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Primary synovial sarcoma of the heart

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Abstract

Primary synovial sarcoma of the heart is very rare, accounting for 5% of cardiac malignancies. Of the few cases reported in the literature to date, nearly all have had a very poor outcome. We present a further case. This uncommon malignancy has no specific symptoms during its development, which results in delayed diagnosis. Echocardiography, chest computed tomography, and magnetic resonance imaging can provide effective information about this tumor. With the identification of the characteristic and diagnostic chromosomal abnormality t(X; 18), this malignancy will become increasingly recognized. Synovial sarcoma of the heart requires surgical intervention to improve the prognosis. Adjuvant and/or genetic therapy pre- or post-operation can help prolong life. Chemotherapy is usually recommended as it may benefit the patients. The key to treatment in the future is to find new therapeutic agents. Further elucidation of the effects of this chromosomal abnormality may lead to better-directed therapies in future. (Cardiol J 2011; 18, 2: 128–133)

Key words: heart, pathology, surgery, synovial sarcoma, tumor

Introduction

The incidence of primary malignant tumor of the heart is extremely low: about 0.02% in a series of autopsies [1, 2]. The incidence among the general population varies between 0.001% and 0.03% [3]. Nearly all are sarcomas: the commonest are angiosarcomas (31%), followed by rhabdosarcomas (21%), malignant mesotheliomas (15%) and fibrosarcomas (11%) [4, 5], with synovial sarcomas only accounting for 5% of malignant tumors of the heart [6–8]. Primary synovial sarcoma of the heart is mentioned in the literature mainly as case reports. It is easy for diagnosis to be delayed due to the non-specific clinical symptoms. No effective treatment measures exist, and the prognosis is very poor, with most patients succumbing within 12 months of diagnosis. We describe a new case and review the previous reports.

Case report

A 39 year-old male patient was referred to our hospital after four months of continuous coughing, expectoration and hemoptysis, initially presumed to be a lung infection, but unresponsive to anti-infective drugs. A chest computed tomographic (CT) scan revealed an enlarged heart with a right ventricular mass. The electrocardiogram showed normal sinus rhythm with complete right bundle branch block and abnormal T-wave. Transthoracic echocardiography detected echo zones in the right ventricular chamber, in the free wall and pericardial cavity outside the right ventricle (Fig. 1A). A subsequent 64-slice CT scan accurately demonstrated a 9.5 cm × 6.2 cm right ventricular mass with intraventricular and extraventricular extensions. The right ventricular wall and the ventricular septum were invaded. Slight pericardial and bilateral pleural effusions

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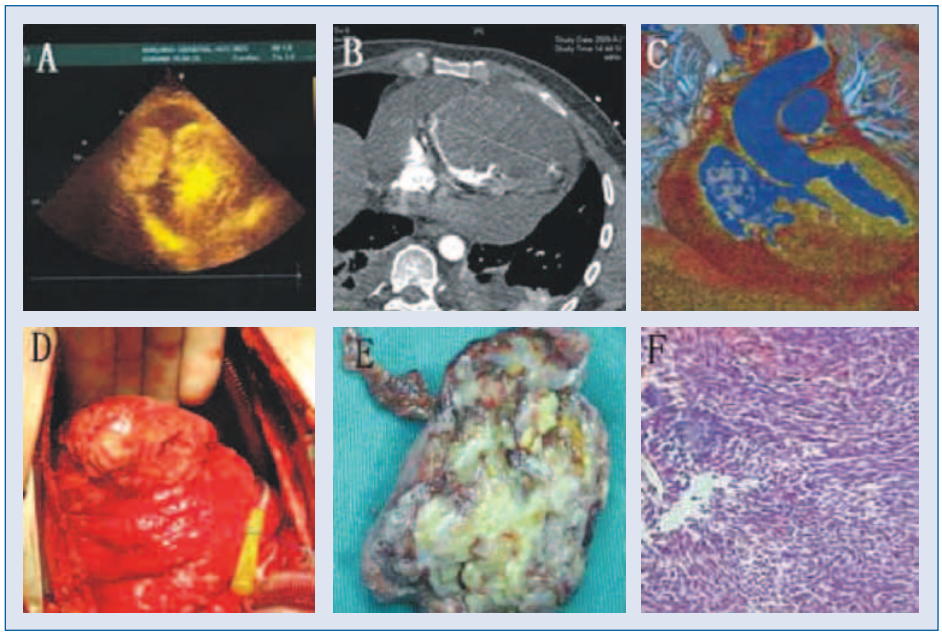

