Case reports

Pulmonic stenosis caused by a malignant tumor of the heart

A case report

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Acquired pulmonic stenosis is among the rare disorders of the heart. The causes mentioned in the literature are reviewed in a publication by Babcock and associates.[1] Tumors arising from the heart or localized near its base can produce such a stenosis. This paper describes a female patient with a sarcoma of the heart and pulmonic stenosis, diagnosed during life on the basis of an exhaustive examination.

Case report

The patient was a 38-year-old nurse with symptoms dating back to 1963, when she repeatedly had a sensation of fainting during a hike in the mountains. Later, she noticed occasional acceleration of the heartbeat in association with fatigue. During that period, she developed dyspnea at moderate exertion, e.g., walking upstairs. In view of these relatively unimportant symptoms, she consulted her physician. A systolic murmur was heard and she was given a cardiological examination.

At that time, the pulse was regular. The blood pressure was 115/80 mm. Hg, recumbent as well as standing. A systolic murmur was audible at the heart, with maximum intensity in the second and third intercostal spaces to the left of the sternum, with some conduction to the back. The heart sounds were normal. Routine laboratory findings were normal.

The electrocardiogram (ECG) showed a sinus rhythm, normal conduction times, and a vertical position of the heart axis. There was an S in V_6, but no other indication of hypertrophy of the right ventricle.

X-ray examination disclosed a rather large heart with an effaced waistline. In the right oblique projection some slight bulging of the conus arteriosus was seen. In the left-oblique projection the configuration of the heart was normal.

Phonocardiography disclosed a holosystolic diamond-shaped murmur with a late systolic maximum intensity. The amplitude was small. The punctum maximum was localized over the third intercostal space to the left of the sternum. The pulmonary component of the second sound was virtually invisible. The carotid pulse tracing was normal, as was the left ictus tracing. The venous pulse was normal apart from a slightly high A wave.

At heart catheterization in March, 1964, linear oxygen saturations were found in the right heart. The oxygen saturation in the radial artery was 95 per cent. The pressure in the right atrium averaged 2 mm. Hg. Right ventricle: inflow tract 68/2, outflow tract 42/2, pulmonary artery 42/6, peripheral segment 8 mm. Hg. This meant a fall of pressure in the outflow tract of the right ventricle by 26 mm. Hg at rest (Fig. 1).

The patient was discharged with a diagnosis of infundibular pulmonary stenosis of relatively little hemodynamic significance, and resumed work. In the autumn of 1964, the symptoms gradually progressed to distinct dyspnea at the slightest exertion,

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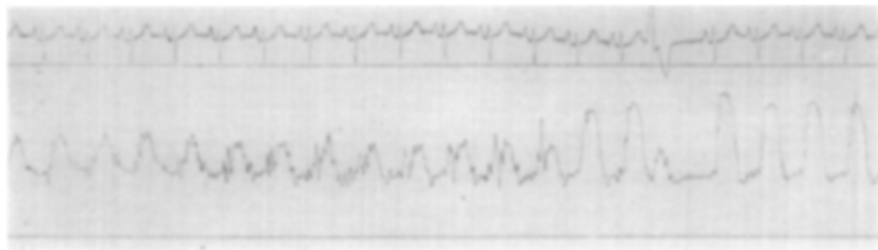

Fig. *1*. Heart catheterization, March, 1964; withdrawal tracing from pulmonary artery to right ventricle

