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■ CASE REPORT ■

Primary Monophasic Synovial Sarcoma Arising in the Mesentery: Case Report of an Extremely Rare Mesenteric Sarcoma Confirmed by Molecular Detection of a *SYT–SSX2* Fusion Transcript

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Synovial sarcoma arises in the para-articular tissues, and it can also occur in various unexpected sites. We report a rare case of primary monophasic synovial sarcoma (MSS) arising in the mesentery. A 59-year-old man presented with a palpable abdominal mass. On microscopic examination, the entire tumor comprised a dense proliferation of the spindle cells without epithelial components. The tumor cells were positive for transducin-like enhancer of split 1, bcl-2, epithelial membrane antigen and CD99 but negative for CD34, CD117, alpha-smooth muscle actin, cytokeratin, and calretinin on immunohistochemistry. The reverse transcriptase-polymerase chain reaction revealed a single 151-bp fragment representing the *SYT-SSX2* fusion transcript. Because mesenteric MSS is extremely rare and many cases display histologic findings that overlap with those of more frequently involved tumors such as hemangiopericytoma and gastrointestinal stromal tumor, there is a chance of making an incorrect diagnosis that can result in an inappropriate treatment.

Key Words: Synovial sarcoma; Mesentery; Spindle cell sarcoma; Immunohistochemistry; Reverse transcriptase polymerase chain reaction

Synovial sarcoma is an aggressive malignant tumor that commonly arises in the para-articular tissues in adolescents and young adults. However, it may also arise in unexpected sites, such as head and neck regions[1] and even the genitourinary tract.[2] Primary intra-abdominal or retroperitoneal synovial sarcoma is a rare condition. To our knowledge, only one case of monophasic synovial sarcoma (MSS) of the mesentery has been previously reported in the English literature.[3] Given the very low incidence of the primary MSS that arises in the mesentery and intra-abdominal cavity, there is a chance that it may not be considered in differential diagnosis. This eventually results in a misdiagnosis as another type of spindle cell tumor. It is therefore important to be aware of the possibility of primary MSS of the mesentery. It is also necessary to perform further evaluation such as immunohistochemistry or molecular studies for detection of *SYT-SSX* fusion transcripts, which is essential for avoiding misdiagnosis. We describe a rare case of primary MSS of the mesentery around the jejunum, which was confirmed by the detection of *SYT-SSX* fusion gene transcripts using the reverse transcriptase-polymerase chain reaction (RT-PCR).

CASE REPORT

A 59-year-old man was admitted to the hospital because of a 3-month-history of huge abdominal palpable mass in the right lower quadrant. However the patient presented with no other symptoms, such as abdominal pain or indigestion. Physical examination showed a smooth, bulging mass in the right lower abdomen, but revealed no other physical abnormalities. A magnetic resonance imaging of the abdomen revealed a well-defined heterogeneously enhanced giant mass involving the lower abdomen adjacent to the jejunum (Fig. 1). The suspected preoperative diagnosis was a sort of mesenteric or omental tumor, such as gastrointestinal stromal tumor (GIST), hemangiopericytoma

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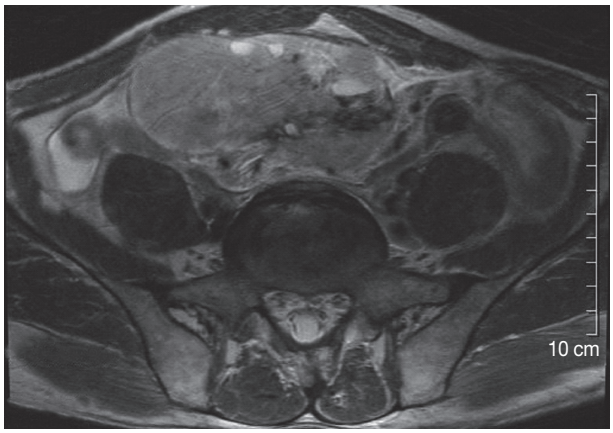

Fig. 1. A T2-weighted magnetic resonance imaging shows a heterogeneous tumor involving the lower peritoneal cavity.

or leiomyosarcoma.

