COMPLETE RESECTION OF A PRIMARY CARDIAC RHABDOMYOSARCOMA

Case Report, Review of the Literature, and Management Recommendations

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A case of primary cardiac rhabdomyosarcoma in a 23-year-old white man was managed by complete excision and combination chemotherapy. The pathologic features of the tumor are described. Based on a review of the English literature, the natural history of this tumor is discussed and a plan of therapy is proposed, which consists of (1) resection of the tumor if feasible, (2) chemotherapy with Actinomycin D, vincristine sulfate, and cyclophosphamide, and (3) cardiac radiation for residual unresected or locally recurrent tumor.

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Primary tumors of the heart are variously reported as occurring in 1 in 4,000 to 1 in 10,000 necropsies.[1-4] Only 20 to 30% are malignant, and those are nearly equally divided between angiosarcoma, fibrosarcoma, and rhabdomyosarcoma.[4-6] Histologic criteria for the diagnosis of these sarcomas has been controversial, and systems of classification have changed.[7-9] In a review of the English literature, we could find reports of only 40 cases of primary cardiac rhabdomyosarcoma.[1-3,5-8,10-42]

We recently cared for a patient with a primary cardiac rhabdomyosarcoma who was unusual in two respects. First, the diagnosis was established by echocardiography and cardiac catheterization while the patient was alive and prior to any tumor embolization or apparent metastasis; and second, complete surgical resection of the tumor was possible. Complete excision of a primary malignant cardiac tumor has been previously reported only once.[15]

CASE REPORT

A 23-year-old white man presented to his station dispensary with a history of cough and dyspnea of several weeks' duration. He was initially treated for an upper respiratory infection without improvement. Over the following six weeks his symptoms progressed to dyspnea on minimal exertion, two-pillow orthopnea, nearly continuous non-productive cough, and a 12-pound weight loss. He particularly noted that lying on his left side was intolerable because of severe dyspnea. During that time, a number of diagnoses were considered. These included viral pneumonitis, atypical myocarditis, alcoholic cardiomyopathy, and flail mitral valve. The favored diagnosis at the time of his referral to us was congestive heart failure due to flail mitral valve.

Physical examination on admission showed an acutely ill man in moderate distress due to dyspnea. The temperature was normal; the blood pressure was 110/80 mm Hg and the pulse was 110 and regular. The neck veins were distended to the angle of the jaw in the 30° head-up position, and rales were heard in all lung fields. Cardiac examination showed the PMI in the 5th intercostal space at the mid-clavicular line. There were no thrills or thrusts. The first heart sound was normal. The pulmonic component of the second heart sound was split physiologically. There was a Grade 2/6 systolic ejection murmur along the left sternal border best heard in the supine position, and a Grade 2/6 diastolic blowing murmur along the left sternal border. A harsh Grade 2/6 late systolic plateau-shaped murmur was heard at the lower left sternal border and apex radiating to the left axilla. A Grade 3/6 apical diastolic rumble was evident when the patient was in the left lateral decubitus position. In the sitting position, a prominent opening sound or "knock" was heard approximately 0.08 seconds after the second heart sound. The remainder of the physical examination was normal.

Hematologic and blood chemistry surveys were normal except for a WBC of 12,500 with a normal differential and a sedimentation rate of 56 mm/hr. An EKG showed sinus rhythm, left atrial enlargement, and nonspecific ST-T wave changes. A chest X-ray film revealed left atrial enlargement and pulmonary edema. An echocardiogram disclosed echodensities in the left atrium and in the mitral valve during diastole, establishing the diagnosis of a left-sided intracavitary mass.

At cardiac catheterization the cardiac index was 2.0 L/min/m^2. Pulmonary artery pressure was 90/50 mm Hg ($\overline{m}$ 65 mm Hg), and the PA wedge showed an A wave of 40 mm Hg, a V wave of 65 mm Hg, and a mean pressure of 45 mm Hg. Aortic pressure was 95/60 mm Hg ($\overline{m}$ 75 mm Hg), and the left ventricular pressure was 95/12 mm Hg. Gradients across the mitral valve were 31 mm Hg end-diastolic and 35 mm Hg mean. Evaluation of simultaneous left ventricular and pulmonary artery wedge curves showed findings consistent with Sungs Type I intracardiac tumor.[43] There was notching of the systolic upstroke on the left ventricular curve, and a peaked V wave with a rapid y descent on the pulmonary artery wedge curve. Levophase pulmonary angiogram in the 30° RAO position demonstrated a dumbbell-shaped filling defect in the left atrium extending through the mitral valve orifice and into the left ventricle.

