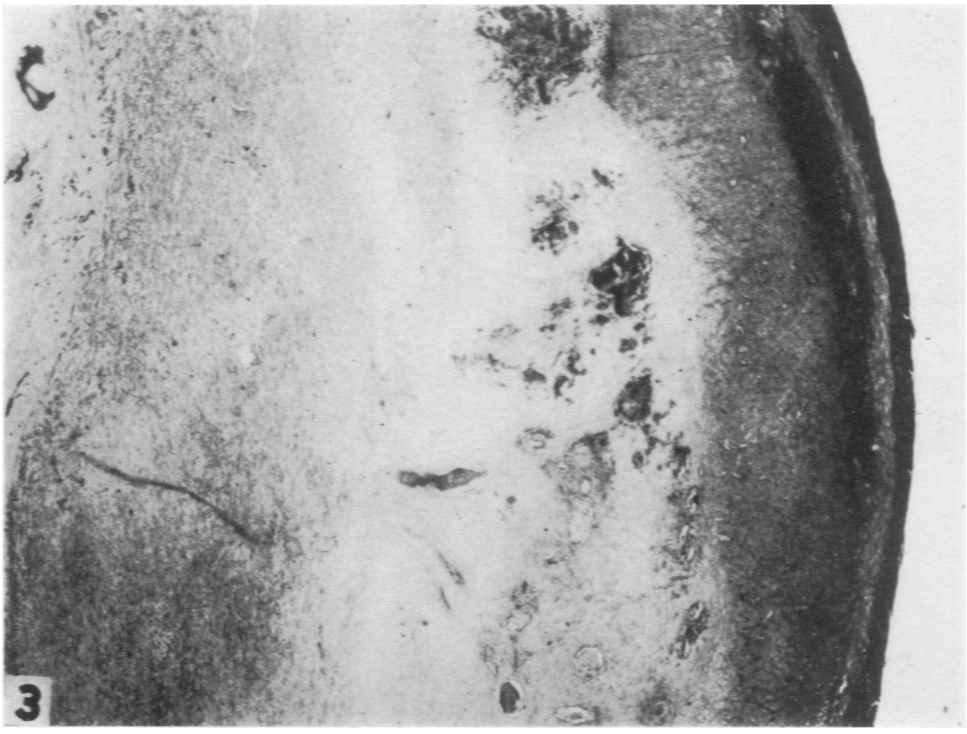
PLATE 53

FIG. 3. Low power photomicrograph through the smallest of the three polyps and showing the continuity of the growth with the pulmonary arterial wall. The cellular areas of the tumor were just beneath the surface and along the line of attachment. × 22.

FIG. 4. Wall of the pulmonary artery at a point near the attachment of the polyp. Note the arteritis, ulceration and deposit of hyaline fibrin on the surface. × 30.