Wide excision and segmental resection of the jejunum were performed. A large tumor was located in the mesentery, primarily around the jejunum, and it adhered to the outer wall of the jejunum. Postoperative adjuvant chemotherapy was performed using a combination regimen of adriamycin with cis-diamminedichloroplatinum for six cycles. Gross examination revealed a relatively well-circumscribed mass measuring 12×10×5 cm, and it was located throughout the outer wall of the small intestine and mesentery. The cut surface showed a tan, fish-like fleshy appearance with multifocal hemorrhage and friable areas (Fig. 2A). Microscopically, the tumor was well defined by a thin fibrous capsule and it grew into the outer wall of the jejunum from the mesenteric wall. There were dense cellular sheets with alternating hypocellular areas (Fig. 2B). Spindle cells were small, uniform and closely packed with scant cytoplasm. Relatively frequent mitotic figures were observed (more than 10/10 high power fields). Hemangiopericytomatous vascular arrangements were also identified in some areas. Stromal hyalinization was found in a small portion of the neoplasm (Fig. 2C). On immunohistochemistry, the tumor cells were positive for transducin-like enhancer of split 1 (TLE1; 1:20, Santa Cruz Biochemicals, Santa Cruz, CA, USA) (Fig. 2D), CD99 (1:100, Labvision, Neomarkers, Fremont, CA, USA) (Fig. 2E), bcl-2 (1:100, Dako, Glostrup, Denmark) (Fig. 2F), epithelial membrane antigen (EMA; 1:100, Dako) (Fig. 2G) and S-100 protein (1:1,000, Dako), but negative for alpha-smooth muscle actin (1:200, Labvision, Neomarkers), CD34 (1:200, Labvision, Neomarkers), cytokeratin AE1/AE3 (1:400, Biogenex, San Ramon, CA, USA), calretinin (predilution, Labvision, Neomarkers) and CD117 (1:200, Dako) (Fig. 2H). Ki-67 (1:100, Labvision, Neomarkers) was expressed in 5% of tumor cells.

For identification of *SYT-SSX* fusion gene transcripts, an additional RT-PCR of t(X;18) was performed. Total RNA was isolated from a 4-μm paraffin-embedded tissue section. The cDNA was synthesized with SuperScript II RNase Reverse Transcriptase (GIBCO BRL Life Technologies, Gaithersburg, MD, USA) in the presence of random primers for an hour at 42℃. The cDNA was amplified using the forward and reverse primers: 5′-CCAGCAGAGGCCTTATGGATA-3′; 5′-GGTGCAGTTGTTTCCCATCG-3′ for *SYT*; 5′-GGTGCAGTTGTTTCCCATCG-3′ for *SSX1*; 5′-GGCACAGCTCTTTCCCATCA-3′ for *SSX2*. The RT-PCR was carried out under the following thermocycling conditions: 35 amplification cycles, each consisting of denaturation at 94℃ for 30 seconds, annealing at 61℃ for 30 seconds and elongation at 72℃ for 30 seconds, with an extension at 72℃ for 1 minute. The amplified products were electrophoresed on a 1.5% agarose gel and then stained with ethidium bromide. The RT-PCR produced a band for the *SYT-SSX2* fusion gene transcript (151 bp) (Fig. 3). The final diagnosis was primary mesenteric synovial sarcoma with monophasic fibrous type. Two years later, the patient presented with a recurrence of the multiple masses in the mesocolon. The patient is currently being treated with a combination chemotherapy regimen consisting of etoposide, ifosfamide, and cisplatin.

DISCUSSION

Given the rarity of spindle cell tumor in the intra-abdominal cavity, it would be difficult to make a diagnosis of it. A total of 50 cases of intra-abdominal synovial sarcoma has been reported up to present.[4,5] Of these, there was only one case of primary mesenteric synovial sarcoma with monophasic subtype according to a review of the English literature.[3] A diagnostic approach to biphasic synovial sarcoma can also be made even without ancillary tests such as immunohistochemistry or molecular study. But this does not always apply to MSS, that arising in an unusual location. Because the MSS of the mesentery is a very rare, its diagnosis cannot be established before more frequently encountered spindle cell tumors including GIST and other kinds of sarcomas could be completely ruled out. This can be rather worrisome because patients may receive an inappropriate treatment if pathologists or physicians make an incorrect diagnosis of it, particularly in cases of MSS occurring in an uncommon site. As mentioned by Fisher *et al.*,[6] MSS is commonly confused with other spindle cell malignancies such as fibrosarcoma, malignant hemangiopericytoma or malignant peripheral nerve sheath tumor (MPNST) as well as GIST according to micro-

