Primary Pericardial Synovial Sarcoma With Detection of the Chimeric Transcript SYT-SSX

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We report a case of a 19-year-old woman with a primary pericardial synovial sarcoma that extended from the right ventricular free wall to the posterior aspect of the left anterior thoracic wall. Synovial sarcoma was diagnosed by the detection of the chimeric transcript SYT-SSX using reverse transcriptase-polymerase chain reaction (RT-PCR). This transcript is generated by reciprocal translocation between chromosomes X and 18, and is specific to synovial sarcoma that usually occurs in the extremities of young adults. When pathological and immunohistochemical diagnosis of synovial sarcoma is difficult, the molecular biological technique using RT-PCR becomes a powerful method of confirmation of this neoplasm. (Jpn Circ J 1999; 63: 330–332)

Key Words: Chimeric transcript, Primary pericardial tumor, Reverse transcriptase-polymerase chain reaction (RT-PCR), Synovial sarcoma, SYT-SSX

Primary malignant tumors of the heart and pericardium are rare, and most of them are sarcomas. In particular, synovial sarcoma that primarily arises from the heart and pericardium is extremely rare.1–3 In the last few decades, chromosome analysis of malignant tumors, especially hematologic neoplasms such as leukemia and lymphoma, has been widely used for diagnosis and assessment of disease prognosis. More recently, a number of cytogenetic abnormalities have been reported in solid tumors. One of them is the reciprocal translocation, t(X;18), associated with synovial sarcoma of the extremities. Primary cardiac synovial sarcoma with t(X;18) has also been reported.2,3 The breakpoint of t(X;18) is cloned, and this translocation results in fusion of the SYT gene of chromosome 18 to either of 2 genes, SSX1 or SSX2, at Xp11.2.4 This rearrangement of genes produces a chimeric SYT-SSX transcript that can be detected by reverse transcriptase-polymerase chain reaction (RT-PCR).

A primary pericardial synovial sarcoma with the chimeric transcript SYT-SSX is presented here. Detection of this chimeric transcript by RT-PCR is considered to be a useful tool for diagnosis of synovial sarcoma.

Case Report

A 19-year-old woman was admitted to our hospital presenting with dyspnea and general fatigue. She had no history of cardiac disease. Physical examination revealed a heart rate of 76 beats/min and blood pressure of 100/74 mmHg with pulsus paradoxus. Jugular venous distention was present, but no Kussmaul sign. Cardiac examination...
Pericardial Synovial Sarcoma Diagnosed by RT-PCR

revealed distant heart sounds and a weak apex beat. The liver was not palpable and pitting edema was absent in both legs. Hemogram and biochemical profiles were almost within normal limits and arterial blood gas analysis showed hypoxia. Chest radiography on admission showed cardiomegaly but no abnormality in the lung fields. An electrocardiogram demonstrated normal sinus rhythm and low voltage. An echocardiogram revealed a massive pericardial effusion with a wide-based mass adjacent to the right ventricular free wall.

A computed tomography (CT) scan of the chest showed a large pericardial effusion and an non-homogenously enhanced large mass occupying the anterior part of the left thoracic cavity between the chest wall and the anterior wall of the heart (Figs 1A,B). No lymph node enlargement was seen. Magnetic resonance imaging (MRI) demonstrated normal sinus rhythm and low voltage. An echocardiogram revealed a massive pericardial effusion with a wide-based mass adjacent to the right ventricular free wall.

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Fig 2. A photomicrograph of the primary pericardial tumor showing fasciculi of the spindle cells and a glandular structure. (Hematoxylin-eosin, original ×120).

Fig 3. Detection of fusion SYT/SSX transcripts by RT-PCR. M, 1kb ladder; lane 1, a biphasic synovial sarcoma; lane 2, the present case; lane 3, a malignant mesothelioma; lane 4, an adenocarcinoma of the lung.