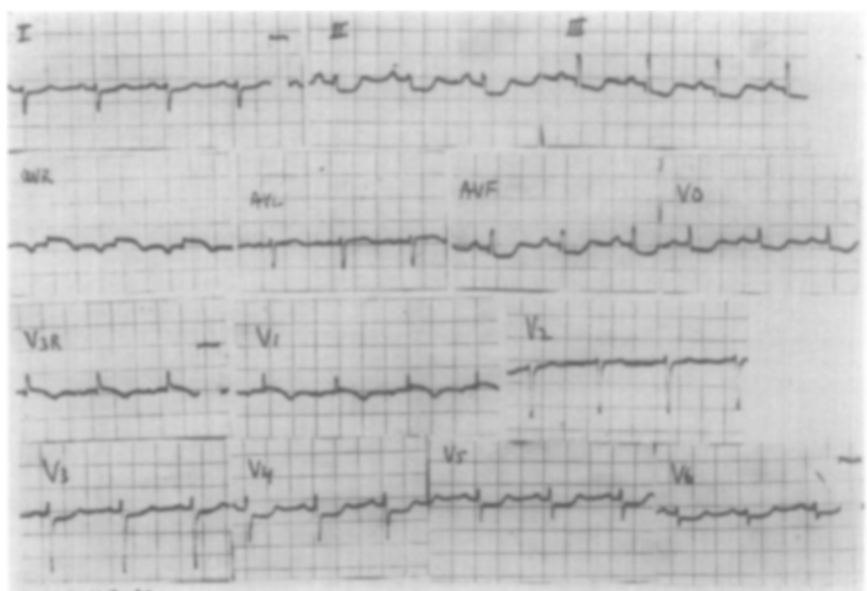

Fig. *2*. Electrocardiogram, June, 1965.

with attacks of dyspnea also at rest. Cyanosis gradually became apparent also. By the end of 1964, the patient began to suffer from presternal pain, radiating to the back.

In February, 1965, the patient developed a fever which lasted a few days, and the symptoms increased. She was hospitalized in Austria, where she was working at the time. The blood pressure was 100/60 mm. Hg and x-rays disclosed unequivocal enlargement of the heart. The temperature had returned to normal. Pericardial friction rub was audible on the fourth day. The erythrocyte sedimentation rate (ESR) was 74 to 115 mm. after 1 and 2 hours, respectively. The antistreptolysin titer (AST) was normal: 220 U. Pericarditis was diagnosed. Antibiotics, and later prednisone, seemed to lead to improvement. After a month, however, the condition obviously deteriorated. The patient complained of severe dorsal pain and the dyspnea increased. In May, she was taken to the Netherlands.

The patient was admitted to our department on June 1, 1965. The predominant symptom was pain in the back at the level of the scapulae and often simultaneously in the anterior aspect of the thorax. The pain was sometimes localized on the inside of the right upper arm, or occasionally in the left arm. There was no radiation to the cervical region. The pain was independent of respiration but clearly correlated to the position of the body; in particular, there was aggravation when the patient was lying on the left side; she was unable to sit up straight for any length of time. The pain was least severe when she was lying on the right side. Oxygen inhalation alleviated the pain. Any exertion produced dyspnea, but spontaneous attacks of dyspnea had ceased. The patient did not cough. There was no dysphagia and no hoarseness, no attacks of dizziness, and no tendency to collapse.

Examining this patient, we saw a woman in good nutritional condition and with intact mental faculties. There was unmistakable cyanosis of the skin and mucosa but the fingers were not clubbed. The

pulse was regular at a rate of 90 beats per minute. The blood pressure (upper arm) was 120/70 mm. Hg. The veins in the cervical region showed moderate overfilling. A brief systolic murmur was audible over the cervical region. The carotid arterial pulsations were normal. The thorax was symmetrical, apart from a slightly more pronounced curvature to the left than to the right of the sternum. The apex beat was felt in the midclavicular line. The heart sounds were normal, with a rather loud first sound at the apex. There was a systolic murmur with maximum intensity from the first to third ribs to the left of the sternum, and much less distinct over the apex. In the lateral recumbent position, a possible diastolic murmur was heard over the apex. Percussion and auscultation of the lungs revealed no abnormality. The liver did not seem to be enlarged, and no edema was found. The peripheral arterial pulses were intact. The spine and limbs showed normal mobility. Palpation and percussion elicited pain nowhere. Further physical findings were all normal.

