Alveolar Rhabdomyosarcoma Involving the Heart
An Echocardiographic, Angiographic and Pathologic Study

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SUMMARY
A 12-year-old girl, who had had an above-knee amputation of the left leg for a soft tissue sarcoma six years prior to this admission, presented with syncope, angina, and signs of aortic stenosis. Echocardiography demonstrated a mass arising from the interventricular septum with obstruction of the left ventricular outflow tract and aortic valve. Cardiac catheterization and angiography confirmed these findings. At operation, a tumor was found involving the interventricular septum. Histologically, it was an alveolar rhabdomyosarcoma, and it appeared similar to the previous tumor. The patient was treated by partial surgical resection, cytotoxic drugs and localized radiation therapy and has been followed by serial echocardiography.

PRIMARY OR SECONDARY cardiomas are uncommon in infancy and childhood. The rhabdomyoma is the most frequent neoplasm in the pediatric age group; in 50% of cases this tumor occurs in association with tuberous sclerosis and is usually found in children less than two years of age.

The clinical presentation resulting from cardiac tumors is variable and depends partly upon the anatomic location. Left ventricular outflow obstruction has been documented in some cases.

Echocardiography has been useful in suggesting the diagnosis of various cardiac tumors such as right and left atrial myxomas, right atrial extension of Wilms' tumor and ventricular rhabdomyoma.

The purpose of this report is to describe the echocardiographic diagnosis, angiographic features, and clinical pathologic correlation of a tumor that obstructed the aortic valve in a child.

Case Report
A 12-year-old white female was referred for evaluation in May 1975. She had experienced a syncopal episode preceded by chest pain after she had run down some stairs at school. Several other episodes of chest pain and dizzy spells on exertion had been noted in the weeks prior to the syncopal episode. Six years previously, she had undergone an above-knee amputation of the left leg for a soft tissue sarcoma which was interpreted at that time as a liposarcoma. There had been no further therapy and yearly follow-up examinations failed to reveal any evidence of recurrence or metastasis.

The physical examination showed an anxious, preadolescent female with a prosthetic left leg. Palpation of the amputation stump revealed no evidence of a locally recurrent mass and the lymph nodes in the left inguinal region and elsewhere were not enlarged. Excluding the cardiovascular system, there were no other detectable abnormalities on clinical examination of the organ systems.

By palpation, the radial and femoral pulses were of normal volume and character. Blood pressure in the right arm was 95/60 mm Hg. There was no elevation of the jugular venous pressure. The apex beat was palpable in the fifth intercostal space within the midclavicular line. A systolic thrill was palpable over the left precordium and over the carotid artery. On auscultation, the first heart sound was normal. A soft ejection click followed by a grade IV/V systolic ejection systolic murmur was heard best along the left sternal border and in the neck. Paradoxical splitting of the second heart sound was noted by several observers. No diastolic murmurs were audible.

The chest roentgenogram revealed no evidence of cardiomegaly or prominence of the ascending aorta and the lung fields were within normal limits. An electrocardiogram showed left ventricular hypertrophy.

Other investigations, including hemogram, urinalysis, skeletal survey, intravenous pyelography and tomograms of the skull, were normal.

Echocardiogram
An echocardiogram was performed with the patient in the supine position and the transducer positioned in the third and fourth left intercostal spaces. A 2.25 MHz transducer and Ekoline 20A machine interfaced with a Honeywell strip chart recorder were used for the recordings.

The parallel echoes of the aortic wall were located. Aortic cusps were filled during systole by a dense band of echoes which disappeared in diastole when a normal central diastolic aortic cusp echo could be seen (fig. 1). The left atrium did not show any abnormal echoes. On angling the transducer inferiorly toward the mitral valve, a dense mass of echoes was recorded anterior to the mitral valve partly separated from the interventricular septal echo (fig. 2). More inferiorly, this mass of echoes became continuous with the septum (fig. 3), while in the lowermost portion of the ventricle, normal septal and ventricular posterior wall were recorded without any abnormal intervening echoes (fig. 4).
ing the left ventricular outflow tract and aortic valve. A right ventriculotomy was performed and the tumor seemed to have a wide base involving the entire ventricular septum and extending onto the right side. On frozen section examination, a diagnosis of malignant mesenchymal tumor was made. The tumor was partially resected from the left side through the left atrium leaving some residual tumor in the interventricular septum. The postoperative course was uneventful except for a period of transient complete heart block.

