Pericardial Synovial Sarcoma: A Case Report and Review of Literature

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Abstract

Pericardial Synovial Sarcoma (PSS) is a rare malignant soft-tissue tumor. Early diagnosis and multimodal management could be improving patient outcome. PSS diagnosis is difficult due to localization but and aggressive disease. Using all the available medical methods is important to avoid progression and recurrence of this kind of tumors. Multidisciplinary treatment is necessary and radiotherapy is a good and safe option. We present our experience of a forty-year-old man with this tumor.

Keywords: Pericardial; Sarcoma; Treatment

Introduction

Pericardial Synovial Sarcoma is a type of sarcoma uncommon [1]. It is usually diagnosed in young adults. Patient’s present unspecified symptoms, similar to fever, cough, pain chest and fatigue. In other cases, patients present pericardial effusion and cardiac tamponade. Only 30 cases of synovial sarcoma of the pericardium have been reported in the English language literature, 20 included follow-up [2,3].

Case Report

Figure 1: CT with pericardial mass.

A 40-year-old man visited our Hospital in June 2014 due to chest pain. The physical examination had no abnormal findings. After admission, the chest X-ray indicated cardiomegaly and echocardiography showed dates of pericardial effusion. The patient received treatment and was discharged from hospital after one week with pericarditis diagnosis. Four months later, he started with similar symptoms and echocardiography showed massive pericardial effusion with a tumorous region in the pericardial space.
Echocardiography showed a big mass with compression of right cavities without stenosis, gradient valve tricuspid of 3,7mmHg. The chest CT, as well as confirming the effusion, revealed a pericardial cystic mass with pericardial thickening (Figure 1). Is suggested of neoplasm similar to mesothelioma or sarcoma. Pericardiocentesis was performed and 1000 mL of pericardial fluid was drained (Figure 1).

According to these findings, surgical resection through pericardiotomy with median sternotomy was performed on October 2014 with pathology study. The tumor was located in the pericardial space, with irregular morphology; size of 14x5.7x6 cm and 1500mL serohematic pericardial fluid. Histological analysis showed spindle cells-type sarcoma, necrosis and 18 mytosis. Immunohistochemical analysis showed that the tumor cells were positive for bcl-2, CD99, vimentin and the Ki-67 proliferative index was 50%; however, staining for S100 proteins, CD34, CK AE1/AE3, EMA, enolasa, muscle-specific actin (HHF35) and desmin was negative. On the other hand, fluorescence in situ hybridization revealed a moderate prevalence (64%) of cells with interruption of the SYT gene (18q11.2). Final diagnosis was monophasic synovial sarcoma with poorly differentiated areas with unspecified margins. Patient had a good clinical evolution but the control CT scan three months later, showed tumor persistence, 7.5x11x2.8cm with compression in right ventricle. The tumor grew from the inner surface of the pericardium near the origin of the pulmonary artery and ascending aorta with invasion of left atrium and right coronary. The study was completed with angiography scan. The case was evaluated in multidisciplinary committee. The specialist decided re-intervention but complete resection was not possible because of the proximity and attachment to the great vessels. In CT scan after surgery, the mass was reduced around 50%. In multidisciplinary committee, we discussed the possibility of adjuvant radiation therapy. Finally, patient received radiation treatment with prescription dose of 45Gy; 1.8Gy daily (Figure 2). He didn’t had any toxicity (Figure 2).

After three months, patient had a new recurrence. In committee we decided not surgery, patient received chemotherapy. Finally patient had a new recurrence and died in 12 months after diagnosis (Figure 3).

Discussion

Pericardial Synovial Sarcoma (PSS) is a rare primary malignant tumor of the heart and has an unclear prognosis. Primary cardiac tumours are uncommon, occurring less frequently than metastatic tumours with an incidence in autopsy series ranging only from 0.001-0.03 % [4]. Most of the primary cardiac tumours are benign and approximately 25 % of them are malignant, of which the majority are sarcomas but originating from the pericardium are exceedingly rare accounts for approximately 4.2 % of primary cardiac sarcomas. In descending order of frequency, these are angiosarcoma, fibrosarcoma, rhabdomyosarcoma, and malignant fibrous histiocytoma [5]. It is more frequent in young adults between 15 and 35 years of age [6].