Pathological Findings

The resected mass was soft, 11×14×7 cm in size and 460 g in weight. Gross section of the tumor showed a mixture of necrotic, hemorrhagic and cystic changes. The tumor was histologically composed of short fasciculi of spindle cells. A hemangiopericytomatous, herringbone pattern, with palisading of the tumor cell nuclei were also noted. A glandular structure was found in only one slide (Fig 2). Nuclei of the spindle cells were spindle to ovoid in shape and darkly stained. Immunohistochemically, a majority of the tumor cells reacted positively to vimentin (Bioscience; Emmenbrucke, Switzerland), and a small number had a positive reaction to keratin (wide spectrum screening, DAKO; Glostrup, Denmark). Staining was negative to epithelial membrane antigen (EMA, DAKO) and S-100 protein (DAKO).
Detection of the Chimeric Transcript, SYT-SSX

To confirm the tumor diagnosis, the biopsied material of the recurrent lung tumor was subjected to RT-PCR analysis. A synovial sarcoma of the extremity forming a biphasic pattern, a malignant mesothelioma of the chest wall and an adenocarcinoma of the lung were included in the assays and served as control specimens. Total RNA was extracted with ISOGEN® (Nippon gene) and 1 μg of RNA was reverse transcribed using random hexamers and the GeneAmp® RNA-PCR kit (Perkin Elmer), in accordance with the manufacturer’s protocol. The resulting cDNA was amplified by PCR using SYT (5'-CAACAGCAAGATG-CATACCA-3’) and SSX (5’CATTTGCTATGACCT-GATG-3’) primers. Amplification was carried out using AmpliTaq® polymerase (Perkin Elmer) and a Perkin Elmer thermal cycler. Thirty amplification cycles were performed, each consisting of 1 min at 93˚C (denaturation), 1 min at 55˚C (annealing) and 1 min at 72˚C (extension). The amplified products were separated by agarose (3%) gel electrophoresis and stained with ethidium bromide. The RNA identified products were separated by agarose (3%) gel electrophoresis and stained with ethidium bromide. The RNA from both the biphasic synovial sarcoma and the present case yielded a major, 585 bp DNA fragment (Fig 3).

Sequencing of the amplified DNA revealed the same in-frame junction between the SYT and the SSXI gene previously described by Crew et al. This confirmed the diagnosis of synovial sarcoma.

Discussion

Primary tumors of the heart and the pericardium are rare. Approximately 37% of such tumors are malignant. Among these, sarcomas including angiosarcoma, malignant fibrous histiocytoma (MFH) and leiomyosarcoma are most frequent. Among primary pericardial tumors, mesothelioma is most common, while synovial sarcoma is extremely rare.2,3

Synovial sarcoma ordinarily arises from the large joints of the extremities, but can also arise in the neck, tongue, esophagus, retroperitoneum and other areas. This neoplasm is histologically classified into 4 types: biphasic, monophasic fibrous, rare monophasic epithelial, and poorly differentiated types.10 The biphasic type, as a classical type of synovial sarcoma, is recognized by the coexistence of an epithelial component and a fibroblast-like spindle-cell area. However, diagnosis is difficult in the case of the monophasic fibrous type with a predominantly spindle-cell pattern and only a minute focus of the epithelial component. This type is frequently confused with fibrosarcoma, malignant hemangiopericytoma, or malignant peripheral nerve sheath tumor.

Cyogenetic studies have been used for differential diagnosis of neoplasms and many sarcomas have been characterized by specific chromosome translocations that seem to be etiologically significant. Cloning of their breakpoints revealed that these translocations result in the production of novel chimeric transcripts. These chimeric transcripts provide tumor-specific markers that can be detected by RT-PCR. In synovial sarcoma, more than 80% of the cases have the reciprocal translocation t (X;18) (p11.2;q11.2), resulting in fusion of the SYT gene at 18q11 to SSX at Xp11.2.2 There are 2 subtypes of SSX; SSXI and SSX2, which encode closely related proteins (81% identity) of 188 amino acids.3 In the present case, detection of this synovial sarcoma-specific chimeric transcript, SYT-SSXI, led to the final diagnosis of synovial sarcoma. As the tumor was predominantly composed of short fasciculi of spindle cells (a glandular structure was found in only one slide), this case was diagnosed as the monophasic fibrous type. To our knowledge, this is the first case of a primary pericardial synovial sarcoma confirmed by a molecular biological technique. The primary occurrence of synovial sarcoma in the pericardium reinforces the theory that this neoplasm arises not only from synovium but also from mesenchymal elements.

The prognosis of primary cardiac sarcoma is generally poor. Its complete resection is required for improved survival, but this is difficult because most of the tumors are found at the advanced stage. Adjuvant chemotherapy and irradiation are of little effect because of the frequent recurrence and metastasis of the neoplasm.

In summary, we described a primary pericardial spindle-cell sarcoma with detection of the chimeric transcript SYT-SSX. This specific transcript has been reported in synovial sarcoma of the extremities and greatly contributed to the diagnosis of primary pericardial synovial sarcoma in this case.

References