After a short convalescence period to allow for wound healing, she was treated with 3,500 rads of radiation therapy to the heart with a reduced field concentrating on the interventricular septum. Initial chemotherapy consisted of actinomycin D (0.015 mg/kg/day intravenously for five days); vincristine sulfate (2 mg/m² intravenously weekly for 12 weeks); on the sixth week cyclophosphamide was started at 2.5 mg/kg/day orally. The plan is to continue the five day courses of actinomycin D at 12 week intervals for one year and the oral cyclophosphamide for 2 years.

Pathologic Examination

Frozen section preparations were made from fragments of the tumor obtained from the ventricular septum during the course of the surgical procedure. A neoplasm of small basophilic cells was identified on microscopic examination.

The gross specimen consisted of a lobulated, rubbery, pinkish-grey mass which measured 4.3 × 2 cm and had a glistening outer surface (fig. 7). The cut surface had an irregular, slightly trabeculated appearance. Histologically, the tumor had an alveolar pattern very similar to that of the neoplasm resected from the leg six years previously (fig. 8). There was infiltration and replacement of the myocardium by tumor cells. Extensive myxoid and hyaline degeneration of the stroma was a prominent feature of the mass in the area which projected through the aortic valve. In these foci, the histologic appearance resembled superficially that of a cardiac myxoma. A diagnosis of an alveolar rhabdomyosarcoma was made.

The original soft tissue tumor in the lower extremity was

<table>
<thead>
<tr>
<th>Table 1. Cardiac Catheterization Data</th>
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<tbody>
<tr>
<td>Pressure (mm Hg)</td>
</tr>
<tr>
<td>Right atrium a = 8, v = 8, x = 4, y = 4, mean = 5</td>
</tr>
<tr>
<td>Right ventricle 32/0.8</td>
</tr>
<tr>
<td>Pulmonary artery 32/10, mean = 24</td>
</tr>
<tr>
<td>Right lower lobe wedge, a = 20, v = 14, x = 11, y = 11, mean = 14</td>
</tr>
<tr>
<td>Left ventricle 190/0-20</td>
</tr>
<tr>
<td>Aorta 110/75</td>
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</table>

FIGURE 4. Echocardiogram with transducer angled inferiorly toward left ventricular cavity below mitral valve. Normal septum and left ventricular posterior wall recorded with no abnormal echo mass from the septum or in the left ventricle. IVS = interventricular septum, LV = left ventricle.

FIGURE 5. Aortogram showing nonopacified filling defect within the aortic valve during systole (A), while in diastole (B) normal aortic sinuses can be seen.
located in the gastrocnemius region and described as a partially hemorrhagic and mucoid mass. There was no evidence that the bone was involved by the tumor. Microscopic sections showed a highly cellular malignant neoplasm composed for the most part of uniform cells which were arranged in loose clusters within fibrovascular septa. An alveolar pattern was the result of the segregation of tumor cells by the septa (fig. 8A). Large neoplastic cells, some with conspicuous amounts of brightly acidophilic cytoplasm were noted among the smaller cells. Cytoplasmic cross-striations were identified in a few of the multinucleated cells. Although the tumor was circumscribed at the periphery, it lacked a capsule. Invasion of the blood vessels was not observed. Interpretation of the neoplasm was that it represented an alveolar rhabdomyosarcoma and not a liposarcoma.

Postoperative Echocardiograms

Echocardiograms have been performed at monthly intervals since surgery (now nine months ago). While initially there was some residual thickening of the interventricular septum, this is now less obvious. Septal motion is normal. Aortic cusps, aortic root, left ventricular outflow tract and mitral valve are all normal (figs. 9, 10).

Discussion

The clinical presentation of a cardiac tumor is variable. In addition to nonspecific constitutional symptoms such as malaise and weight loss, cardiac problems such as arrhythmias, pericarditis with or without effusion, embolic phenomena and left or right-sided inflow or outflow obstruction have been described. Obstructive phenomena are dependent upon the anatomic location of the tumor. Subaortic stenosis has been documented in cases of rhabdomyoma in infancy and in left ventricular myxoma or clot in adults.

Our patient presented with syncope, angina, and signs of severe aortic stenosis. Although a phonocardiogram was not recorded, several experienced observers documented an aortic ejection click and paradoxical splitting of the second sound. We believe the ejection sound was produced by the sudden impact of the tumor against the aortic valve and surrounding structures during early systole. This is similar in origin to the diastolic opening sound described in cases of left atrial myxoma. The paradoxical splitting of the second sound suggests severe aortic stenosis, although it could have been produced by mechanical interference with valve closure.

The echocardiographic findings documented in this case were different from those seen in congenital valvar or membranous subvalvar stenosis or in idiopathic hypertrophic obstructive cardiomyopathy. During ventricular systole, a dense mass of echoes filled the aortic valve while during diastole a normal central closure line of the aortic cusps was seen. Below the aortic valve a dense mass of echoes involving the interventricular septum and left ventricular outflow tract.