PSS was first described in 1978 [7]. The signs and symptoms caused by the primary cardiac sarcoma are extremely variable and nonspecific. Clinical manifestations can be divided into four categories: systemic; embolic; cardiac; and secondary to metastasis. The most common systemic manifestations are fever, chills, fatigue, night sweats and weight loss. Embolic manifestations occur mainly in sarcomas invading the cardiac cavities, causing pulmonary or systemic embolism. Cardiac manifestations depend on the location of the tumor: predominantly pericardial, intramural or intracavitary. In the case of pericardial sarcoma, the most common initial clinical picture results from massive hemorrhagic pericardial effusion and cardiac tamponade [4]. The organs most often affected by primary cardiac sarcoma metastases are the lungs, brain and bones.

The tumors are classified into three histologic subtypes: monophasic, biphasic and poorly differentiated [6]. The histologic type was judged to be monophasic in the current case. Biphasic PSS tumor composed of spindled and epithelioid areas or as a monophasic tumor, characterized by the spindle cell component only. Although immunological characteristics, such as positivity for bcl-2 and CD99, are not exclusive to synovial sarcoma, a definitive diagnosis can be made based on the presence of the chromosomal change t(X;18) (p11;q11), the cytogenetic hallmark of synovial sarcoma. The SS18 gene on 18q and either the SSX1 or SSX2 gene on Xp undergo reciprocal translocation, forming a fusion gene, SS18-SSX, with the subsequent production of fusion proteins; more than 90% of synovial sarcomas present with this characteristic...
molecular signature. In addition, biphasic synovial sarcoma has a 
SYT-SSX1 fusion transcript, whereas SYT-SSX2-positive tumors are 
monophasic synovial sarcomas [6].

It is most frequent presenting symptom is signs of
cardiac tamponade; subsequent diagnostic imaging, including
echocardiography or chest CT, reveals a pericardial mass requiring
biopsy for diagnosis [8]. An important survival factor is complete
resection, but it is rare. Radiotherapy and chemotherapy are
indicated in incomplete resection to prevent locoregional
recurrence. While broad surgical resection is the first choice for
treatment, chemotherapy and radiotherapy are carried out when
surgical resection is unsuccessful; however, the prognosis of this
disease is poor [9]. Median survival was around 15-25 months in
some series.

Due to its extreme rarity, the most effective therapeutic strategy
for treating pericardial synovial sarcoma could not be determined,
and the complete or near total excision of the tumor was performed
in only five of the reported cases. The pericardial tumor observed
in the present case was also considered to be unresectable, due to
its strong attachment to the visceral pericardium [6]. Management
of synovial sarcoma of pericardial origin is challenging and needs
a multimodal approach. It is an aggressive tumor with a poor
prognosis. Most patients have a short survival time (In Table 1
describes published cases in literature). One exception is the case
report of a patient whose survival exceeded 14 years and involved 
recurrences and multiple surgical resections. Surgical resection can
lead to curative therapy. Most often, due to the site of origin, tumors are
adherent to adjacent vital organs and are non-resectable at the
time of diagnosis. Therefore, External Beam Radiotherapy (EBRT) and
less commonly neo-adjuvant chemotherapy are used to make the
tumor resectable. In our patient, we could not attempt complete
surgical resection. Therefore, after the initial biopsy and pericardial
window, neo-adjuvant chemotherapy was done with six cycles of
high dose ifosfamide (2000mg/m2) and mesna. Due to the rarity of these
tumors, it is very difficult to establish an optimal regimen for
chemotherapy. In general synovial sarcomas are chemo-sensitive to
ifosfamide and show a good response. A case series of 13 patients
with synovial sarcoma treated with high-dose ifosfamide showed
a response in all patients, with 4 clinical remissions achieved.
Combining doxorubicin with ifosfamide may achieve a higher
response rate (58%) but patient tolerability and side effects need
to be considered. The initial favorable response to neoadjuvant high
dose ifosfamide in our patient made the tumor resectable and may
be a viable alternative to EBRT alone in non-resectable tumors [5].