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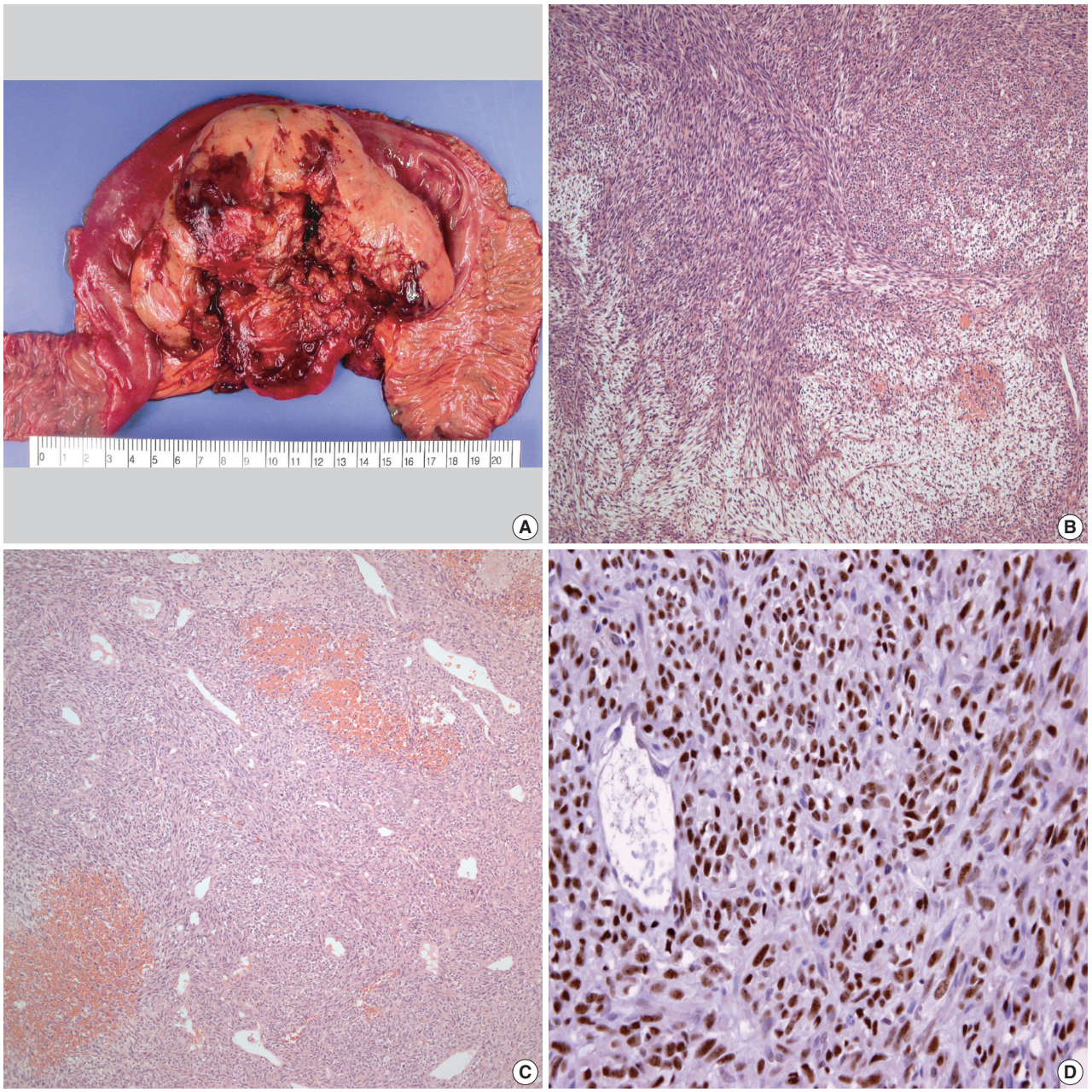

Fig. 2. Gross and microscopic findings. (A) Gross specimen showing a well-circumscribed tumor with a hemorrhage in the mesentery. (B) Alternating dense and scanty spindle cells with a herringbone-like pattern. (C) Hemangiopericytomatous vascular arrangement and hyalinized stroma. The immunohistochemical findings for (D) transducin-like enhancer of split 1. (*Continued to the next page*)

scopic findings due to the overlap of histological features. In the current case, the immunohistochemistry and microscopic findings were most compatible with MSS, rather than the sarcomas mentioned above. No immunoreactivity for cytokeratin AE1/AE3 was identified in the current case, although it is not an uncommon finding in those of MSS. According to Begueret *et al.*,[7] only 58.3% of total cases of MSS had a focal positive reaction to cytokeratin AE1/AE3. These authors also noted that EMA expression was more commonly found in cases of MSS. Immunoreactivity for TLE1, CD99 and bcl-2 in spindle cells is not suggestive of fibrosarcoma but it is consistent with the immunohistochemical findings of synovial sarcoma,[8] despite the presence of identical morphologic findings such as herringbone arrangement of spindle cells in some areas. In addition, there are often distinctive morphologic features in cases of MSS and these include thick collagen or a hemangiopericytomatous vascular