FIGURE 6. Left ventriculogram in early systole (A) showing nonopacified defect in left ventricular outflow tract and aortic valve. During diastole (B), multiple nonopacified filling defects are seen within the left ventricle.

FIGURE 7. Gross anatomy of the tumor showing cut (A) and smooth external surface (B). Tumor size is 4.3 × 2 cm. The constricted area in the middle of the specimen was thought to represent a point where the tumor was compressed by the left ventricular outflow tract and aortic valve ring.
zation and ranged from 24 to 46 ml/m² (mean 36). LVEF and LV outputs were normal in all four infants.

The single patient (E.S.) with TI secondary to possible Ebstein's anomaly based on the angiocardiographic appearance of tricuspid displacement and the prolonged QRS duration on ECG initially had the most abnormal RA max volume and RVEDV. These values decreased toward normal in relative and absolute values during the six month period between the first and second catheterization. It was possible that the quantitative differences in RA max volume and RVEDV in this infant from the other three represented only a difference in the severity of the TI since it is unlikely that these values would differ depending on the etiology of the TI. In those infants with the most severe TI, the absolute values of the RA max volume and RVEDV corrected for BSA actually decreased.

Discussion

Cineangiocardio graphic volume data have proven to be useful and objective means of quantitating chamber volume, ejection fraction and stroke volume. As indicated in figures 5 and 6, three of the four infants initially had significantly increased RA maximal volume and RVEDV. The clinical severity of the tricuspid insufficiency seemed to correlate with the degree of abnormality of these values. One infant with clinically moderate TI but massive cardiomegaly had increased RA maximal volume but a normal RVEDV. These results suggest that RA maximal volume and RVEDV might be useful in quantitating TI in certain patients. Those patients with mild incompetence may have elevated RA max volume and normal RVEDV, while in

- Table 2. Compilation of the Angiographically Determined Right Heart Volumes Corrected for Body Surface Area and the Intensity of the Systolic Murmur

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age</th>
<th>RA max vol (ml/m²)</th>
<th>RVEDV (ml/m²)</th>
<th>Grade of murmur*</th>
</tr>
</thead>
<tbody>
<tr>
<td>G.H.</td>
<td>3 days</td>
<td>50</td>
<td>45</td>
<td>I/VI</td>
</tr>
<tr>
<td></td>
<td>18 months</td>
<td>51</td>
<td>56</td>
<td>I/VI</td>
</tr>
<tr>
<td>K.H.</td>
<td>2 days</td>
<td>97</td>
<td>151</td>
<td>III/VI</td>
</tr>
<tr>
<td></td>
<td>15 months</td>
<td>63</td>
<td>119</td>
<td>I/VI</td>
</tr>
<tr>
<td>M.S.</td>
<td>2 days</td>
<td>227</td>
<td>76</td>
<td>III/VI</td>
</tr>
<tr>
<td></td>
<td>4.5 months</td>
<td>81</td>
<td>40</td>
<td>I/VI</td>
</tr>
<tr>
<td>E.S.</td>
<td>1 day</td>
<td>271</td>
<td>137</td>
<td>IV/VI</td>
</tr>
<tr>
<td></td>
<td>6 months</td>
<td>136</td>
<td>67</td>
<td>II/VI</td>
</tr>
</tbody>
</table>

*Intensity of the systolic murmur graded on a I–VI scale.

- Figure 5. The right atrial maximal volumes, expressed as a percent of normal for a corresponding body surface area and calculated from the initial and follow-up angiograms of all four patients, are plotted as a function of age at the time of study. The normal range is depicted by the shaded area.

- Figure 6. The right ventricular end-diastolic volumes, expressed as a percent of normal for a corresponding body surface area and calculated from the initial and follow-up angiograms of all four patients, are plotted as a function of age at the time of study. The normal range is depicted by the shaded area.
Figure 8. Histology of alveolar rhabdomyosarcoma of the lower extremity (A) showing large mono- and binucleated tumor cells with intensely acidophilic cytoplasm. Smaller mononuclear cells were loosely adherent to the delicate fibrovascular septa that produced the alveolar appearance. Histology of the heart (B) showed a similar arrangement of the tumor cells although the alveolar pattern was less apparent. Some of the cells with cross-striations were considered entrapped in myocardial fibers. (Hemotoxylin and eosin A × 125, B × 175.)

Figure 9. Postoperative echocardiogram showing a recording of aortic cusps during systole and diastole with no abnormal echoes.