Table 1: Cases reports with follow-up.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age</th>
<th>Gender</th>
<th>Clinical</th>
<th>Surgery</th>
<th>CT (type)</th>
<th>RT (dose/ Gy)</th>
<th>Immunohistochemically positive antigens and molecular analysis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muramatsu et al. [6]</td>
<td>57</td>
<td>M</td>
<td>Cardiomegaly</td>
<td>Incomplete</td>
<td>Ifosfamide, adriamycin</td>
<td>500y</td>
<td>CK, CD99 and bcl-2 Fusion SYT/SSX negative.</td>
<td>Died at 3y</td>
</tr>
<tr>
<td>Phatak et al. [5]</td>
<td>27</td>
<td>M</td>
<td>Dyspnea, cough</td>
<td>Incomplete</td>
<td>Ifosfamide and MESNA</td>
<td>Yes</td>
<td>BCL-2, CD 99, vimentin, FLI1, enolase. EMA.SYT gene: rearrangement</td>
<td>Recurrence at 9m. Second line CT. Stable at 18m</td>
</tr>
<tr>
<td>Bezerra et al. [2]</td>
<td>29</td>
<td>F</td>
<td>Dyspnea, chest pain</td>
<td>Incomplete</td>
<td>2-cycles</td>
<td>No</td>
<td>Spindle cells No analysis</td>
<td>Died before second cycle of CT</td>
</tr>
<tr>
<td>Cheng et al. [9]</td>
<td>31</td>
<td>M</td>
<td>Fever, cough</td>
<td>Biopsy</td>
<td>No (refused)</td>
<td>No</td>
<td>EMS, CK7, 19, AE1/AE3 SYT gene: rearrangement</td>
<td>Alive at the theat the 12m follow up</td>
</tr>
<tr>
<td>38</td>
<td>M</td>
<td>Chest distress, shortness of breath</td>
<td>Biopsy</td>
<td>-</td>
<td>-</td>
<td>Vimentin, bcl-2, calponin, CD99. SYT gene: rearrangement</td>
<td>Awaiting heart transplantation</td>
<td></td>
</tr>
<tr>
<td>54</td>
<td>F</td>
<td>Malaise, fever, chest pain</td>
<td>Incomplete</td>
<td>Ifosfamide</td>
<td>No</td>
<td>EMA, vimentin, VER EP4, bcl2, CK AE1/AE3 SYT-SSX fusion gene</td>
<td>Died after 26-m</td>
<td></td>
</tr>
<tr>
<td>Mooorjani et al. [12]</td>
<td>61</td>
<td>M</td>
<td>Dysnea</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>EMA, CK AE3</td>
<td>Alive after 2-m of surgery</td>
</tr>
<tr>
<td>Katakura et al. [13]</td>
<td>70</td>
<td>F</td>
<td>Coughed, dysnea</td>
<td>Complete</td>
<td>No</td>
<td>No</td>
<td>SYT-SSX fusion gene</td>
<td>Died 79-d after operation</td>
</tr>
<tr>
<td>Korula et al. [14]</td>
<td>49</td>
<td>M</td>
<td>Dyspnea, chest pain</td>
<td>Biopsy</td>
<td>Yes</td>
<td>No</td>
<td>EMA, CK(AE1/AE3), bcl2</td>
<td>Palliative care</td>
</tr>
<tr>
<td>29</td>
<td>M</td>
<td>malaise</td>
<td>Incomplete</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>Alive at 13-m</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>M</td>
<td>Dyspnea</td>
<td>Biopsy</td>
<td>-</td>
<td>-</td>
<td>EMA, CD34, CD99, vimentin and MNF116. FISH</td>
<td>Palliative care</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reference</th>
<th>Patients</th>
<th>Gender</th>
<th>Age</th>
<th>Symptoms</th>
<th>Type</th>
<th>Chemotherapy</th>
<th>Additional Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hing SN et al. [16]</td>
<td>15</td>
<td>M</td>
<td>10-80</td>
<td>Cough, tight chest</td>
<td>Incomplete</td>
<td>Cisplatin, doxorubicin, cyclophosphamide</td>
<td>No</td>
<td>EMA, vimentin, bcl2 SYT-SSX fusion gene</td>
</tr>
<tr>
<td>Van der Mieren et al. [17]</td>
<td>26</td>
<td>M</td>
<td>22-76</td>
<td>Cardiac tamponade</td>
<td>Yes</td>
<td>Doxorubicin, hydrochloride</td>
<td>Yes</td>
<td>EMA, vimentin, CK SYT-SSX transcript</td>
</tr>
<tr>
<td>Yano et al. [18]</td>
<td>22</td>
<td>F</td>
<td>22</td>
<td>Shortness of breath, cough</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>EMA, vimentin SYT-SSX2 expression</td>
</tr>
<tr>
<td>Anand et al. [19]</td>
<td>29</td>
<td>M</td>
<td>19</td>
<td>Acute breathlessness</td>
<td>Incomplete</td>
<td>Yes</td>
<td>Yes</td>
<td>EMA, CD99</td>
</tr>
<tr>
<td>Val-Bernal et al. [20]</td>
<td>76</td>
<td>F</td>
<td>37</td>
<td>Unspecific symptoms</td>
<td>Autopsy</td>
<td>No</td>
<td>No</td>
<td>EMA, cytokeratin 5,6,7, thrombomodulin</td>
</tr>
<tr>
<td>Dos Santos et al. [21]</td>
<td>37</td>
<td>M</td>
<td>19</td>
<td>Fever</td>
<td>Incomplete</td>
<td>No (refused)</td>
<td>No</td>
<td>-</td>
</tr>
<tr>
<td>Otzumi et al. [22]</td>
<td>19</td>
<td>M</td>
<td>19</td>
<td>Dyspnea, fatigue</td>
<td>Complete</td>
<td>-</td>
<td>-</td>
<td>Vimentin SYT-SSX transcript</td>
</tr>
<tr>
<td>Al-Rajhi et al. [23]</td>
<td>19</td>
<td>M</td>
<td>18</td>
<td>Shortness of breath</td>
<td>Incomplete</td>
<td>No</td>
<td>Yes</td>
<td>SYT-SSX fusion gene</td>
</tr>
</tbody>
</table>