Laboratory findings. Blood tests revealed a hemoglobin concentration of 15.1 Gm. per 100 ml., 4.3 million erythrocytes per cubic millimeter, 14,700 leukocytes per cubic millimeter (with a differential count of 2 eosinophils, 1 staph cell, 73 segmented cells, 17 lymphocytes, and 7 monocytes), and an ESR of 17 mm. after 1 hour and 30 mm. after 2 hours. The concentration of urea was 0.22 Gm. per liter, of creatinine 8.0 mg. per liter, and of bilirubin 5.4 mg. per liter. The thymol turbidity was 1.2 U., and the alkaline phosphatase was 195 μmole per minute per liter. Enzyme activities were as follows: serum glutamic oxalacetic transaminase (SGOT), 16 U.; serum glutamic pyruvic transaminase (SGPT), 17 U.; lactic dehydrogenase (LDH), 290 U.; β-hydroxybutyrate dehydrogenase (HBDH), 202 U.; creatine phosphokinase (CPK), 0 U. The total protein value was 8.0 Gm. per liter, with fractions as follows: albumin, 55 per cent; α_2-globulin, 11 per cent; β-globulin, 12 per cent; γ-globulin, 15 per cent. The glucose concentration was 1.10 Gm. per liter.

Tests of the urine revealed the following findings: Albumin negative, glucose negative, urobilin trace, bilirubin negative; sporadic leukocytes in the sediment.

The ECG (Fig. 2) showed a sinus rhythm (100 per minute), AV interval 0.16 sec., QRS width 0.06 sec., vertical position electrical axis. There was a prominent P wave in Lead II; high R in aV_R; RsR′ in V_{3R} and V_1 S as far as V_6. ST depression in Leads II, III, aV_F, V_6, and V_3 through V_6.

Radiological findings. The lung fields were clear, without infiltrative changes. The vascular pattern in the right lung seemed diminished (Fig. 3). In the anteroposterior (AP) projection, the heart shadow showed a large bulge at the site of the conus arteriosus. The right heart contour also bulged. The right oblique projection showed an excurvation of the posterior aspect immediately above the diaphragm. The left atrium did not seem dilated. The bulge at the side of the conus arteriosus projected ventrally here. The left oblique projection disclosed bilateral broadening of the heart, but with normal contours.

At phonocardiography (Fig. 4), we recorded a normal first sound followed immediately by a diamond-shaped murmur with a late maximum, the decrescendo of which overlapped the second aortic sound. The murmur was most pronounced on 2L1. No ejection sound was visible anywhere. A small pulmonic sound occurred 0.14 second after the second aortic sound. A low-frequency atrial sound occurred on 4L1. The carotid pulse tracing was normal, with a prominent dicrotic wave. The upstroke time of the femoral artery pulse tracing was 0.10 second. The venous pulse tracing showed a narrow x descent. In the lateral recumbent position, a few pulsation curves of normal aspect were recorded along the left sternal border. The ejection time measured from the carotid pulse tracing was 83 per cent.

In view of these data, and especially because of

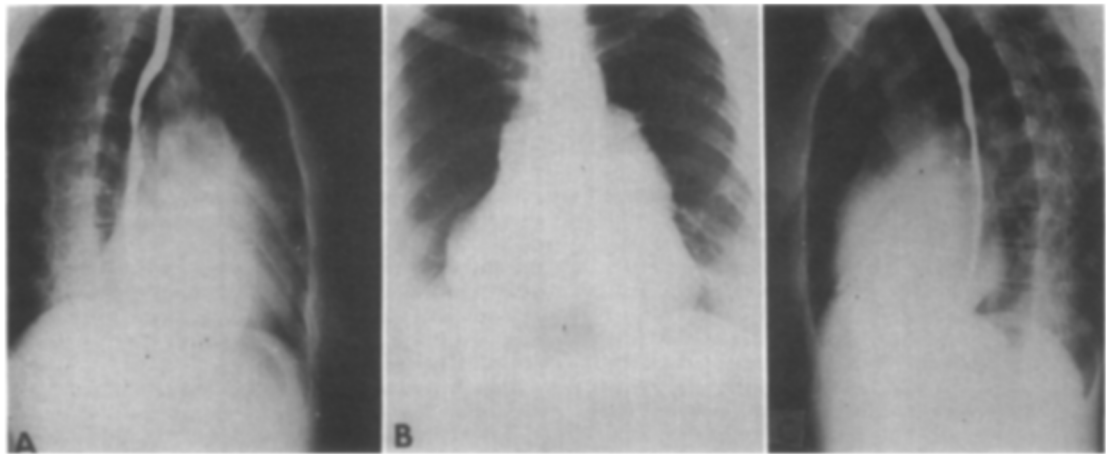

Fig. 3. X-rays, June, 1965. *A*, Right oblique position, *B*, posteroanterior direction, and *C*, left oblique position.

