Primary cardiac synovial sarcoma is a rare disease. A 51-year-old man visited our hospital with the chief complaint of palpitations and shortness of breath while exercising. Copious bloody pericardial effusion and a multicystic intrapericardial tumor were detected. A primary cardiac malignant tumor was suspected, an open-chest tumor resection was performed with the objectives of diagnosis and treatment. Histologically, the tumor cells were uniformly spindle-shaped with an ovoid or oval nucleus, they had proliferated in fascicular fashion. In addition myxoid degeneration, a hemangiopericytomatous vascular pattern and pseudorosette formation were seen in some areas of the tumor. Based on the histopathological and immunohistochemical findings and reverse transcription polymerase chain reaction detection of SS18-SSX1 fusion transcripts, a monophasic fibrous type synovial sarcoma was diagnosed. Postoperative radiation therapy was administered and there had been no recurrence 9 months after the surgery.

The most common malignant tumor that develops from the pericardium is a malignant mesothelioma, accounting for about 50% of primary pericardial tumors. The incidence of synovial sarcomas of the pericardium was reported to be about 5%.1

Here, we report our experience with a Japanese patient who developed a synovial sarcoma that originated in the epicardium and grew in the direction of the pericardial cavity. Because of its site of origin and the histological images, it was necessary to distinguish this tumor from sarcomatoid malignant mesothelioma and other spindle cell sarcomas. Molecular genetic analysis was very useful for reaching a definitive diagnosis of this synovial sarcoma. We also present a discussion of the literature.

CLINICAL SUMMARY

The patient was a 51-year-old man. Three months before presentation, he had experienced a fever that persisted for approximately one month. From about one week prior to presenting, the patient experienced palpitations and became breathless when he was walking. Plain chest X-rays revealed a striking enlargement of the heart. Cardiac ultrasonography showed copious pericardial effusion and an intrapericardial solid, nodular tumor with the formation of multiple cysts. Pericardial drainage was immediately performed, yielding approximately 2 L of bloody pericardial effusion. A chest CT showed, in the late arterial phase, a deeply stained, large tumor with dimensions of 6.2 × 6.2 × 6.0 cm in the pericardial cavity between the left atrium and the left main pulmonary artery. The ventral portion of the tumor contained a large cyst of approximately 2 cm in diameter (Fig. 1a,b). Pericardial drainage was performed three times, and the results of cytological studies on the pericardial effusions were always...
negative. Gallium scintigraphy did not find any evidence of a lesion that could be a primary focus or a metastasis in any other organs. Thoracotomy was performed to resect the intrapericardial tumor in order to prevent heart failure and achieve a definitive diagnosis.

Operative findings were of a solid, nodular tumor observed in the pericardial cavity, posterior to the left atrium (Fig. 2). The tumor was a polyoid mass that was pedunculated and grew from the epicardium near the bifurcation of the left anterior descending branch and the circumflex branch of the coronary artery. The tumor was removed by severing the stalk.

Postoperative radiation therapy was administered and there had been no recurrence 9 months after the surgery.

PATHOLOGICAL FINDINGS

The tumor was divided into more than 20 fragments. Macroscopically, the tumor was seen to be light brown in color, while it was solid, elastic and soft, with partial cystic changes accompanied by hemorrhage. Histologically, the tumor cells were uniformly spindle-shaped, with an ovoid or oval nucleus, and they proliferated in fascicular fashion. Multiple mitoses were observed (Fig. 3a–c). The cells did not show clear epithelial features and there was no calcification. Cyst-like structures, due to myxoid degeneration, were seen in some areas (Fig. 3d). In addition, a hemangiopericytoma-like vascular pattern (Fig. 3e) and pseudorosette formation (Fig. 3f) were observed at some sites. Immunohistochemical staining showed the tumor cells to be diffusely positive for vimentin, and also focally positive for cytokeratin and epithelial membrane antigen. The cells were diffusely, strongly positive for bcl-2 and CD56. Approximately 5% of the cells were positive for calretinin, mesothelin and thrombomodulin (Fig. 4a–f), whereas the cells were negative for S-100, desmin, α-smooth muscle actin (αSMA) and CD34.

Electron microscope findings were that the tumor showed a high degree of nuclear atypia, and desmosomes; tight junctions and microvilli were observed (Fig. 5). The microvilli were long and slender, and some cells had cilia. No basal membrane was seen.

Molecular genetic analysis using reverse transcription polymerase chain reaction (RT-PCR) performed with paraffin-embedded tissue blocks detected the SS18-SSX1 fusion gene transcript (Fig. 6).

