Primary synovial sarcoma of the heart. A clinicopathologic study of one case and review of the literature

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Introduction

Primary cardiac tumors are much less common than metastatic lesions of the heart. Most of them are histologically benign and count for 70-80% of all tumors that arise in the heart, whereas malignant primary tumors represent only 25% of all primary cardiac tumors. Most of them are sarcomas. They are in decreasing order of frequency: angiosarcomas, mesotheliomas, and fibrosarcomas.

Primary synovial sarcoma of the heart is extremely rare: only thirteen cases have been reported in the literature. We describe the fourteenth case, which is confirmed by an immunohistochemical study, and review the cases reported previously.

Case report

In July 1997, a 45-year-old man presented with symptomatic heart failure for a 6-week period with dyspnea, orthopnea accompanied by a dry cough. Chest X-ray showed a marked opacification of the basis of the right lung. A computed tomography revealed a right atrial tumor associated with a right septated pleural effusion. An echocardiogram showed a large solid tumor filling almost the entire right atrium and obstructing the tricuspid valve (Fig. 1). At surgery (2 August 1997), the tumor was polypoid and lobulated with a smooth external surface. It was attached to the top lateral wall of the right atrium by a 5-mm diameter pedicle.
Extensive surgery was undertaken with complete resection of tumor and of a small margin of normal endocardium around the fibro vascular stalk that required patch reconstruction of the atrial wall. The patient did not receive adjuvant treatment after surgery. Five years after, the patient is well with no evidence of tumor recurrence or metastases.

**Materials and methods**

Tissues from the cardiac tumor were fixed in Bouin, stained with hematoxylin and eosin and reviewed through light microscopic examinations. The tumor is graded according to the system proposed by the “Fédération Nationale des Centres de Lutte Contre le Cancer” (FNCLCC), which is based on tumor differentiation, tumor necrosis and mitosis count.

Immunohistochemistry, using the streptavidin-biotin complex, was performed for the following antigens: cytokeratin (Immunotech; prediluted), epithelial membrane antigen (EMA) (Immunotech; prediluted), vimentin (Immunotech; prediluted) and S100 (Immunotech; prediluted).

**Results**

**Gross pathology**

Macroscopically, the tumor presented as a 7.0x5.0x3.0 cm lobulated solid mass surrounded by a thin smooth capsule interrupted at the point of implantation. The cut surface showed a white-grayish appearance with some hemorrhagic areas. Its consistency was firm but friable (Fig. 2).

**Pathological findings**

The tumor showed a biphasic growth pattern of epithelial and spindled areas with a focal hemangiopericytomatosus-like pattern (Fig. 3).

The epithelial cells formed solid cords and nests. They were predominantly columnar, characterized by large round or oval nuclei with granular chromatin pattern, one or two small nucleoli and abundant slight eosinophilic cytoplasm with distinct cellular borders (Fig. 4). The spindle-cell component was composed of densely packed elongated, fusiform cells with oval to round nuclei and scant cytoplasm. Nuclei were mildly
pleomorphic with a granular chromatin pattern and one nucleolus.
The tumor exhibited 5 mitotic figures per 10 high-power fields (HPF). Mast cells were intermingled with spindle cells (Fig. 5). No necrosis was observed. The tumor was classified as grade II. The pedicle and the excision margin were free of the tumor.
The tumor cells immunostained positively for both cytokeratin marker and epithelial membrane antigen (EMA) in the epithelial component, and focally within the spindle cell component. Vimentin was strongly positive only in the spindle cell component. The spindle cells and focally the epithelial cells stained positively for S100 protein.
Multiple cytogenetic studies attempts on paraffin-embedded material in order to look for the X:18 translocation, characteristic of synovial sarcomas, were unsuccessful because the cardiac tumor was fixed in Bouin.

**Discussion**

The synovial sarcoma of the heart is extremely rare with only thirteen cases previously reported. Cardiac synovial sarcomas exhibit the same histological, histochemical and immunohistochemical characteristics in other locations of synovial sarcomas.
The cytogenetics studies have revealed that a high proportion of synovial sarcomas is characterized by the presence of the reciprocal chromosomal translocation t(X;18)(p11.2;q11.2) or SYT-SSX fusion transcript. In unusual clinical settings, molecular and genetic techniques are particularly helpful in mesenchymal lesion diagnosis.

