CONGENITAL RHABDOMYOMA OF THE HEART *

REPORT OF A CASE

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Von Recklinghausen [1] in 1862 was the first to report a case of congenital rhabdomyoma of the heart. Since then reports of 49 other cases have appeared in the medical literature. In America, cases have been recorded by Knox and Schorer (1906),[2] Wolbach (1907),[3] Farber (1931),[4] and Ill and Gray (1934).[5] The case here reported makes the 5th in American and the 51st in the general medical literature.

REPORT OF CASE

Clinical History: The mother of the infant to be discussed was a white woman, 24 years of age. The past history was irrelevant. The Wassermann reaction was negative. She had a normal spontaneous delivery of a child, now living and well, on May 9, 1934. A spontaneous abortion at 3 months occurred in August, 1934.

Later, the birth of a male infant, weighing 4215 gm., occurred on April 29, 1937, on the obstetrical service of Bellevue Hospital. At birth the child was cyanotic. Respiration was artificially established 3 minutes after birth, but the cyanosis continued. Normal temperature could be maintained only through the application of external heat. Physical examination of the baby was negative except for cyanosis and a short systolic murmur which was heard over the pulmonary cardiac area. The baby lived only 3 hours.

POSTMORTEM EXAMINATION

The body is that of a well developed white male infant weighing 4215 gm. and measuring 53.3 cm. in length. The skin appears normal except for a moderate amount of postmortem lividity in the dependent portions of the trunk.

With the exception of the heart and brain, other organs show nothing of importance.

Heart: The heart is enlarged to twice its normal size and weighs 49 gm. The epicardium appears normal. On the left border of the

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heart, close to the apex, there is a raised nodule 1 cm. in diameter, which on section is seen to be composed of a circumscribed area of soft brown tissue arranged in whorls.

The pulmonary artery is dilated and measures 1 cm. in diameter at its base. The ductus arteriosus is dilated also, measuring 8 mm. in diameter, but the ascending aorta measures only 5 mm. It would appear that the main flow of blood was through the ductus arteriosus rather than through the ascending aorta. The descending aorta appears normal.

On sectioning the heart the right auricle and tricuspid valves appear to be normal. A rudimentary interauricular septum imperfectly separates a rudimentary left auricle, measuring 1.5 cm. in thickness, from the right auricle. The foramen ovale cannot be identified. The left auricle through the atretic mitral valves communicates with a small cavity 1.5 cm. in diameter representing the left ventricle. The aortic valves are bicuspid. The right ventricle is lined with glistening endocardium. The papillary muscles are hypertrophied and the base of one of the muscles within the right ventricle has been invaded by a tumor measuring 1.5 cm. in diameter. The left ventricle is lined with glistening gray endocardium 2 mm. in thickness. Adjoining the endocardial lining is a layer of dense gray tissue 2 mm. thick. The wall of the right ventricle is 1 cm. thick. The wall of the myocardium representing the interventricular septum measures 3 cm. and separates the rudimentary left ventricle from the large right ventricle.

On section of the interventricular septum two distinct tumor masses are seen. One measures 2.5 by 1.5 cm. It is well encapsulated, gray in color, and extends into the base of the papillary muscle as mentioned above. The cut surface of the tumor presents a grayish, granular dimpled appearance with faint, peripheral radial striations adjacent to the capsule. The capsule is 1 to 2 mm. thick and is smooth, gray and glistening.

The second tumor, 2 by 2.5 cm., is adjacent to the one described above and extends through the remainder of the interventricular septum and the anterior wall of the right ventricle. The tumor is not encapsulated but is well defined from the surrounding myocardium. It is composed of smooth, firm, glistening gray tissue somewhat fibrous in appearance. Scattered through the myocardium at the apex of the heart are a number of well circum-

scribed, light brownish islands of tissue of the same consistence as the myocardium.

Brain: On opening the cranium a moderate amount of subarachnoid edema is found and the cerebral vessels appear moderately congested. On section of the brain the subependymal tissue of the lateral ventricles is markedly thickened. On the floor of the left lateral ventricle extending posteriorly through the left occipital lobe is a tumor 6 by 2 cm. composed of well circumscribed reddish brown tissue. The tumor is firmer in consistence than the surrounding brain tissue. There is a moderate degree of internal hydrocephalus.