At exploration of the left atrium, a large tumor was found originating from a fibrous stalk, 2.8 cm in diameter, which was attached to the posterior atrial wall between the orifices of the right and left pulmonary veins. The tumor filled the left atrium, passed through the mitral valve, nearly occluding it, and occupied much of the left ventricular cavity. There was no evidence of attachment to the intraatrial septum. Because of the size of the tumor, it was necessary to detach it from its point of fixation by cutting across the fibrous stalk before it could be delivered from the heart. The remaining stalk, with a margin of normal left atrial posterior wall, could then be excised. The resulting defect, which extended from the right pulmonary veins to the left pulmonary veins, was repaired with a composite patch of pericardium intracavitary and Dacron velour extracavitary. The right-sided chambers were inspected through a right atriotomy to rule out other unsuspected involvement.

The postoperative course was entirely uneventful, and the patient was discharged on the eighth postoperative day. He was reevaluated for metastases after a period of convalescence at home. Brain, bone, and liver-spleen scans were negative for metastasis. All blood chemistries were normal, and an EKG and echocardiogram were normal. In spite of the fact that the tumor had been completely excised, and the metastatic work-up was normal, the decision was made to use adjuvant chemotherapy because of the usual poor prognosis in rhabdomyosarcoma of any site of origin. He was begun on vincristine sulfate, 2.0 mg/m^2 I.V. weekly for 12 weeks; Actinomycin D, 0.015 mg/km/day for 5 days, to be repeated every 3 months for a total of 5 courses; and cyclophosphamide, 2.5 mg/kg daily for 2 years.

The patient underwent a 6-month postoperative evaluation, at which time he was asymptomatic and had tolerated his chemotherapy well.

There was no evidence of metastatic disease or of local recurrence. However, 1 month later he presented with mild confusion, and on CAT scan was found to have three brain metastases. Local irradiation to the brain metastases was instituted.

PATHOLOGIC DESCRIPTION

The specimen weighed 120 gm and measured 10 x 8 x 6 cm. It was a tannish-white to dark brown smooth-surfaced mass with a 2.8 x 2.6 cm pale white to light yellow stalk. The distal end of the mass consisted of numerous smooth-surfaced, edematous, grey-white, botryoid structures attached by long stalks to the main tumor mass. The cut surface of the longest stalk, which measured 4.0 x 1.4 cm, showed a hemorrhagic, necrotic region in its most distal aspect. The cut surface of the main tumor mass showed focal areas of hemorrhage surrounded by a pale white to light yellow smooth slippery parenchyma. A 2.5 x 2.0 cm friable area of necrosis was seen (Fig. 1).

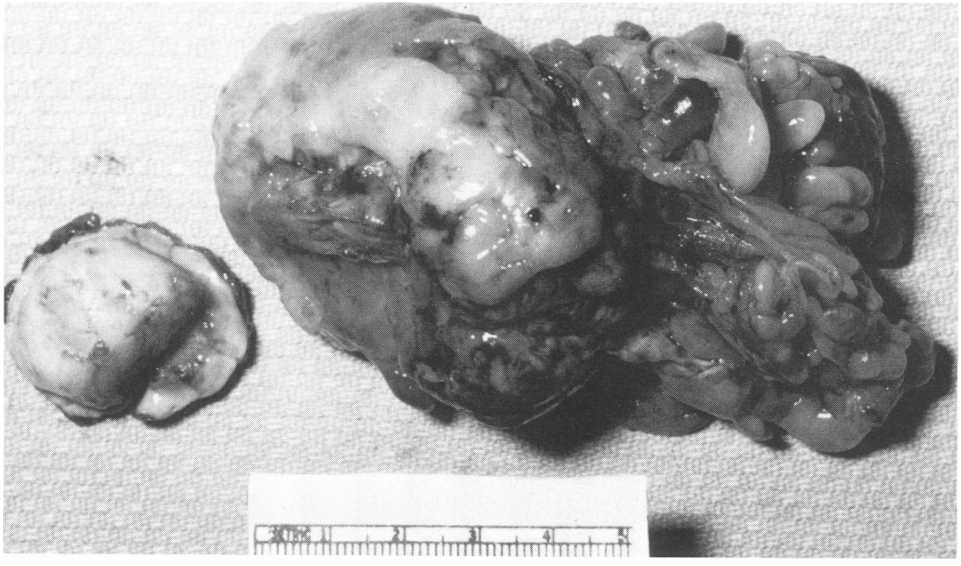

Fig. 1 Gross photograph of resected tumor.