the electrocardiographic evidence of right ventricular strain, it was assumed that the pulmonary stenosis had rapidly increased in severity and that, in addition, a right-to-left shunt had developed—probably at an atrial level through a patent foramen ovale or an atrial septal defect overlooked at the first heart catheterization. The probable aggravation of the stenosis, in conjunction with the abnormal x-ray findings, seemed to suggest tumor growth in the outflow tract of the right ventricle. In order to achieve maximum certainty in ruling out a reversible abnormality, heart catheterization was carried out in combination with angiocardiography.

Low oxygen values were found in the right heart. The catheter (introduced via the right great saphenous vein) could be passed into the left atrium through the atrial septum. In the left atrium, and also in a pulmonary vein, normal oxygen saturation was found. The saturation in the femoral artery proved to be greatly diminished. The saturation and pressure values found are shown in Table I. The withdrawal curve from the left pulmonary artery to the right ventricle shows two systolic pressure increases: one of 26 mm. Hg in the trunk of the pulmonary artery, and another of 32 mm. Hg in the outflow tract of the right ventricle (Fig. 5). It was impossible to reach the right pulmonary artery. The pressure curve of the right ventricle disclosed mechanical alternation. The diastolic pressure was slightly increased. The right atrial

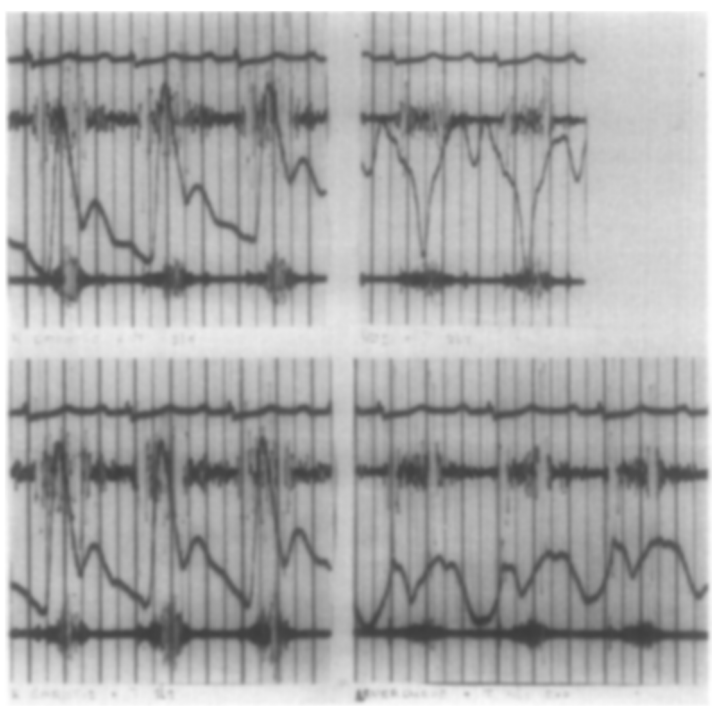

Fig. 4. Phonocardiogram, June, 1965. Above, left, carotid tracing with sound tracing above the pulmonary area; above, right, venous tracing with sound tracing same area. Below, left, carotid tracing with sound tracing below left clavicular bone; below, right, pulse tracing taken over hepatic area with sound tracing at left lower sternal border.