Figure 1. A. Transthoracic echocardiography detected an echo zone (78 mm × 46 mm) in the right ventricle, an echo zone (20 mm × 15 mm) in the anterior wall of the right ventricle, and an echo zone (48 mm × 36 mm) in the pericardial cavity outside the right ventricle; **B.** 64-slice computed tomographic (CT) scan demonstrated a right ventricular mass with intra-ventricular and extra-ventricular extension and septum invasion. Slight pericardial and bilateral pleural effusion was also found; **C.** Three dimensional reconstruction of 64-slice CT demonstrated a large tumor occupying the right ventricular chamber; **D.** A reddish extra-ventricular tumor covering the anterior wall of the right ventricle with old thrombi on the surface; **E.** The surgical specimen with the tumor section represented as fish flesh; **F.** Photomicrograph demonstrating spindle-shaped cells with abundant mitotic activity.

were found as well (Figs. 1B, C). Laboratory findings showed: erythrocyte sedimentation rate (ESR) was 54 mm/h (0–15 mm/h); C-reactive protein was 117.2 mg/L (< 8 mg/L); neuron specific enolase (NSE) was 47.74 μg/L (0–16.3 μg/L); hemoglobin was 109 g/L; leukocyte was 17.7×10^9/L; neutrophilic granulocyte proportion was 0.81; while liver and kidney functions, as well as all other tumor markers, were within the normal range. No abnormal lesions were observed in head or abdominal scanning. A tumor biopsy under the guidance of digital subtraction angiography (DSA) revealed some eosin staining exudates without a definite pathological outcome. The decision was made to perform a tumor resection, both for diagnosis and restoration of hemodynamic stability. Following median sternotomy, the pericardium was dissected to reveal slight pericardial effusion and a 5 cm × × 4 cm × 4 cm reddish extraventricular tumor covering the anterior wall of the right ventricle with old thrombi on the surface (Fig. 1D). The coronary artery was unaffected. After instituting cardiopulmonary bypass via the vena cava and ascending aorta, systemic cooling to 32 degrees centigrade, complete aorta and pulmonary artery block, and cardioplegia to arrest the heart, the right atrium was incised. Through the enlarged tricuspid annulus, it was noticed that the intraventricular portion of the tumor almost completely filled the right ventricle; part of the right ventricular septum was invaded. The tricuspid valve and right ventricular outflow tract were seriously obstructed by the tumor. The large tumor size and the important surrounding heart structures prevented a complete surgical resection of the tumor. A partial removal of the tumor was finally carried out. Most of the intraventricular tumor was resected to relieve the right ventricular inflow and outflow tract obstruction. The extraventricular part was completely removed, and part of the right ventricular free wall was cut off, leaving a 4 cm × 3 cm × × 3 cm defect. The right ventricular reconstruction was performed with a vascular graft patch (InterVascular, a Datascope company, Montvale, NJ, USA). Tricuspid annuloplasty was performed. Eventually a 6 cm × 5 cm × 4 cm part of the tumor was resected (Fig. 1E) and a reconstructive right ventricle and unblocked right ventricular inflow and outflow tract were achieved. The patient received

effective palliation after the operation, and was discharged home without complications on the tenth post-operative day. Pathological analysis proved the diagnosis of synovial sarcoma in the right ventricle (Fig. 1F). Immunohistochemical stainings showed Syt++, CK5/6–, CD21/35–, S100–, Calretinin–, CK–, CD34–, Des–, EMA–, Melan-A–, CKpan–, SMA–, HMB45–, CD117–. Adjuvant chemotherapy was advised, but refused by the patient. A follow-up telephone call six months after the surgery showed that the patient was living with slight edema.

Discussion

Synovial sarcoma is an uncommon malignancy. It occurs most frequently in the para-articular regions of the extremities and arises from the primitive arthrogenous mesenchyme with the capacity to differentiate toward both mesenchymal and epithelial cell lines. However, it is encountered in areas without any relationship to synovial structures [9]. Primary synovial sarcoma of the heart is extremely rare, with very few reports of cases in the literature. A thorough retrieval up to the end of December 2009 found 35 reported cases of primary synovial sarcoma arising from the heart or pericardium in 33 reports in the English language literature [4–6, 8, 10–38]. Clinical features of all such cases are listed in Table 1.

Clinical manifestations

The male to female ratio was 27:8 with a mean age of 34.8 years (range 13–67). The synovial sarcoma of the heart was initially asymptomatic in early development and presented with dyspnea and breathlessness as the commonest complaints during the later course. The period from morbidity to admission was 2.3 (range 0.1–8) months on average. Corresponding clinical symptoms and physical signs did not present until the tumor invaded surrounding tissues, causing arrhythmias and tamponade; or obstructed the blood flow, causing dyspnea, heart failure; or embolized the cerebral, coronary, and retinal vascular beds, causing embolic episodes. Patients had no specific physical signs. Cardiac murmurs could sometimes be heard, and dysfunctions of the liver were occasionally detected.