Figure 10. Postoperative echocardiogram recorded at the junction of the left ventricular outflow tract and left ventricle showing normal interventricular septum and mitral valve. The preoperative echo mass is not present.
was visualized. This mass of echoes was anterior to the mitral valve echo which was consequently distorted. The echocardiographic findings in our cases are similar in some respects to those described in a recent case of left ventricular myxoma or thrombus and to a previously reported case of left ventricular rhabdomyoma involving the left ventricle in infancy. However, the echo mass in our case was far more extensive and clearly obstructed the aortic valve. The lack of any abnormal echoes within the left atrium or mitral valve appeared to exclude the possibility of a pedunculated left atrial myxoma being extruded through the mitral valve.

Aortography and left ventricular cineangiography confirmed the presence of a large multilobed mass within the left ventricle which could be seen to obstruct the aortic valve during systole. These findings are similar to those previously documented in tumors within the left ventricle.

Rhabdomyosarcoma of the heart is one of a number of morphologically distinct neoplasms which have been reported in this location. The benign tumors are well characterized, by cell type, as rhabdomyomas, fibromas and myxomas. The classification of cardiac sarcomas is less definite. While malignant soft tissue tumors of the extremities can usually be classified as fibromas, liposarcomas or rhabdomyosarcomas, the cardiac sarcomas are frequently poorly differentiated and the basic cell type uncertain. This situation is best exemplified by Whorton's review of 100 primary malignant tumors of the heart. Forty-seven of the cases were designated as "spindle-cell," "polypoid" or "round cell sarcoma." When the tumor is sufficiently differentiated, it is generally recognizable as smooth or striated muscle or consisting of vascular spaces, i.e., leiomyosarcoma, rhabdomyosarcoma and angiosarcoma, respectively.

Our patient had a polypoid neoplasm infiltrating the interventricular septum and projecting into the left ventricular cavity. The histopathologic features were unquestionably those of an alveolar rhabdomyosarcoma. Grossly, the tumor in our patient was typical of the growth pattern and configuration associated with primary neoplasms of the heart.

In general, the heart is an uncommon site for rhabdomyosarcoma; most occur in the pelvis, head and neck, and limbs. Approximately 40 primary rhabdomyosarcomas of the heart have been reported in the literature; of these approximately 25% occurred in patients less than 20 years of age.

The clinical and pathologic problem of distinguishing between a primary or metastatic carcinoma is well illustrated in this case. Rhabdomyosarcoma frequently metastasizes to the heart. An argument could be raised on the basis of prior experience with metastatic rhabdomyosarcoma that our patient developed a second primary tumor which, by chance, showed the same histologic pattern as the neoplasm excised six years previously. The points favoring the conclusion that the second tumor was primary and not a metastasis from the first tumor include the prolonged period of time separating the development of clinical manifestations of the second tumor from the removal of the first, the absence of other metastatic foci, and the solitary nature of the tumor in the heart.

The treatment of this patient has included partial surgical resection and combined radiation and cytotoxic therapy. These modalities have resulted in complete relief of symptoms and have reduced the risk of sudden death from severe left ventricular outflow obstruction. Long-term control of this patient is a distinct possibility with the use of combined therapy. Echocardiography afforded precise diagnostic data in the preoperative phase of this patient's care and is now being applied as a noninvasive approach to assessment of her postoperative course.

Acknowledgment

We are grateful to Cheryl Lawrence for technical assistance.

References

27. Manson G, Rundkopf W: Bilateral adolescent mamnopathy as a presen-
28. Nicol AG, McAndrew GM: Cardiac leiomyosarcoma: primary or secon-
29. Lawrence W, Jegge G, Foote FW: Embryonal rhabdomyosarcoma: A
30. Nadas AS, Ellison RC: Cardiac tumors in infancy. Am J Cardiol 21: 363,
1968
31. Pratt CB, Dugger DL, Johnson WW, Ainger LE: Metastatic involvement
of the heart in childhood rhabdomyosarcoma. Cancer 31: 1492, 1973
32. Enzinger FM, Shiraki M: Alveolar rhabdomyosarcoma. An analysis of
110 cases. Cancer 24: 15, 1969
33. Fernandez CH, Sutow WW, Merino OR, George SL: Childhood rhab-
domyosarcoma. Analysis of coordinated therapy and results. Am J
Roentgen Radium Ther Nucl Med 123: 588, 1975
Alveolar rhabdomyosarcoma involving the heart. An echocardiographic, angiographic and pathologic study.
G S Orsmond, L Knight, L P Dehner, D M Nicoloff, M Nesbitt and F B Bessinger, Jr

Circulation. 1976;54:837-843
doi: 10.1161/01.CIR.54.5.837

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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