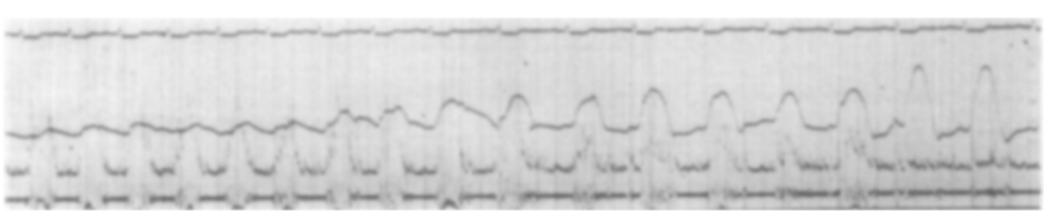

Fig. 5. Heart catheterization, June 10, 1965; withdrawal tracing from left pulmonary artery to right heart chamber. ECG, pressure curve and intracardiac phonocardiogram.

curve showed increased pressure; a deep y descent was seen.

At cineangiocardiography, contrast medium injected into the superior vena cava was seen to flow to the left heart at the level of the atrium. Some filling defects were visible in the trunk of the pulmonary artery. Especially in the left oblique projection, the trunk showed a distinctly reduced diameter. The right pulmonary artery did not fill: only a trace of contrast medium was visible at the beginning of this vessel. The left heart shadow, originally mistaken for the conus arteriosus, extended far laterally beyond the limits of the contrast medium. The left main branch seemed slightly dilated. From the left atrium, the left ventricle, and aorta filled in the normal manner (Fig. 6).

The data obtained by heart catheterization and angiocardiography indicated occlusion of the right pulmonary artery—a supravalvular and infundibular stenosis—caused by an expanding process; the heart shadow showed an extraluminal expansion to the left at the site of the conus arteriosus, and a right to left shunt existed at an atrial level.

On the basis of these findings, we diagnosed a malignant tumor of the heart, chiefly affecting the outflow tract of the right ventricle and also invading the pulmonary artery.

The patient's condition remained unchanged until the sudden death on June 15, 1965.

Postmortem findings. The mediastinum contained a tumor the size of a coconut, growing from the heart. The heart with the tumor weighed a total of 1,150 grams. Tumor tissue covered two-thirds of the heart surface, and a large nodular mass had formed, mainly at the site of the conus arteriosus. Here, the tumor had penetrated the muscular wall of the right ventricle, causing stenosis of the infundibulum (Fig. 7). The tumor had also invaded the wall of the pulmonary artery, constricting this artery to a mere crevice (Fig. 8). The intra-arterial tumor follows the course of this artery and, beyond the bifurcation, causes complete obstruction of the right pulmonary artery. Between the greatly dilated right atrium and the normal left atrium, the foramen ovale is wide open (the diameter of the round opening is 1 cm.). The right ventricle shows marked hypertrophy and its muscular wall is 1.3 cm. thick. The wall of the left ventricle is of normal thickness. The aortic valves are intact, as is the aorta, although this vessel is completely enveloped in tumor tissue.

The microscopy of the tumor is that of a polymorphous round cell sarcoma with extensive necrosis (Fig. 9).

Both the liver and the spleen are enlarged (weights of 1,800 and 190 grams, respectively), and microscopically both show congestion. No metastases are to be found.

Table I. *Data of heart catheterization Oct. 6, 1965*

Situation of catheter tip	*Oxygen saturation (per cent)*	*Pressure (mm. Hg)*
Vena cava inferior	46.5	—
Vena cava superior	44.40	—
Right atrium	43	10/6
Right ventricle	42	86/4/12
Right ventricle outflow tract	—	54/8/14
Pulmonary artery trunk	35	50/20
Left pulmonary artery	—	28/17
Vena pulmonalis	99	—
Left atrium	96.5	10/6
Left ventricle	—	72/0/4
Femoral artery	77	—

Discussion

Primary tumors of the heart are known to be rare. Cases reported in the literature are reviewed in a few publications.[2-6] The diagnosis is impeded by the frequent absence of clinical symptoms or the lack of specific symptoms. A tumor localized in or near a heart valve can produce symptoms of stenosis or insufficiency of the