Medical imaging features

Chest radiography and echocardiography can be used to primarily evaluate the tumor. A chest CT scan and magnetic resonance imaging (MRI)

Table 1. Clinical features of 35 cases of primary synovial sarcoma of the heart.

Variable	Result
Age (years)	34.8 ± 15.0 (13–67); n = 35
Sex (male/female)	27/8
Clinical manifestations:	
Dyspnea	25 (71.4%)
Cough	7 (20.0%)
Syncope	5 (14.3%)
Fatigue	5 (14.3%)
Palpitation	5 (14.3%)
Chest pain	5 (14.3%)
Emaciation	4 (11.4%)
Edema	4 (11.4%)
Abdominal pain	3 (8.6%)
Vomiting	2 (5.7%)
Headache	2 (5.7%)
Fever	2 (5.7%)
Hemoptysis	2 (5.7%)
Embolism	1 (2.7%)
Admission time from onset (months)	2.3 ± 2.0 (0.1–8); n = 18
Right heart	1.8 ± 1.3 (0.1–4); n = 8
Left heart	2.6 ± 1.6 (0.75–4); n = 5
Pericardium	2.9 ± 3.2 (0.25–8); n = 5
Physical sign:	
Cardiac murmur	10 (28.6%)
Jugular vein	5 (14.3%)
Ascites	3 (8.6%)
Edema	3 (8.6%)
Hepatomegaly	3 (8.6%)
Paradoxical pulse	3 (8.6%)
Laboratory examination	3 slight liver dysfunction
Location:	
Right atrium	11 (29.7%)
Right ventricle	7 (18.9%)
Left atrium	5 (13.5%)
Left ventricle	2 (5.4%)
Pericardium	12 (32.4%)
Diameter [cm]:	7.6 ± 4.2 (2.0–20.0)
Right heart	7.0 ± 3.4 (2.9–15.0)
Left heart	4.1 ± 1.1 (2.0–5.1)
Pericardium	11.2 ± 4.0 (8.0–20.0)
Attachment:	
Pedicled	7 (24.1%)
Sessile	22 (75.9%)
Local recurrences	7 (20.0%)
Metastasis:	11 (31.4%)
Lung	6 (54.5%)
Others	5 (45.5%)
Surgical operation:	
Complete resection	11 (33.3%)
Partial resection	17 (51.5%)
Undocumented	5 (15.2%)
Adjuvant therapy	17 (48.6%)
Pathological outcome:	
Biphasic type	14 (51.9%)
Monophasic type	13 (48.1%)
Diagnostic measure:	
Immunohistochemistry	12 (44.4%)
Genetic test	15 (55.6%)

could further help demonstrate the local extension of the tumor and provide effective information for surgery. Miller et al. [27] reported a left atrial synovial sarcoma found three months after coronary artery bypass grafting. No abnormality was visualized through the transthoracic echocardiography before the first surgery. This showed that the tumor grew fast, and transthoracic echocardiography could provide little information about the changes in the left atrium. CT or MRI inspection should be regularly carried out after surgery to enable earlier detection of recurrences or metastases.

Special tumor location and large tumor size

Our review found most primary synovial sarcomas of the heart are located in the right heart. The right to left ratio is 18:7. Tumor volume is large, with an average diameter of 7.6 cm. According to the statistics in the table, the average diameter of tumors from different parts of the heart varies from 4.1 cm (left heart) to 11.2 cm (pericardium). Tumors of the left heart are of a smaller volume. It is considered that tumors of the left heart would more easily lead to the hemodynamics obstacle and therefore symptoms appear earlier. The tumors are of different shapes: most have wide fundus and a sessile lobular shape, while pedicled tumors only account for 24.1% (7/29) and more commonly arise from the valve or cardiac septum.