Microscopic Examination

Heart: A hematoxylin and eosin stain of tissue taken from the interventricular septum shows a tumor with a thin connective tissue capsule which varies in thickness, and in a few areas the tumor lies directly superimposed on myocardial tissue. A number of fair sized blood vessels with thin walls are seen within the capsule. Short connective tissue septums dip into the tumor, carrying small and medium sized blood vessels. A few small or medium sized arteries are also found within the tumor.

The myocardium immediately overlying the capsule is composed of delicate and elongated muscle fibers with prominent nuclei and cross striations and separated by slender connective tissue fibers containing a few fresh red blood cells and leukocytes.

The tumor is characterized by many, usually rounded vacuolated spaces which vary in size (Figs. 1 and 3). The tissue between them is composed of large polygonal branching cells with a finely granular and eosinophilic cytoplasm (Fig. 3). A fine fibrillar network is associated with these cells. Three or four cytoplasmic processes spring from the surface of each cell body and many of the cells contain round, deeply staining nuclei. In some instances the cells appear to lie within the vacuoles, the cytoplasmic processes spreading out to subdivide the space (Fig 2).

With high magnification the vacuolated spaces are seen to be lined by a thin rim of amorphous tissue. Often the lining of these spaces appears to be derived partially from the cytoplasmic process of an adjacent large granular cell (Fig. 3). The spaces appear to be extracellular and the large polygonal branching cells

lie between them. The majority of the spaces are clear but a few, however, contain several small round eosinophilic cells with bilobed dark nuclei resembling polymorphonuclear leukocytes (Fig. 1).

The cytoplasm of the cells contains many fine eosinophilic granules arranged to produce cross striations (Figs. 1 and 2). Under oil immersion the cross striations become even more evident and are seen to extend from the main body of the cell into the branching processes, which number two to six per cell. Most of the cells contain a single, large round nucleus with prominent nucleoli and chromatin granules. A few of the cells contain two nuclei.

Sections of the apparently normal myocardium disclose small foci of tumor tissue similar to that described above. A section of the second tumor mass shows tissue resembling a fibromyxoma, representing, probably, degenerative changes.

Brain: On microscopic examination the tumor in the occipital lobe is found to be a spongioblastoma with unipolar, bipolar and multipolar cells. Between the spongioblasts are large numbers of small, oval and round nuclei which cannot be identified. Every portion of the brain examined shows some deviation from normal. The main changes are noted in the occipital and frontal poles on both sides. Here the cortical architecture is distorted. Many abnormal nerve cells are present as well as enormous astrocytes and numerous undifferentiated cells. No ependymal cells are found lining the ventricles, but replacing them is a dense layer of glia fibers. No myelin formation is noted in any of the sections.

Other Organs: The lungs are congested and show focal hemorrhages with foci of aspirated amniotic fluid. Icterus is present in the liver. The kidneys are congested. The spleen shows acute splenitis.

Pathological Diagnoses: Primary congenital rhabdomyoma of the heart with multiple tumors; congenital malformation of the heart with atrial septal defect, hypoplasia of the aorta, mitral stenosis, dilatation of the pulmonary artery and ductus arteriosus, bicuspid aortic valve, and rudimentary left auricle and left ventricle; and tuberous sclerosis of the brain with cerebral tumor.

Discussion

In Table I are summarized the cases reported to date of congenital rhabdomyoma of the heart.

Of the 51 cases the tumor was classified as single in 8, multiple in 36, and diffuse in 3. Two cases showed two nodules, 1 case showed no tumor in gross, and 1 other case is unquestionably a rhabdomyoma from the photographs. Tuberous sclerosis of the brain was found associated with the tumor of the heart in 29 cases. In 4 cases tuberous sclerosis was not found and in 18 cases no mention of this lesion is made. Other congenital lesions were found also in association with the rhabdomyoma of the heart. Thus, in 24 cases tumors or cysts of the kidneys were reported. Cutaneous tumors were seen in 3, an enlarged liver or spleen in 3, and harelip or cleft palate in 1 case. Thirty-one cases had some associated lesion in organs other than the brain or heart. The age distribution of this tumor was found to be as follows: newborn, 10; under 1 year, 15; 1 to 3 years, 8; 3 to 15 years, 11; and over 15 years, 5. The age was not given in 2 cases.