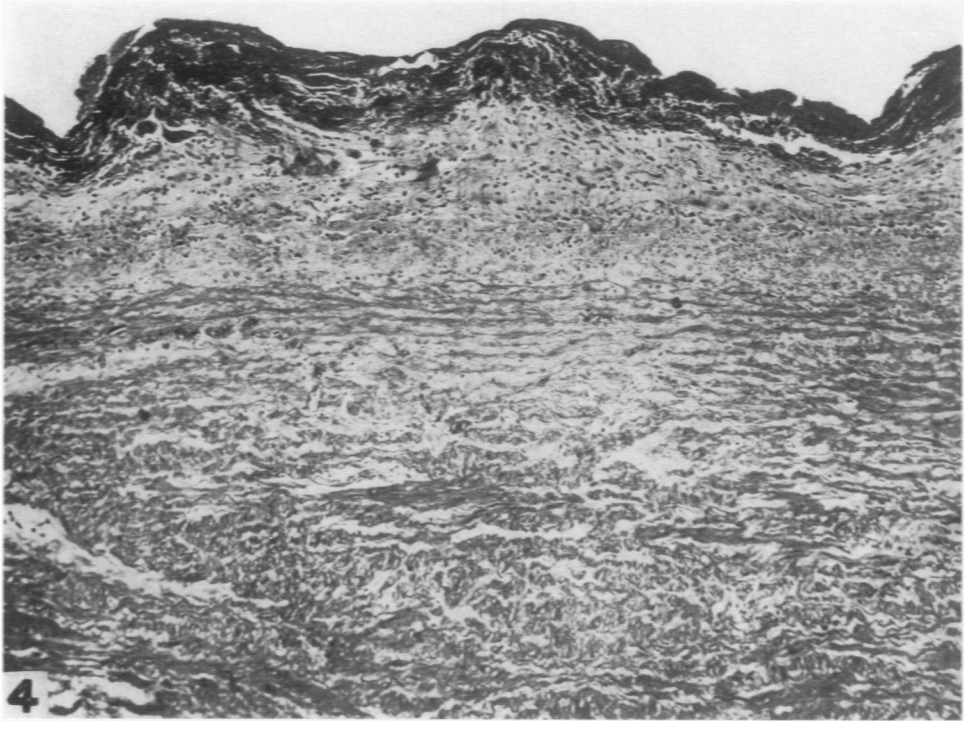


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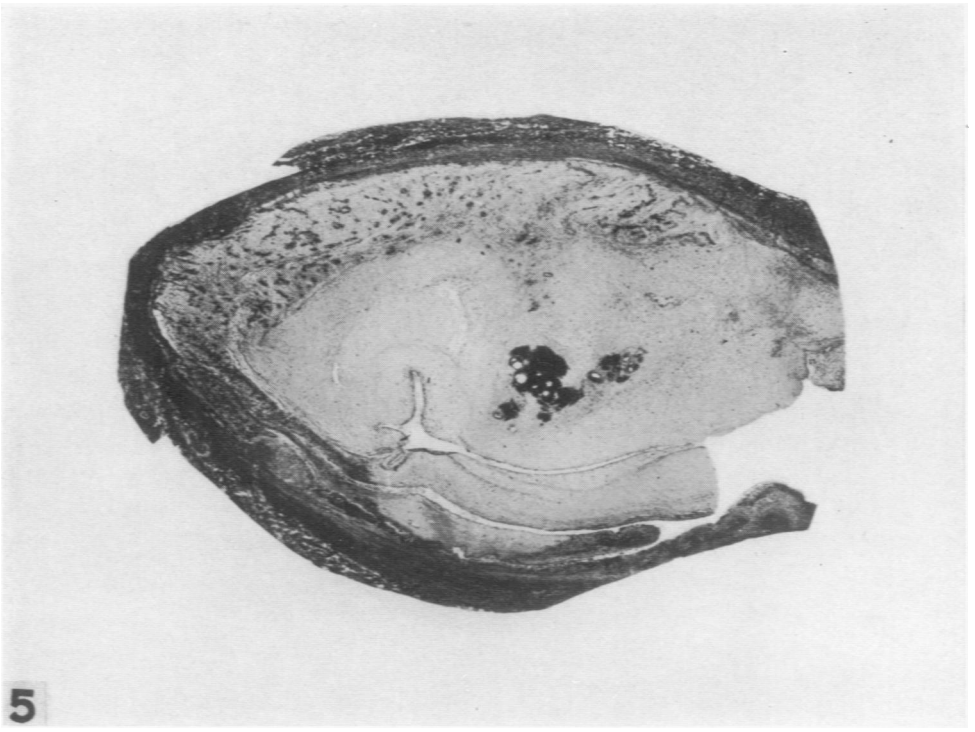
PLATE 54

FIG. 5. Section of the pulmonary artery containing a secondary myxomatous growth. The vessel is, for the most part, occluded, although parts of the tumor are growing as long, filamentous polyps. × 8.5.

FIG. 6. A small branch of a pulmonary artery, the wall of which was penetrated at several points by direct extensions of the tumor into the parenchyma of the lung. × 30.