Low surgical resection rate and high recurrence rate

As with other malignant tumors of the heart, surgical resection is still the mainstay of treatment for synovial sarcoma of the heart [8]. The awkward tumor site and large tumor volume at presentation make complete removal of the tumor hard to achieve in most cases. Auto transplantation after the tumor removal and orthotopic transplantation has been employed in a few limited cases. The complete removal rate was 33.3% (11/33). However, partial removal of the tumor could relieve the symptoms and prolong life. In our case, a complete resection of the tumor could not be achieved. Instead, most of the tumor, along with part of the right ventricular wall, was resected. The surgery turned out to have a positive outcome. Removal of the tumor and surrounding tissues benefits patients by alleviating symptoms and reducing recurrence. Protecting normal cardiac structures, including the atrioventricular ring, may reduce post-operative complications. The local recurrence rate after operation was 20.0% (7/35), and the metastasis rate was 31.4% (11/35). As the commonest metastatic part, lung metastases were detected in six of the 11 patients with definite records. Metastases to cranium, extremities, pleura and liver, could also be seen in some cases. If a diagnosis of synovial sarcoma was considered before surgery, further inspections to identify distant metastases would be necessary.

Pathological findings

Histologically, synovial sarcoma includes two different cell types: spindle cells and epithelial cells. It can be classified into four subtypes depending on the relative proportion of its two cell types: (1) biphasic type; (2) monophasic fibrous (spindle cell) type; (3) monophasic epithelial type; and (4) poorly differentiated type [39]. Immunohistochemical and genetic tests are important in obtaining a diagnosis. More than 90% of patients with synovial sarcoma have a t(X; 18) translocation mutation, which is not associated with other sarcomas [40]; 27 cases with definite histological outcomes have been recorded, the biphasic to monophasic type ratio being 14:13.

Poor prognosis

Synovial sarcoma of the heart has a poor outcome. As with other primary sarcomas of the heart, most patients with synovial sarcoma of the heart die within one year of diagnosis, more than 50% of them from local recurrences [8]. One patient with a primary synovial sarcoma arising from the pericardium had the longest survival of over 14 years proved by long-term follow-up. Patients with complete tumor removal surgery had a better prognosis. In patients with complete tumor resection, 20% (2/10) died during follow-up, and the survivors had a mean follow-up of 35.9 months (mean 35.9 ± 52.8, range 2–168, median 11.0); in the patients with incomplete tumor resection, 37.5% (6/16) died during follow-up, and the survivors had a mean follow-up of 8.8 months (mean 8.8 ± 7.1, range 1.4–22, median 5.5). Some reports have suggested that tumors of the left heart had a better prognosis, but this is not confirmed in the set of patients we have reviewed. Statistics in the table show that tumors arising from the pericardium had a better outcome compared to those from other parts of the heart.

Of the patients with synovial sarcomas of the right heart, 33.3% (4/12) died during follow-up, and

the survivors had a mean follow-up of 14.5 months (mean 14.5 ± 17.8, range 3–60, median 8.5); of the patients with synovial sarcomas of the left heart, 40.0% (2/5) died during follow-up, and the survivors had a mean follow-up of 3.8 months (mean 3.8 ± ± 1.9, range 1.4–6, median 4.0); of the patients with synovial sarcomas of the pericardium, 33.3% (3/9) died during follow-up, and the survivors had a mean follow-up of 35.4 months (mean 35.4 ± 58.8, range 2–168, median 13.0). Adjuvant radiotherapy may be useful in preventing local recurrence, but the burden of treatment in terms of toxicity is often unacceptable because of the large size of the area requiring treatment. Adjuvant chemotherapy could obviously improve the prognosis, and ifosfamide and amycin have shown consistent efficacy in the chemotherapy regime for synovial sarcoma of the heart.

In the set of patients we reviewed, in the patients with adjuvant therapy, 15.4% (2/13) died during follow-up, and the survivors had a mean follow-up of 24.1 months (mean 24.3 ± 45.8, range 2–168, median 12.0); in the patients without adjuvant therapy, 50% (7/13) died during follow-up, and the survivors had a mean follow-up of 14.4 months (mean 14.4 ± 20.6, range 1.4–60, median 5.5). In cases with metastatic lesions, no specific chemotherapy drugs were found.

Conclusions

Primary synovial sarcoma of the heart is extremely rare and has a poor prognosis. The clinical symptoms are not specific. Echocardiography is the procedure of choice to detect the tumor. But transthoracic echocardiography can provide little information about changes in the left atrium. CT and MRI can provide a precise view of local extensions of the tumor before operation. Genetic tests can distinguish synovial sarcoma of the heart from other diseases. Surgical resection is still the mainstay of treatment, with patients who receive complete tumor removal having a better prognosis. Adjuvant therapy pre- or post-operation helps prolong life. As for all tumors with a low incidence, multicenter studies are the only way to improve the care of patients. The key to treatment in the future is to find new therapeutic agents. Genetic therapy has been reported to have some efficacy [41]. Further elucidation of the effects of this chromosomal abnormality may lead to better-directed therapies in future.

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