As evidence of the congenital nature of rhabdomyoma of the heart, its occurrence in the newborn and its association with congenital anomalies have been noted. Cleft palate, harelip, cystic kidneys, tuberous sclerosis, multiple gliomas of the brain, hypernephroma, sebaceous gland adenomas, embryonic rests in the kidney, and embryonic malformation of the pancreas are among the more important congenital anomalies found associated with rhabdomyoma of the heart. Neuropathologists have noted that congenital anomalies are often associated with tuberous sclerosis of the brain.

Steinbiss [6] believes that the congenital rhabdomyomas of the heart cannot be regarded as true tumors. They do not show any evidence of proliferative activity, and degenerative changes such as fibrosis and calcification have been noted in older lesions. In the case here reported, a small portion of the tumor showed fibrotic degenerative changes. Malignant transformation of the tumor has not been recorded and probably does not occur. Farber [4] gives an excellent review of this controversial question. He believes that the evidence is against a neoplastic nature of the tumor. Rehder,[7] and Schmincke,[8] as well as Steinbiss believe that

TABLE I

Data on Cases of Congenital Rhabdomyoma of the Heart Reported in the Literature to Date

(Enlarged after Farber)

Number	Author	Year	Age	Sex	Histological findings		
					Heart	Brain	Other organs
1	Von Recklinghausen [1]	1862	Newborn	–	Multiple nodules in both ventricular walls	Tuberous sclerosis	Cutaneous tumors
2	Virchow [21]	1864	Newborn	–	Multiple nodules in both ventricular walls	——	Hepatomegaly, multiple skin tumors
3	Hlava [29]	1887	14 days	–	Single tumor in left ventricle	Not examined	——
4	Kolisko [18]	1887	2 mos.	–	Multiple small nodules	——	——
5	Cesaris-Demel [20]	1895	3 yrs.	–	Multiple tumors in both ventricles and septum	Tuberous sclerosis	Small nodular renal tumors, embryonic renal tissue without glomeruli
6	Seiffert [17]	1900	20 mos.	M	Multiple tumors in apex, myocardium and septum	——	Cystic kidney
7		1900	7 mos.	–	Multiple small myocardial tumors	——	——
8	Rothe [26]	1901	–	–	Multiple tumors	Tuberous sclerosis	Multiple breast tumors
9	Ponfick [19]	1901	7 mos.	M	Multiple nodules in both ventricles	Tuberous sclerosis	——
10		1901	3 yrs.	F	Multiple nodules in both ventricles	Tuberous sclerosis	——
11	Bonome [16]	1902	1½ yrs.	–	Multiple tumors	Tuberous sclerosis	——

12	Riedmatten [24]	1904	1½ yrs.	–	Multiple tumors	Tuberous sclerosis	——
13	Knox and Schorer [8]	1906	7 mos.	–	Multiple tumors, one large pedunculated tumor in left ventricle	——	——
14	Wolbach [8]	1907	10 mos.	F	Single tumor in right ventricle	Negative	Neuroglioma of spinal meninges
15	Abricossoff [12]	1909	3¼ yrs.	–	Multiple tumors in both ventricular walls	Tuberous sclerosis	——
16	Ehrnrooth [25]	1911	7 mos.	–	Single tumor in left ventricle	Grossly negative	Negative
17	Bundschuh [26]	1912	2 yrs.	F	Multiple nodules	Tuberous sclerosis	Tumors of kidneys, glioma of dura, adenoma sebaceum
18	Jonas [27]	1912	6 mos.	M	Multiple nodules in both ventricular walls	Tuberous sclerosis	Congenital malformation of kidney, hare-lip, cleft palate
19	Kawamura [9]	1913	4 yrs.	F	Multiple nodules in both ventricles	——	Renal tumors, congenital anomalies in pancreas, esophagus and rectum
20	Schulgin [10]	1913	6 days	–	Multiple tumors in both ventricles	Tuberous sclerosis	Kidney tumors
21			6 yrs.	–	Multiple tumors in both ventricles	Tuberous sclerosis	Kidney tumors
22	Rehder [7]	1914	Newborn	–	Multiple nodules	——	Grossly negative
23	Mönckeberg [11]	1914	14 mos.	–	Multiple nodules	Tuberous sclerosis?	Absent right kidney and ureter
24	Ribbert [28]	1915	1 yr.	–	Multiple nodules	Tuberous sclerosis	Cysts of kidneys
25	Hisinger-Jägerskiöld [29]	1916	7½ mos.	–	Single nodule at apex	——	Tumors of kidneys
26	Amersbach and Handorn [15]	1921	7 days	M	Single nodule	Negative	Negative