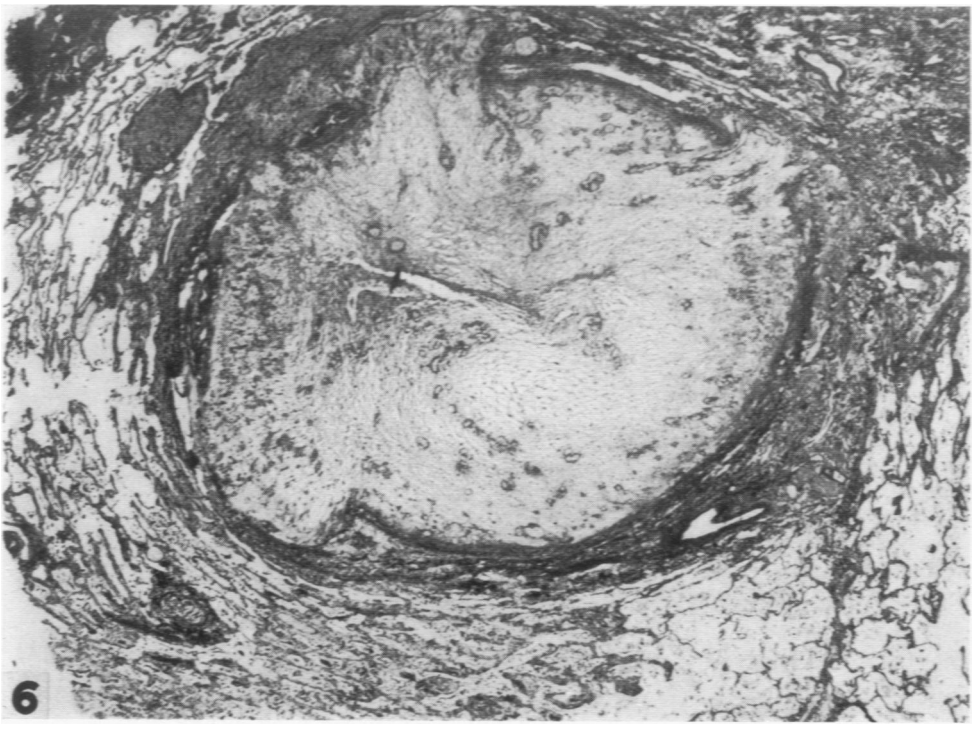


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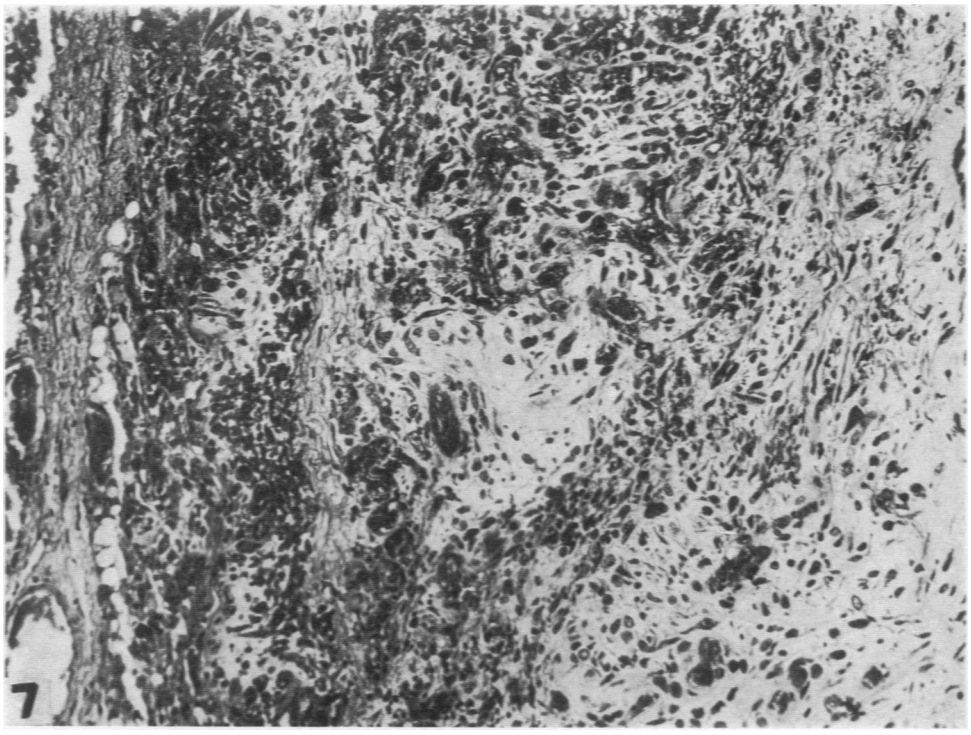
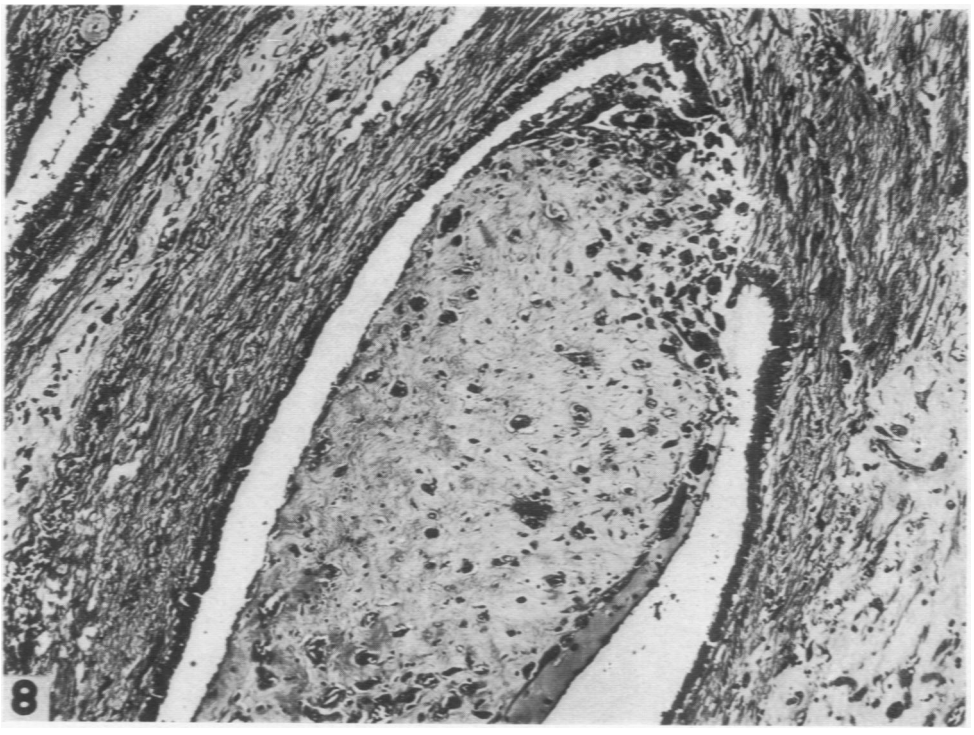
PLATE 55

FIG. 7. High power photomicrograph of one of the secondary tumors of the lung, showing a great variation in the shape and size of the tumor cells and many multinucleated forms. × 180.

FIG. 8. High power photomicrograph of a secondary polyp extending through the wall and growing freely in a small bronchiole. × 180.





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