Histologically, in our case of biphasic synovial sarcoma, the differential diagnosis has included: metastatic synovial sarcoma, adenocarcinoma, carcinosarcoma, metastatic pulmonary blastoma and metastatic mesothelioma.
The distinction of metastatic synovial sarcoma in the heart was easy in the present case, since investigation for extracardiac primary tumor was negative, especially without lung involvement, which is the principle site of metastatic synovial sarcoma.
The adenocarcinoma may enter the differential diagnosis of biphasic synovial sarcoma particularly when the epithelial component is well-developed. However, typically, there must be a primary tumor elsewhere, such as in the lung. In addition, adenocarcinoma lacks the malignant spindle-cell component, hyaline fibrous, and the hemangiopericytomatous patterns observed in synovial sarcomas.
Although pulmonary blastoma is a biphasic tumor, it differs from synovial sarcoma by its primitive epithelial component, that may resemble a well-differentiated fetal adenocarcinoma, and its primitive mesenchymal stroma. In addition, the pulmonary blastoma has occasional foci of osteosarcoma, chondrosarcoma or rhabdomyosarcoma.
In the carcinosarcoma of any site, the glandular element usually shows a significantly greater degree of nuclear pleomorphism than the epithelial component observed in biphasic synovial sarcoma. Similarly, the spindle cell component of carcinosarcoma is usually more cytologically atypical.
Metastatic cardiac malignant pleural mesotheliomas are readily separated since malignant mesotheliomas involve the pleura diffusely and rarely present as a localized mass. Histologically, malignant mesotheliomas with spindled and epithelial areas usually show a grad-
Tab. 1. Heart synovial sarcoma cases.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Presentation</th>
<th>Location</th>
<th>Size/Gross</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8</td>
<td>M</td>
<td>Dyspnea, Syncope</td>
<td>Right ventricle</td>
<td>BSS</td>
<td>None</td>
<td>Diagnosed at autopsy</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>46</td>
<td>F</td>
<td>Not known</td>
<td>Left atrium</td>
<td>BSS</td>
<td>Not known</td>
<td>Not known</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>53</td>
<td>M</td>
<td>Dyspnea cough</td>
<td>Right atrium</td>
<td>BSS</td>
<td>Local excision</td>
<td>Died at 6 months</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>F</td>
<td>Dyspnea, Syncope, Cough, Weight loss</td>
<td>Right atrium</td>
<td>BSS</td>
<td>Local excision months, Transplantation for recurrent disease</td>
<td>Died at 3 months</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>35</td>
<td>M</td>
<td>Pneumonia, Abdominal pain, Syncope, Weight loss</td>
<td>Right ventricle</td>
<td>MSS</td>
<td>Chemotherapy</td>
<td>Died at 9 months</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>38</td>
<td>M</td>
<td>Dyspnea</td>
<td>Right ventricle</td>
<td>MSS</td>
<td>Local excision</td>
<td>Died within the year (extensive metastatic disease)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>13</td>
<td>M</td>
<td>Syncope</td>
<td>Right atrium</td>
<td>MSS</td>
<td>Local excision</td>
<td>Disease free at 10 months</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>45</td>
<td>M</td>
<td>Congestive heart failure, Tamponade</td>
<td>Left atrium</td>
<td>SS</td>
<td>Chemotherapy (metastatic pericardial disease)</td>
<td>Died of metastatic disease</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>40</td>
<td>M</td>
<td>Congestive heart failure, Tamponade</td>
<td>Extensive tumor Involvement of the heart</td>
<td>SS</td>
<td>None (tumor was irresecable)</td>
<td>Died of metastatic disease</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>45</td>
<td>M</td>
<td>Chest pain, Dyspnea, Tamponade</td>
<td>Left ventricle Pericardium</td>
<td>MSS</td>
<td>Partial local excision</td>
<td>Died at 5.5 months, Metastasis in both lung fields and in the mediastinum</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>29</td>
<td>M</td>
<td>Dyspnea Heart Failure</td>
<td>Left atrium</td>
<td>5 cm, extend to the pulmonary veins bilaterally and mitral valve</td>
<td>SS</td>
<td>Local excision</td>
<td>Died at 8 months after 2 recurrences</td>
</tr>
<tr>
<td>12</td>
<td>34</td>
<td>M</td>
<td>Dyspnea</td>
<td>Right atrium</td>
<td>MSS</td>
<td>None (tumor was irresecable)</td>
<td>Died within the post-year diagnosis</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>47</td>
<td>M</td>
<td>Transient ischemic attacks, Bilateral pulmonary nodules</td>
<td>Right atrium</td>
<td>4.5 cm</td>
<td>BSS</td>
<td>Local excision, Biopsies of the lung nodules, Chemotherapy</td>
<td>Uneventful post-operative course</td>
</tr>
<tr>
<td>14</td>
<td>45</td>
<td>M</td>
<td>Dyspnea Cough</td>
<td>Right atrium</td>
<td>7 x 5 x 3 cm polyoid and lobulated</td>
<td>BSS</td>
<td>Local excision and patch reconstruction of the atrial wall</td>
<td>Disease free at 5 years</td>
</tr>
</tbody>
</table>