TABLE I (*Continued*)

Number	Author	Year	Age	Sex	Histological findings		
					Heart	Brain	Other organs
27	Kaufmann [80]	1922	3 yrs.	–	Multiple nodules	Tuberous sclerosis	——
28		1922	7 yrs.	–	Multiple nodules	Tuberous sclerosis	Kidney tumors
29	Mittasch [81]	1922	4 mos.	–	Multiple nodules	Tuberous sclerosis	Kidney tumors
30		1922	14 yrs.	M	Multiple nodules	Tuberous sclerosis	Kidney tumors
31		1922	31 yrs.	M	Multiple nodules	Tuberous sclerosis	Kidney tumors, angiomyolipoma of liver
32	Schmincke [8]	1922	Newborn	–	Diffuse involvement of myocardium	——	Congenital tumor of lungs
33	Steinbiss [6]	1923	5 yrs.	M	Multiple nodules in both ventricles	Tuberous sclerosis	Fibroepithelioma of skin, kidney tumors?
34		1923	8 yrs.	M	Multiple nodules in both ventricles	Tuberous sclerosis	Kidney tumors
35		1923	10 yrs.	M	Multiple nodules in both ventricles	Tuberous sclerosis	Kidney tumors, adenoma sebaceum
36		1923	16 yrs.	M	Nodule in septum and cicatrix	Tuberous sclerosis	Kidney tumors and cysts
37		1923	21 yrs.	F	Two small nodules in right auricle	Tuberous sclerosis	Kidney tumors
38		1923	35 yrs.	–	Single nodule at apex of left ventricle	Tuberous sclerosis	Kidney tumors
39	Omodei-Zorini [89]	1923	2½ yrs.	–	Single tumor in right ventricle	——	——

40	Uehlinger [18]	1925	20 yrs.	M	Multiple nodules in left myocardium	Not mentioned	——
41	Berger and Vallée [14]	1930	2 yrs.	–	Multiple nodules	Not examined	Cysts of kidneys
42	Farber [4]	1931	6 mos.	F	Multiple nodules in both ventricles	Tuberous sclerosis	Cysts of kidneys
43	Reitano and Nucciotti [88]	1933	1 day	–	Multiple, one large nodule almost replacing the entire heart	Not mentioned	——
44	Ill and Gray [5]	1934	48 hrs.	M	Multiple nodules	Not examined	Enlarged liver and spleen
45	Mitani [80]	1934	Newborn	M	Single tumor in interventricular septum and muscle of ventricles and auricles	Tuberous sclerosis	Cysts of kidney
46	Wegman and Egbert [84]	1935	10 mos.	F	Multiple nodules	Negative	Cysts of kidneys
47	Heuper [85]	1935	7 mos.	M	None grossly, microscopic foci of tumor tissue	Tuberous sclerosis	Cysts of kidneys, multiple spongioblastomas of basal ganglia, enlarged liver
48	Pauli [87]	1936	4 mos.	M	Diffuse tumor	Not mentioned	Enlarged liver, hydrocele
49		1936	6½ mos.	M	Diffuse tumor	Not mentioned	Not mentioned
50	Tamura [86]	1936	–	–	From photographs is unquestionably a case of rhabdomyoma	——	——
51	Labate	1939	3 hrs.	M	Multiple tumors in right ventricle and interventricular septum	Tuberous sclerosis with spongioblastoma	Congenital anomaly of heart

the tumor is a malformation and not a true tumor. The form of the embryonal cells composing the tumor is retained but the size is greatly increased. There is retardation of development but hypertrophy of the individual elements.

On the other hand, Wolbach [3] with the aid of the phosphotungstic acid hematoxylin stain demonstrated beginning muscle fibril formation and so considered the rhabdomyoma a true neoplasm. He demonstrated that the walls of the vacuolated spaces contain striated fibrils, analogous to the fibrils of normal heart muscle. These striations were observed in studying our case. Many observers have recalled the analogy between the tumor cells and embryonic heart muscle.