In consideration of the findings described above, the tumor was diagnosed as a monophasic fibrous type synovial sarcoma.

DISCUSSION

Synovial sarcomas are malignant soft-tissue tumors that manifest at juxta-articular sites of the limbs in relatively young patients. Historically, these tumors were named synovial sarcomas because histopathological images resemble synovium accompanied by epithelioid differentiation. However, synovial sarcomas have been reported to develop in the head and neck region, lung, abdominal wall, abdominal cavity, retroperitoneum, and other sites that are devoid of synovium. It is now thought that the origin of these tumors is unrelated to synovial tissue. Histologically, synovial sarcomas are classified into a biphasic type, which is composed of an epithelial component and a spindle cell component, a monophasic type, consisting of only a spindle cell
component, and a poorly-differentiated type, consisting of small round cells.\(^2\)

The patient reported here had an intrapericardial tumor that had originated from the epicardium, and on the basis of the histopathological findings it was thought to be a synovial sarcoma of the monophasic fibrous type. However, because of its site of origin and the histological images, it was necessary to distinguish this tumor from sarcomatoid malignant mesothelioma and spindle cell sarcoma including fibrosarcoma, malignant peripheral nerve sheath tumor (MPNST), leiomyosarcoma, and malignant solitary fibrous tumor.

Figure 2 Thoracotomy was performed to resect the tumor which was located in the pericardium, posterior to the left atrium. The tumor was pedunculated and grew from the epicardium.

Figure 3 Histopathological findings. (a) The tumor is accompanied by hemorrhage and cyst formation. (b) Uniform tumor cells exist densely in a fascicular fashion. (c) The tumor cells are spindle-shaped or polygonal with a high nuclear to cytoplasm ratio and have an ovoid nucleus. Multiple mitoses (60/10 high power field) are seen. (d) Myxoid degeneration is seen. (e) Hemangiopericytoma-like vascular patterns and (f) pseudorosette formation are also seen.

Figure 4 Immunohistochemical staining findings. (a) The cells were focally positive for cytokeratin. (b) A very small number of tumor cells were positive for epithelial membrane antigen. (c) Some of the cells were positive for calretinin. (d) Some of the cells were positive for mesothelin. (e) The cells were diffusely, strongly positive for bcl-2. (f) The cells were also diffusely, strongly positive for CD56.

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Malignant mesotheliomas of pericardial origin proliferate diffusely and cover the surface of the heart, histologically they show strong characteristics of pleomorphism and atypia in comparison with synovial sarcomas. However, our patient developed a nodular mass, and the tumor was composed of uniform tumor cells. Immunohistochemically, our patient's tumor was partially positive for calretinin and mesothelin, but it is known that some synovial sarcomas are also positive for these markers.3 In addition, while bcl-2 is positive in only 0–8% of sarcomatoid malignant mesotheliomas, it has been reported to be diffusely, strongly positive in a high percentage of synovial sarcomas.4 This marker can thus be thought to be useful for distinguishing between sarcomatoid malignant mesotheliomas and synovial sarcomas.

Moreover, the monophasic fibrous synovial sarcoma may resemble a number of other spindle cell sarcoma. The immunohistochemical panel was useful to distinguish our patient's tumor from other spindle cell sarcoma, such as fibrosarcoma, MPNST, leiomyosarcoma, and malignant solitary fibrous tumor.

The t(X;18)(p11.2;q11.2) chromosomal translocation is characteristic of synovial sarcomas, seen in more than 95% of these lesions.2 It is a chimeric gene, and two variants, SS18-SSX1(SYT-SSX1) and SS18-SSX2(SYT-SSX2), have been identified. Both of those variants are detected in monophasic synovial sarcomas, whereas almost all biphasic synovial sarcomas consist of SS18-SSX2. For our present case, RT-PCR performed using paraffin-embedded tissue sections detected the SS18-SSX1 fusion gene. In contrast, it was reported that the SYT-SSX fusion gene is not detected in sarcomatoid malignant mesotheliomas.5 As a result, it can be surmised that detection of SS18-SSX is extremely useful for reaching a definitive diagnosis of synovial sarcoma that has originated from an atypical site.