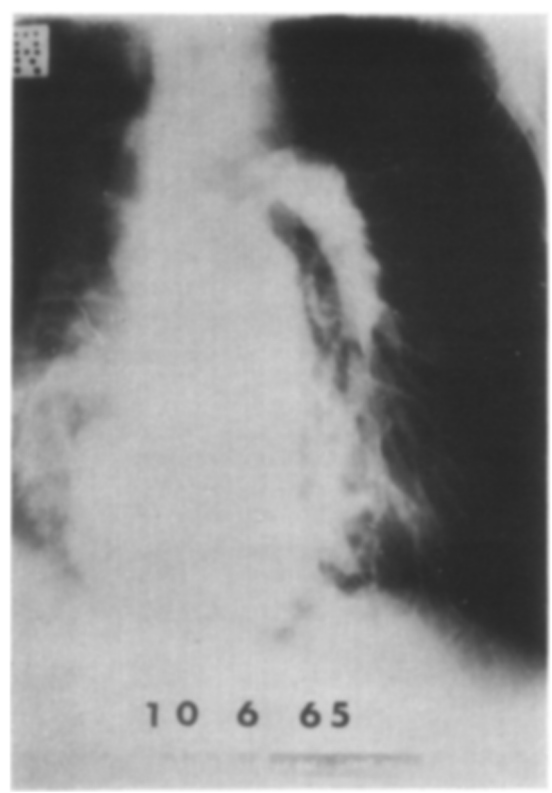

Fig. 6. Angiocardiogram June 10, 1965; contrast injection in superior vena cava, P-A position.

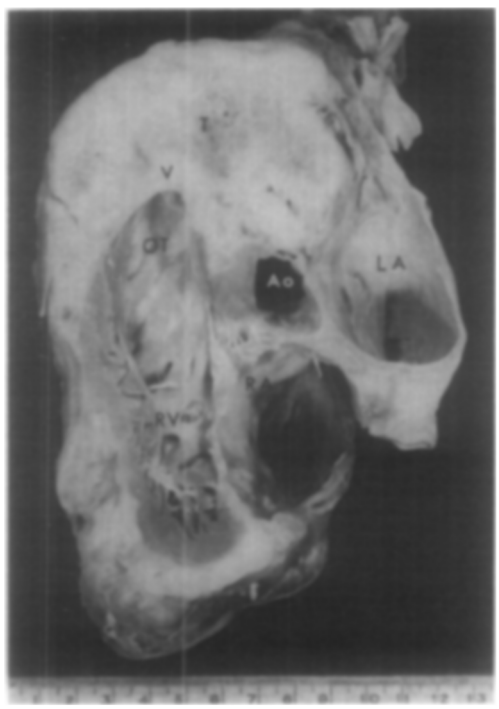

Fig. 7. Cross-section through the heart with right ventricle (*R.V.*), outflow tract (*OT*), and just visible pulmonary valves. The outflow tract is narrowed and surrounded by tumor tissue (*V*).

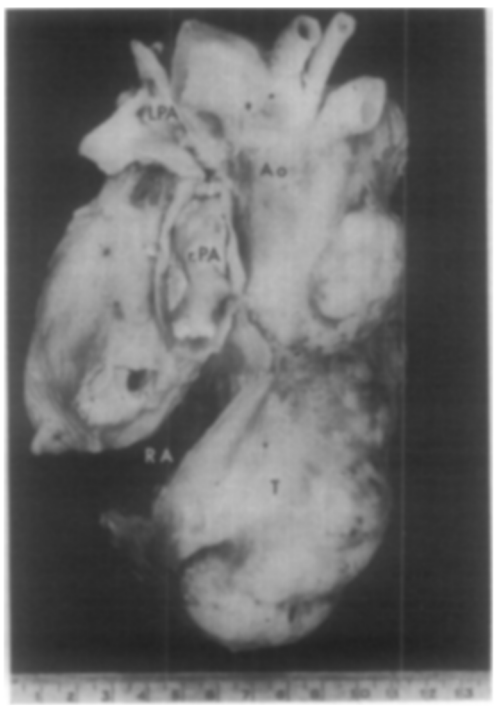

Fig. 8. The pulmonary bifurcation has been opened, the right pulmonary artery is obliterated by tumor tissue.