Knox and Schorer,[2] Kawamura,[9] Schulgin,[10] Mönckeberg,[11] Abricossoff,[12] Uehlinger,[13] and Berger and Vallée [14] believed that the cells of the tumor arise from Purkinje fibers.

Steinbiss claimed that the tumors were found often where the conduction system could not be demonstrated. Amersbach and Handorn [15] also believed that no connection existed between the tumor and the conduction system. Bonome [16] believed that rhabdomyomas develop from embryonic muscle fibers which become isolated through a connective tissue overgrowth replacing adjacent degenerated muscle fibers.

Wolbach, with Mallory's aniline blue connective tissue stain demonstrated that the sarcous elements stain red and the delicate striations between the sarcous elements (membrane of Krause) blue. In tumor tissue stained in this way the delicate fibrils connecting the fuchsin stained bodies are blue. With the phosphotungstic acid hematoxylin stain they are a reddish brown. These facts justify the belief that the granules of the tumor cells are primitive sarcous elements. The orderly arranged dots, most prominent in the tumor cells and the cell processes, are primitive sarcous elements. The fibrillary material taking the blue of the connective tissue stain is to be regarded as an element similar to that of Krause's membrane in normal muscle.

Von Recklinghausen,[1] Seiffert,[17] Kolisko,[18] Ponfick,[19] and Bonome [16] have noted the similarity of the tumor cells to embryonic heart muscle cells.

Von Recklinghausen considered the vacuolated spaces to be lymph or blood spaces, or muscle tubes of pathological origin.

Cesaris-Demel [20] was the first to call attention to the many processed cells lying within the spaces and called them "spider cells." He regarded the spaces as intercellular and similar to those found between anastomosing cells in embryonal hearts. Seiffert considered the spaces to be intracellular and also called attention to the spider-like cells. He compared these cells with the spaces to huge embryonic cells. Virchow [21] was not certain whether the spaces were lymphatic cavities or clear serous cavities. Hlava [22] believed them to be intracellular artifacts produced by alcohol during fixation. Ponfick, Knox and Schorer and Wolbach considered them to be intracellular.

The presence of glycogen in the vacuolated spaces has been a source of dispute as it is dissolved by solutions used in the ordinary methods of preparing sections. Seiffert was convinced of its presence but could not prove it. Rehder and Mönckeberg demonstrated glycogen in the tumor cells. Farber also demonstrated glycogen in the vacuolated spaces in the tumor in his case and states that others also have found this to be true. We were unable to demonstrate any in the vacuolated spaces of the tumor in our case.

Twenty-nine cases (57 per cent) of congenital rhabdomyoma of the heart were associated with tuberous sclerosis of the brain. Ponfick (1901) was the first to call attention to the associated cerebral sclerosis. He believed that the tumor of the heart and the sclerosis of the brain were congenital. Bonome felt that the association of rhabdomyoma of the heart with cerebral sclerosis was dependent upon the same conditions in intrauterine life, *i.e.* disturbances of nutrition with resulting vascular lesions. Steinbiss also noted the coexistence of rhabdomyoma of the heart with cerebral tuberous sclerosis. The latter may result in imbecility and epilepsy and accounts for the frequent occurrence of the tumor in inmates of hospitals for the insane. The cases reported by Steinbiss ranged in age from 5 to 35 years and all occurred in the insane.

Summary

1. The 51st case of congenital rhabdomyoma of the heart has been presented. The tumor occurred in a male infant who lived 3 hours after birth. Multiple tumors were found in the right

ventricle and interventricular septum. The tumor was characterized by many, usually rounded vacuolated spaces. The tissue between them was composed of large polygonal branching cells with a finely granular and eosinophilic cytoplasm. Congenital developmental defects of the heart as well as tuberous sclerosis of the brain with spongioblastoma were found in association with the heart tumor. As evidence of the congenital nature of rhabdomyoma of the heart, its occurrence in the newborn and its association with congenital anomalies have been noted. The true nature of the tumor is not known.