Table 1 lists the 25 cases of synovial sarcoma reported that originated in the heart or pericardium.6–30 The patients' age range is 14–66 years (mean: 34.7 years), with 18 men and 7 women. The site of origin of the synovial sarcoma was the heart in 17 patients and the pericardium in 8 patients. A majority of the primary cardiac tumors occurred in the right atrium. The developmental morphology was described for 15 of the 17 primary cardiac tumors: 11 were intracardiac tumors that grew in the direction of the atrial or ventricular cavity; 4 were extracardiac tumors that had developed in the epicardium and were located in the pericardial cavity. We conclude that the case we have reported here had a rare developmental morphology since it was an intrapericardial tumor that grew extracardially. Many of the tumors reported to date have been giant tumors, with a diameter in excess of 5 cm. Seven of the reported cases had pericardial effusion, and all of their tumors showed extracardiac growth. In addition, cytological studies were performed on the pericardial effusion from three of those seven cases,7,10,17 but malignant cells were not detected. Molecular analysis was described in 12 cases: 11 showed detection of SS18-SSX(SYT-SSX) or t(X;18)(p11.2;q11.2) chromosomal translocation. One case13 did not show these successfully, even though cytogenetic studies of paraffin-embedded material were attempted. Basic treatment for almost all of the 25 patients consisted of surgical removal of the tumor. However, total excision was difficult due to the locations of the tumors and thus many of the patients also underwent other therapies, such as postoperative chemotherapy and/or radiotherapy.