Histologically, this was a highly cellular malignant neoplasm containing focal areas of hemorrhage and necrosis. The tumor cells were arranged in a relatively solid growth pattern with condensation of tumor cells immediately below the tumor surface. The cells were highly pleomorphic, containing irregular hyperchromatic nuclei with prominent nucleoli and atypical mitoses. The cytoplasm was strongly eosinophilic and in many areas had a strap-like appearance. Cross striations typical of myogenous differentiation were easily identified. Tumor cells could not be found within the fibrous stalk, and the cuff of excised atrial wall was free of tumor (Figs. 2 and 3).

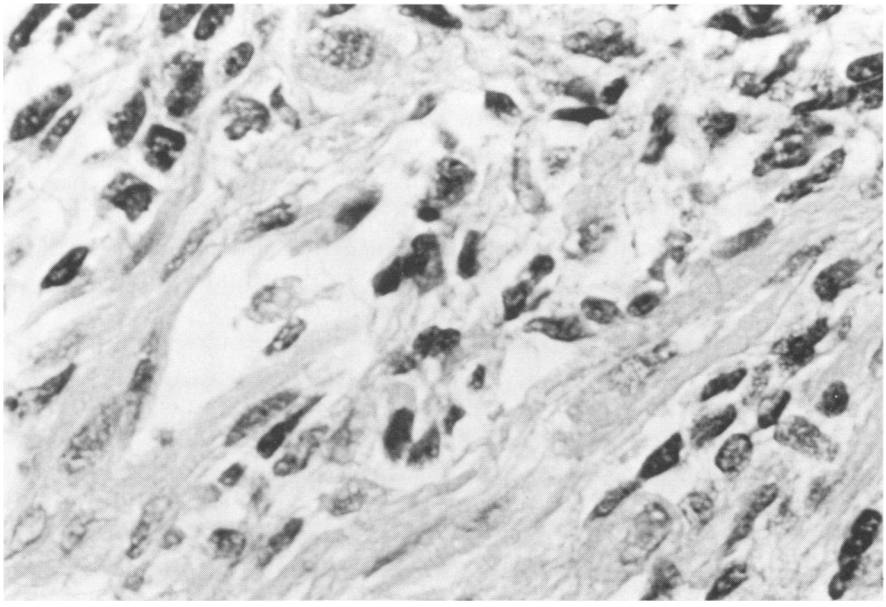

Fig. 2 Photomicrograph showing disorganization of cells, variation in nuclear structure, and cytoplasmic cross-striations. (Hematoxylin and eosin; original magnification x500.)