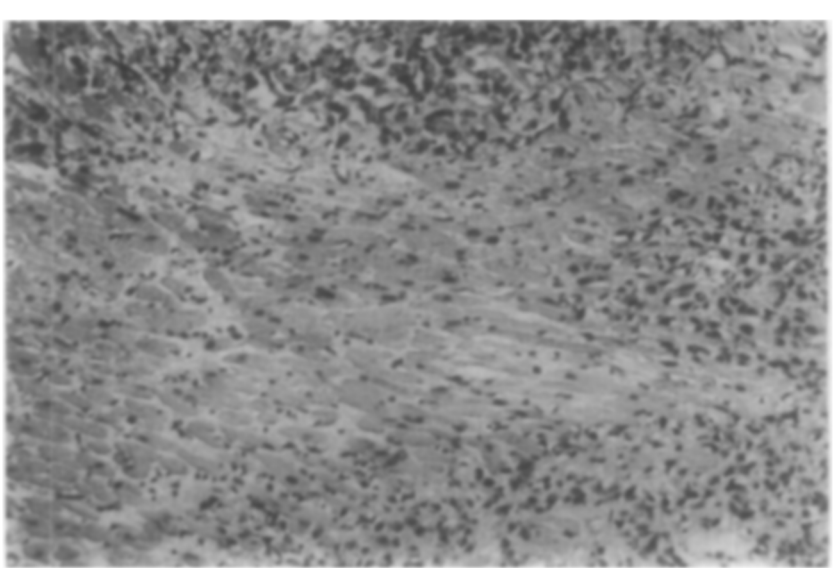

Fig. 9. Microscopical view of the tumor: The tumor invading the myocardial muscle fibers.

valve in question. Of the malignant heart tumors described, a number have been localized in the outflow tract of the right ventricle or in the pulmonary artery. In these cases, the diagnosis was generally not made before autopsy.[7-21] A number of these tumors seemed to grow from the wall of the pulmonary artery.

In the course of subsequent years, improved diagnosis with the aid of heart catheterization and angiocardiography made it possible to detect a few cases of such tumors with pulmonary stenosis in living patients.[22,23] In the case described by Pund and associates,[24] the diagnosis was established on the basis of a cytological study of pericardial and pleural fluid.

In the woman described in this report, the tumor initially manifested itself (at a cardiological study made elsewhere) as an isolated infundibular pulmonary stenosis. In the terminal stage of illness, hemodynamic data in addition demonstrated a supravalvular pulmonic stenosis and a right to left shunt at an atrial level. Angiocardiography disclosed filling defects caused by tumor growth, and confirmed the diagnosis.

The records of the pathological institute proved to include two other reports on primary sarcomas of the heart, which also had caused stenosis of the pulmonary artery. In view of the paucity of clinical data, it is our intention to discuss the pathological anatomical findings in these cases in another publication.

Pathologists have pointed out the existence of benign tumors of the pulmonary valves, many of which are unimportant from a hemodynamic point of view. Catton and co-workers,[25] however, described a case of severe pulmonic stenosis caused by a myxoma, diagnosed on the basis of angiocardiographic findings. Of the benign tumors growing from the right ventricular wall, we would like to mention rhabdomyomas, which are usually localized in the septum and can produce an infundibular form of pulmonic stenosis; these tumors, too, may remain unimportant from a clinical point of view. Angiocardiographic studies have proved useful in these cases also.[26] There are likewise some reports on myxomas arising from the right ventricular wall.[27-30] A critical review of the further pertinent literature has been made by Sakakibara and associates.[30]

Clinical identification of benign tumors is of evident importance with a view to developments in cardiac operation. Extracardiac tumors can cause pulmonic stenosis by compression.[1,31-40] In a number of cases, this has been diagnosed in living patients.[1,35-40]

Summary

A description is given of a case of primary sarcoma growing from the right ventricular wall of the heart, with stenosis of the pulmonary artery as a result of invading tumor tissue. Two other cases are mentioned.

In the case described, the initial manifestation suggested an isolated infundibular pulmonic stenosis. A right to left shunt through a patent foramen ovale developed later.

The diagnosis was established by angiocardiography during the patient's life.

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