RT: Radiotherapy; CT: Chemotherapy

EBRT is a very useful modality of treatment post surgery when the margins of resection are positive. In our patient, EBRT was initiated one month after surgery. Previous reports have shown similar favorable results. To the authors’ knowledge only EBRT has been employed in previous cases. Intraoperative Radiation Therapy (IORT) with a radiation dose of 15–45 Gray appeared to be useful for local control and to be more effective in patients without distant metastases at the first visit in a study that included 24 patients with soft tissue sarcomas (1 case of synovial sarcoma). Close monitoring for recurrence is very crucial in management of this tumor. CT or magnetic resonance imaging should be performed every 6 months to detect subclinical recurrences. We performed CT imaging every three months along with regular clinical follow-up or symptoms. Repeat imaging is essential to be able to diagnose subclinical recurrence and initiate repeat broad surgical resection and follow-up chemotherapy if needed. We used the anti-mitotic agent ifosfamide for treating the recurrence [5]. Cardiac transplant had been an alternative in some cases with more survival but it is controversial due to tumoral etiology.

**Conclusion**

Pericardial Synovial Sarcoma is an extremely rare entity. The prognostic of pericardial synovial sarcoma is very poor, in our case patient has death despite intensity treatment. We need more lines of investigation to improve these results (Table 1).

**References**