BSS: Biphasic Synovial Sarcoma; MSS: Monophasic Synovial Sarcoma; SS : Synovial Sarcoma; IHC : Immunohistochemistry; 14: Current case
Primary Synovial Sarcoma of the Heart

The thirteen cases and the current case of cardiac synovial sarcoma are listed in Table I. The average age was 37.38 years ranging from 13 to 53 years. Eleven of the patients are males and two are females. Synovial sarcoma of the heart is predominantly right-sided (8 cases) with five tumors arising in the right atrium and three in the right ventricle. Only four tumors are left-sided with three arising in the atrium and one in the ventricle.

The clinical presentation is similar to the ones presented in larger series of malignant heart tumors and no specific signs, that could have been related to this rare tumor, were found. The most common symptoms at presentation were dyspnea, syncope and heart failure. Echocardiography and CT scan are often used for the diagnosis of cardiac masses in order to demonstrate the post-operative recurrence.

The average tumor size was 7.4 cm (range 3-15 cm) in 7 cases.

In seven cases, the histological diagnosis was made after local excision and in three cases (cases 5, 8 and 9) by biopsy since the tumor was unresectable. Six tumors were biphasic synovial sarcoma and four monophasic. Our case is a biphasic histological type. Immunoreaction with cytokeratins was cited in six cases (Tab. I). Cytogenetic studies have been performed in two cases (case 5 and 6) and have revealed a chromosomal translocation (X;18). In our case, cytogenetic studies were unsuccessful in spite of repeated attempts because tumor tissues were fixed in Bouin; therefore we cannot exclude the possibility of this chromosomal translocation.

The prognosis of primary cardiac synovial sarcoma is very poor; seven patients died during the first post-diagnosis year. Only one patient was disease-free for 10 months after local excision of the tumor. Our patient is the longest surviving case ever reported (5 years) despite sole surgical treatment. This could be explained by the complete resection of the tumor.

Several factors, influencing the period of survival, have been studied in synovial sarcoma of soft tissue. Cagle et al. have shown that the histological type associated with best survival is the biphasic “highly-glandular” tumor compared to monophasic or biphasic “low-glandular” tumor. Oda et al. did not find significant correlation between histologic type and prognosis.

Cagle and Enzinger have concluded that the mitotic rate is an important prognostic factor. The survival rates were significantly lower among patients with tumors having more than 15 mitoses per 10 HPF. In Oda’s study, large size, high nuclear grade, presence of rhabdoid cells and extensive tumors necrosis are considered negative prognosis factors in synovial sarcoma. In addition, aneuploidy, high proliferating cell nuclear antigen (PCNA) score, increased apoptotic index, p53 mutations and co-expression of hepatocyte growth factor and its receptor (c-MET) have been associated with a poor prognosis. It has also been suggested that synovial sarcoma patients with the SYT/SSX2 fusion transcript are more likely to have a longer disease-free survival than those with the SYT/SSX1 fusion transcript.

The prognosis of cardiac primary sarcomas is very poor with a mean survival of 9 to 16.5 months and no prognostic factor has been clearly established. The histological grading correlates with survival as in non-cardiac sarcomas. Necrosis of more than 50% of the tumor and mitosis, observed in more than 10 cells per 10 high-power fields, seem to be associated with reduced survival. In the 13 cases of cardiac synovial sarcomas, 7 patients died during the first year after diagnosis. Four of them showed a monophasic histological type. As for the longest survival case (current case) the histological type was a biphasic type synovial sarcoma. The mitotic count was less than 10/10 HPF (5 mitoses/10 HPF), the degree of nuclear atypism was moderate (grade II), the tumor size was larger than 5 cm (7.0X5.0X3.0 cm), while necrosis was absent.

As a conclusion, the number of cases of cardiac synovial sarcoma is too low to confirm the usefulness of histologic features relating to prognosis.

References