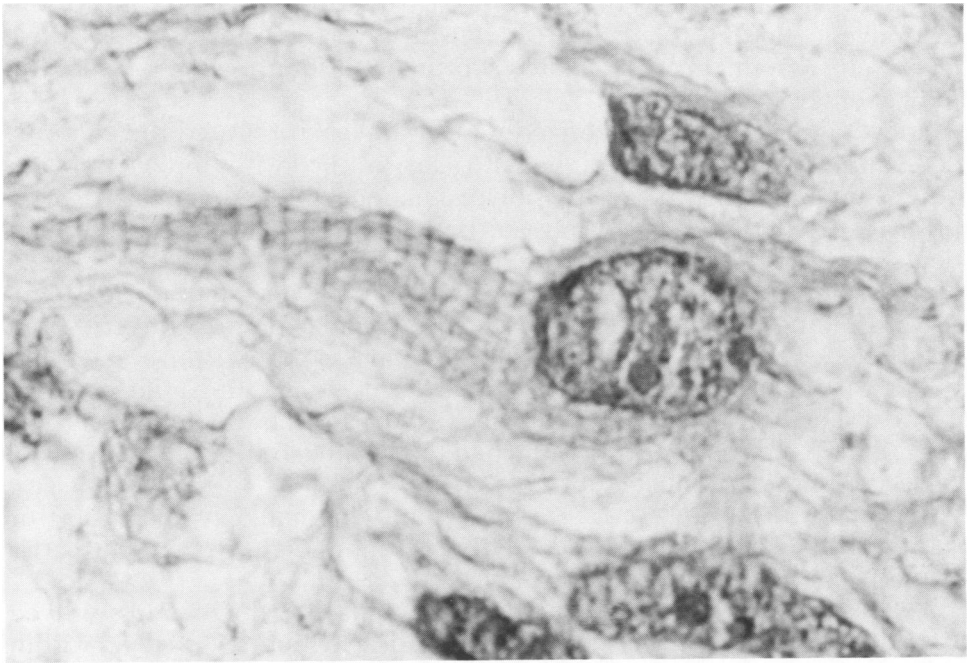

Fig. 3 Photomicrograph showing nuclear detail and prominent cytoplasmic cross-striations. (Hematoxylin and eosin; original magnification x1,250.)

REVIEW OF THE LITERATURE

The English literature was searched to determine the natural history of cardiac rhabdomyosarcoma and to plan the postoperative management for this patient.

Including our patient, 40 case reports of cardiac rhabdomyosarcoma were reviewed.[1-3,5-8,10-42] Twenty-six of the patients were males, and 14 were females. Their ages ranged from a 6 1/2-month gestation stillborn fetus to 81 years, with no particular age group predominating (Table I).

The most common symptoms were dyspnea or orthopnea, cough, easy fatigability and loss of strength, chest pain, and weight loss (Table II). The most common signs were a precordial murmur, respiratory distress, hepatomegaly, tachycardia, and jugular venous engorgement (Table III).

Chest X-ray reports were given in 27 patients, and EKG reports were obtained in 22 patients. These studies did not tend to be of much help. The chest film showed cardiomegaly in 18, but was otherwise non-diagnostic. EKGs showed right axis deviation in six, changes of ischemia in four, AV block in four, atrial flutter/fibrillation in four, and miscellaneous changes in the rest.

Although rarely used in the patients reported, echocardiography and cardiac catheterization have been more useful. Only two echocardiographic reports were found. One showed slight left atrial enlargement in a patient whose tumor arose from the left atrium and atrial septum.[5] The other revealed a "right ventricular intracavitary tumor, slow anterior mitral valve leaflet diastolic closure rate with inverse posterior mitral valve leaflet movement, and a thickened septum with square-wave paradoxical movement."[36]

Four patients were catheterized. One study corroborated the echocardiographic finding that the right ventricle was filled with tumor;[36] and another suggested pericardial effusion in a patient who had pericardial symphysis due to a tumor of the left ventricle.[12] Findings in the other two patients were similar to those in our patient in that they showed left-sided obstruction. The first study was consistent with a diagnosis of mitral stenosis with pulmonary hypertension, right ventricular failure, and tricuspid insufficiency.[31] The second showed pulmonary hypertension, an elevated pulmonary artery wedge pressure with a large V wave, and a filling defect in the left atrium near the mitral valve, which moved during the cardiac cycle. This patient's tumor was attached to the anterior leaflet of the mitral valve and to the intraatrial septum.[15]

Seventeen tumors were intracavitary and originated from the left or right atrium (Table IV). Two of the three tumors that involved both atria arose from the septum.

Twenty-four reports mentioned the length of time the patient survived after the onset of symptoms. Seventeen of these patients were dead within 6 months. Five had symptoms for a period of 13 to 34 months before they died. The outlook was even more dismal when one considered the time of survival after patients sought medical attention: four died within hours of

TABLE I. Age Incidence

Age in Years	Number of Patients
Less than 1	5
1 - 10	1
11 - 20	6
21 - 30	5
31 - 40	4
41 - 50	4
51 - 60	7
61 - 70	6
Over 70	3

TABLE II. Symptoms

Symptom	Number of Patients
Dyspnea/Orthopnea	22
Cough	10
Loss of Strength/Fatigue	9
Weight Loss	9
Epigastric/Abdominal Pain	5
Tachycardia	5
Ankle Edema	4
Fever	4
Anorexia	4

TABLE III. Signs

Sign	Number of Patients
Precordial Murmur	20
Orthopnea/Respiratory Distress	18
Hepatomegaly	16
Jugular Venous Engorgement	13
Tachycardia/Gallop	13
Cyanosis	11
Rales/Pulmonary Edema	10
Cardiomegaly	9
Ankle Edema	7
Fever	7
Hypotension	5

Table IV. Location

Location	Number of Tumors	Myocardial	Intra-cavitary
Right Atrium	7	1	6
Right Ventricle	8	5	3
Left Atrium	11	0	11
Left Ventricle	3	2	1
Both Atria	3		
All Chambers	3		
Right Atrial Epicardium	1		
Pericardial	1		

seeking help, and all but four died within 6 months. Two survived for 1 1/2 and 2 1/2 years respectively, and they were two of only four patients who received treatment.