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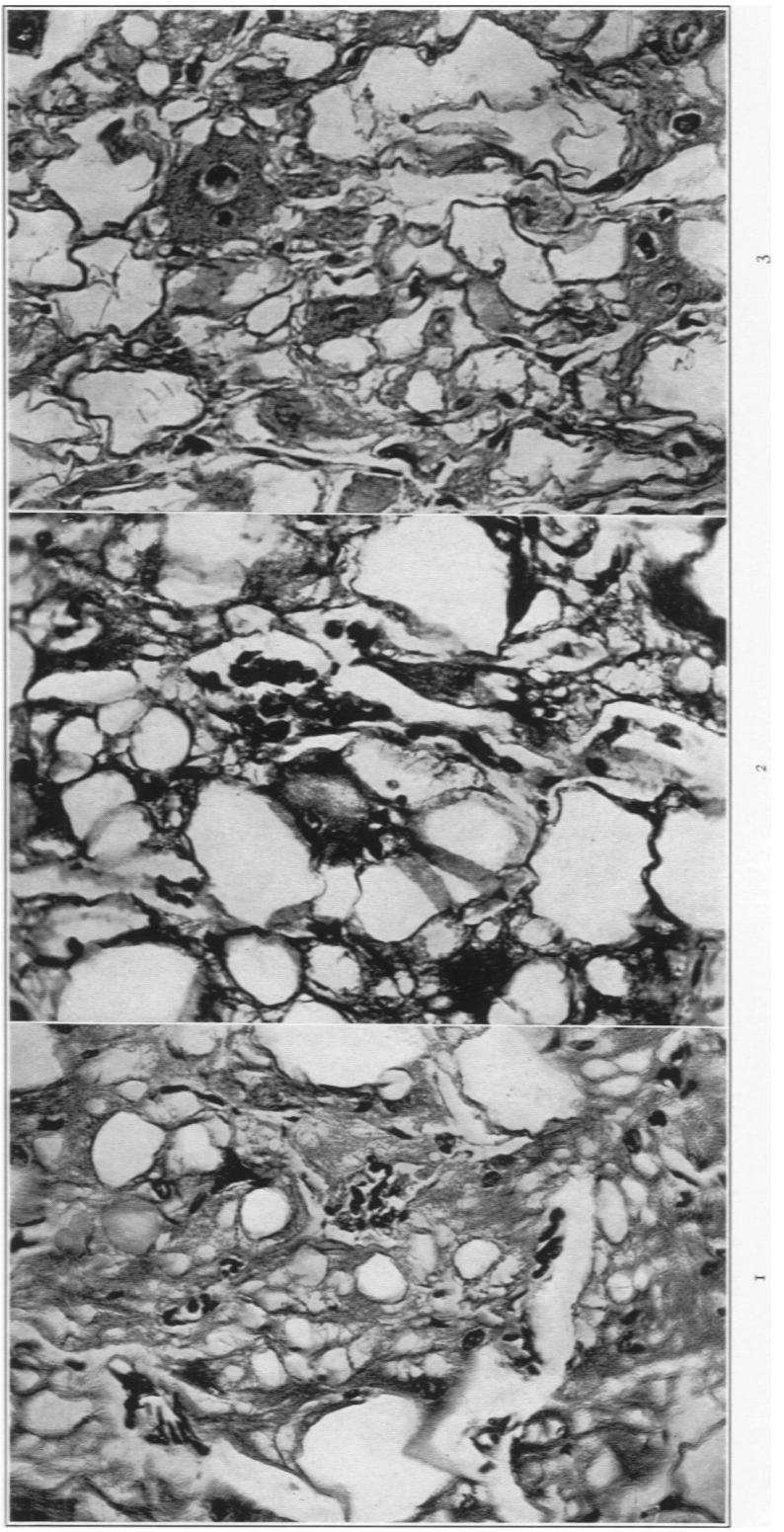
DESCRIPTION OF PLATE

PLATE 28

FIG. 1. Section from tumor showing the granules arranged to produce cross striations. Note the large number of vacuoles. Hematoxylin-eosin stain.

FIG. 2. Note the giant spider-like cell, the cytoplasm of which contains granular cross striations, in the vacuolated space. Foot's modification of the Masson trichrome stain.

FIG. 3. Large intracellular cells are seen occupying the vacuolated spaces. This is a characteristic feature of the tumor. Hematoxylin-eosin stain.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