Synovial sarcomas generally have a poor prognosis, with reported 5-year survival rates of 36–76% and 10-year survival rates of 20–63%.31 More than 50% of patients experience recurrence within 2 years, while approximately 40% develop metastases to the lung, bones, and other locations. The outcomes of the cardiac and pericardial synovial sarcomas were described for 18 of the 25 reported cases: 8 dead;
<table>
<thead>
<tr>
<th>Case</th>
<th>Year</th>
<th>Author</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Chief complaints</th>
<th>Pericardial site</th>
<th>Tumor size (cm)</th>
<th>Histological type</th>
<th>Molecular analysis</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1978</td>
<td>McAllister HA</td>
<td>6</td>
<td>M</td>
<td>Dyspnea, syncope</td>
<td>RV/pericardium</td>
<td>NA</td>
<td>Biphasic</td>
<td>None</td>
<td>Surgery</td>
<td>Died</td>
</tr>
<tr>
<td>2</td>
<td>1988</td>
<td>Sheffield EA</td>
<td>7</td>
<td>M</td>
<td>Dyspnea, cough</td>
<td>RA</td>
<td>5</td>
<td>Biphasic</td>
<td>Monophasic t(X:18)(p11;q11)</td>
<td>Surgery</td>
<td>Died (6 months)</td>
</tr>
<tr>
<td>3</td>
<td>1990</td>
<td>Siebenmann R</td>
<td>8</td>
<td>F</td>
<td>Dyspnea, syncope, cough, weight loss</td>
<td>RA</td>
<td>NA</td>
<td>Biphasic</td>
<td>SYT-SSX1</td>
<td>Heart transplantation</td>
<td>Died (3 months)</td>
</tr>
<tr>
<td>4</td>
<td>1992</td>
<td>Burke AP</td>
<td>9</td>
<td>F</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>1994</td>
<td>Karn CM</td>
<td>10</td>
<td>M</td>
<td>Abdominal pain, weight loss</td>
<td>RV (within the pericardium)</td>
<td>12.5×9×7</td>
<td>Monophasic</td>
<td>t(X:18)(p11;q11)</td>
<td>Surgery</td>
<td>Died (9 months)</td>
</tr>
<tr>
<td>6</td>
<td>1995</td>
<td>Iyengar V</td>
<td>11</td>
<td>M</td>
<td>Shortness of breath</td>
<td>RV</td>
<td>12</td>
<td>Monophasic</td>
<td>SYT-SSX1</td>
<td>Surgery</td>
<td>Alive (10 months)</td>
</tr>
<tr>
<td>7</td>
<td>1997</td>
<td>Nicholson AG</td>
<td>13</td>
<td>M</td>
<td>Syncope</td>
<td>RA</td>
<td>5</td>
<td>Biphasic</td>
<td>None</td>
<td>Surgery</td>
<td>Unsuccessful</td>
</tr>
<tr>
<td>8</td>
<td>1998</td>
<td>Langner K</td>
<td>14</td>
<td>M</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>1999</td>
<td>Al-Rajhi N</td>
<td>15</td>
<td>M</td>
<td>Shortness of breath</td>
<td>Pericardium (right lateral pericardial surface)</td>
<td>10×4×6</td>
<td>Biphasic</td>
<td>SYT-SSX1</td>
<td>Surgery</td>
<td>Died (12 months after radiotherapy)</td>
</tr>
<tr>
<td>10</td>
<td>1999</td>
<td>Kojima KY</td>
<td>16</td>
<td>F</td>
<td>Substernal chest pain, nausea, dyspnea</td>
<td>Pericardium (within the pericardial space)</td>
<td>9.5×7×8.5 (700 g)</td>
<td>Monophasic</td>
<td>SYT-SSX1</td>
<td>Surgery</td>
<td>Died (about 7 months)</td>
</tr>
<tr>
<td>11</td>
<td>1999</td>
<td>Oizumi S</td>
<td>17</td>
<td>F</td>
<td>Dyspnea, general fatigue</td>
<td>Pericardium (adhering to the RV free wall and left anterior thoracic wall)</td>
<td>7×5×6</td>
<td>Monophasic</td>
<td>SS18-SSX1</td>
<td>Surgery</td>
<td>Alive (12 months)</td>
</tr>
<tr>
<td>12</td>
<td>2000</td>
<td>Bittira B</td>
<td>20</td>
<td>M</td>
<td>Right arm weakness, right-sided facial droop, aphasia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>2003</td>
<td>Anand AK</td>
<td>21</td>
<td>M</td>
<td>Breathlessness, chest pain</td>
<td>Pericardium (superior of the RV)</td>
<td>5×4×6.5</td>
<td>Monophasic</td>
<td>SYT-SSX2</td>
<td>Surgery</td>
<td>Alive (14 years), recurrences</td>
</tr>
<tr>
<td>14</td>
<td>2003</td>
<td>McGilbray TT</td>
<td>22</td>
<td>M</td>
<td>Witness seizure, loss of consciousness</td>
<td>MV</td>
<td>Large</td>
<td>Monophasic</td>
<td>SYT-SSX1</td>
<td>Surgery</td>
<td>Alive (13 months), local recurrence</td>
</tr>
<tr>
<td>15</td>
<td>2004</td>
<td>Yano M</td>
<td>24</td>
<td>F</td>
<td>Shortness of breath, leg and facial edema, cough</td>
<td>Pericardium (inner surface of the pericardium)</td>
<td>6×5×7 (460 g)</td>
<td>Monophasic</td>
<td>SYT-SSX1</td>
<td>Surgery</td>
<td>Died (1 month)</td>
</tr>
<tr>
<td>16</td>
<td>2004</td>
<td>Hazelbag HM</td>
<td>25</td>
<td>M</td>
<td>Retrosternal pain, shortness of breath, fever</td>
<td>RA</td>
<td>2.9</td>
<td>Biphasic</td>
<td>SYT-SSX1</td>
<td>Surgery</td>
<td>Alive 6 months</td>
</tr>
<tr>
<td>17</td>
<td>2004</td>
<td>Koletsa T</td>
<td>26</td>
<td>M</td>
<td>Facial edema, distention of neck veins, hypertension</td>
<td>Pericardium (superior of the RV)</td>
<td>5×4×3.4</td>
<td>Monophasic</td>
<td>SYT-SSX1</td>
<td>Surgery</td>
<td>Alive 18 months</td>
</tr>
<tr>
<td>18</td>
<td>2004</td>
<td>Provenzano SC</td>
<td>28</td>
<td>M</td>
<td>Fever, vomiting, headache, tiredness, abdominal pain, nocturnal dyspnea</td>
<td></td>
<td></td>
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<tr>
<td>19</td>
<td>2004</td>
<td>Zhao Q</td>
<td>29</td>
<td>M</td>
<td>Shortness of breath, chest pain</td>
<td>RA/LA (biatrial mass)</td>
<td>2.5×2.4×7.2 cm</td>
<td>Monophasic</td>
<td>fibrous</td>
<td>Surgery</td>
<td>Alive (9 months), recurrence</td>
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<tr>
<td>20</td>
<td>2005</td>
<td>Miller DV</td>
<td>30</td>
<td>M</td>
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<tr>
<td>21</td>
<td>2006</td>
<td>Miller DV</td>
<td>50</td>
<td>M</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>22</td>
<td>2006</td>
<td>Miller DV</td>
<td>65</td>
<td>M</td>
<td>Excessive fatigue</td>
<td>RA</td>
<td>4.0×1.0</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Note: LA, left atrium; LV, left ventricle; MV, mitral valve; NA, not available; RA, right atrium; RV, right ventricle.
and 10 survived. Seven of eight patients died within 1 year of onset. Concerning survival, five of 10 patients were still alive for more than 1 year, and one of them survived for more than 14 years in spite of repeated instances of recurrence and resection.23

In conclusion, we report a rare case of synovial sarcoma that originated in the epicardium and grew in the direction of the pericardial cavity. For accurate pathological diagnosis it is necessary to take into consideration the possibility that a synovial sarcoma has developed even in the heart, and it is also important to perform molecular genetic analysis.

REFERENCES