The first patient was treated by superficial excision of the tumor and radiation therapy.[31] The second was treated with radiation for involvement of the mediastinum, left upper lobe, and hilum. The primary site of that tumor was not known when the patient was tested.[21] A third patient had total excision of a tumor involving the intraatrial septum and the anterior leaflet of the mitral valve. A Starr-Edwards mitral prosthesis was inserted and no other treatment was given. The patient died 8 months later when recurrent tumor nearly filled the left atrium.[15] The last patient to receive treatment had a partial resection of a tumor which involved the intraatrial septum followed by 3,500 rads of radiation to her heart with a field concentrating on the intraventricular septum. In addition, she was treated with Actinomycin D, vincristine sulfate, and cyclophosphamide on a schedule similar to that used in our patient.[33] A year later she developed another rhabdomyosarcoma of the thigh, which was irradiated. One year thereafter she died suddenly at home. No autopsy was done (personal communication from F. Blanton Bessinger, M.D.).

Nineteen patients were reported to have had metastases to one or more sites. Most commonly involved were lung, liver, mediastinum, kidney, and brain, but many other sites were occasionally involved. Metastases were not present in eleven patients, and in nine the point was not commented upon (Table V).

DISCUSSION

As is unfortunately the case with so many malignancies, the majority of malignant cardiac tumors are beyond the bounds of effective palliation or potential cure by the time the patient is sufficiently symptomatic to seek medical attention. However, this case illustrates that an occasional patient may be helped, at least to the extent of being palliated. With no reported instance of even long-term survival, it is probably not reasonable to hope

TABLE V. Metastatic Sites

Site	Number of Tumors
None	10
Lung	7
Liver	5
Mediastinum	5
Kidney	4
Brain	4
Pulmonary Artery	3
Adrenal	2
Intestine	2
Diaphragm	2
Bone	2
None Stated	8
Thoracic Inlet	1
Pancreas	1
Breast	1
Thyroid	1
Cervical	1
Lymph Nodes	1
Mesentery	1
Stomach	1
Subcutaneous Tissue	1
Intercostal Muscle	1
Thymus	1

for a cure of any patient with a primary cardiac malignancy. Nevertheless, that is our goal, and it can only be achieved by early diagnosis and definitive treatment by surgical extirpation and appropriate adjuvant therapy. As is true in diagnosing the more common benign myxoma, one must first consider the diagnosis when faced with a puzzling patient and do the appropriate study—an echocardiogram. We recently resected a benign left atrial myxoma in a patient who had been having small tumor emboli for 9 months while being treated with steroids for a presumed diagnosis of polyarteritis nodosa. A house officer thought of the diagnosis, and for completeness ordered the echocardiogram which established the correct diagnosis. The echocardiogram can be expected to be abnormal in a large percentage of patients with intracavitary tumors. A cardiac catheterization should then be done to confirm the diagnosis and to define better the anatomy in all patients except those who require immediate surgery as a life-saving measure.

With a diagnosis of tumor, the patient should then be explored and as much tumor as possible resected without further compromising the patient from a cardiac standpoint.

Because primary cardiac rhabdomyosarcoma is such a rare entity, it is not possible to make definitive statements about the proper role of adju-

vant radiation or chemotherapy in the post-resection period. A number of reports have established that radiation to the primary tumor can result in some palliation without resulting in an unacceptable amount of myocardial fibrosis.[21,31,44-47] In addition, combined chemotherapy has been shown to have a significant role in the management of skeletal muscle rhabdomyosarcoma.[48]

Based on these observations, our recommendations for the adjunctive therapy of patients with cardiac rhabdomyosarcoma are these: (1) Patients who are believed to be free of disease after surgical resection should be treated with chemotherapy, using Actinomycin D, vincristine sulfate, and cyclophosphamide on a schedule such as that outlined above. (2) Patients with either residual local tumor, or those with locally recurrent tumor, should, in addition to combined chemotherapy, have local radiation to the heart.

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