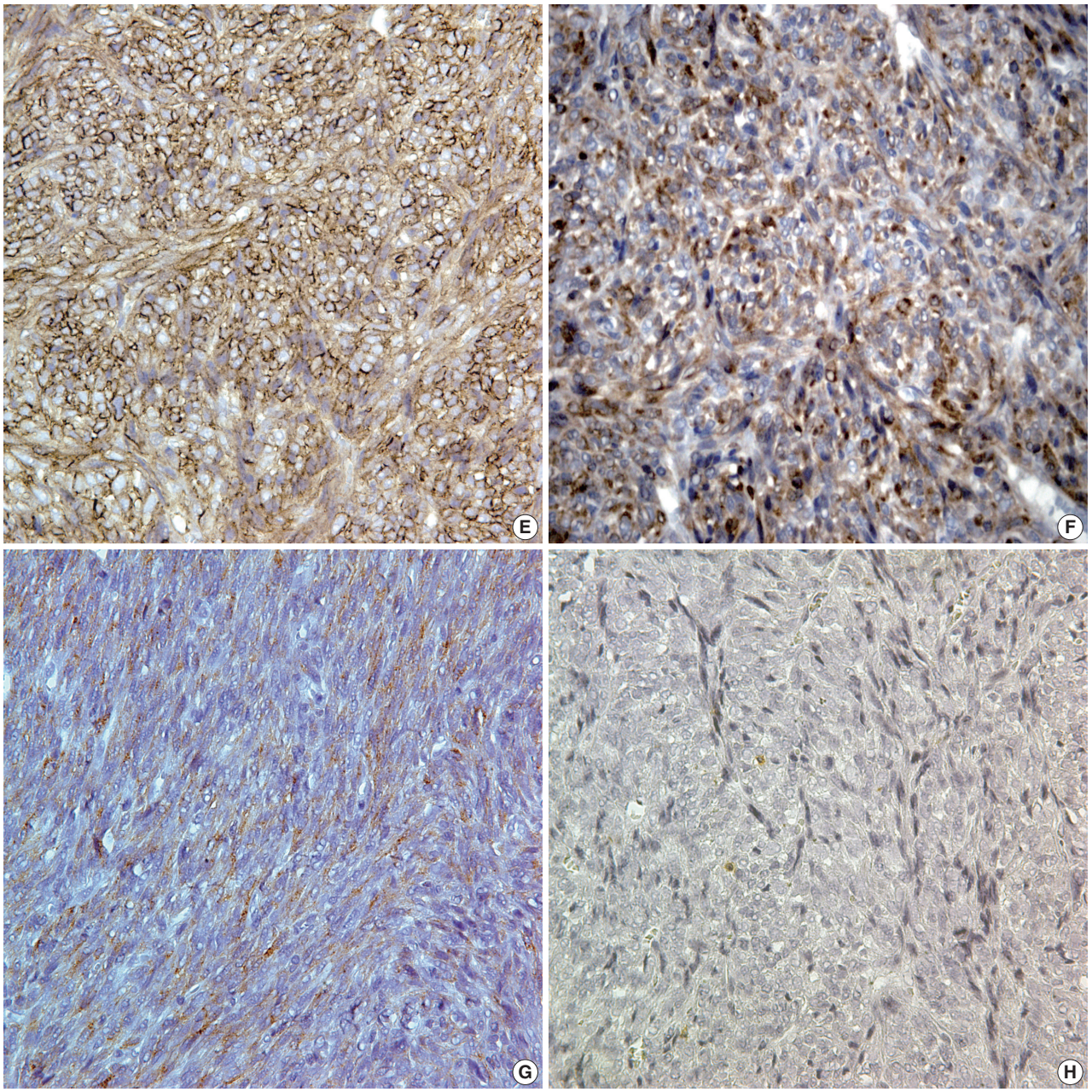

Fig. 2. (*Continued from the previous page*) (E) CD99, (F) bcl-2, and (G) epithelial membrane antigen. (H) Negative expression of CD117 in the tumor cells.

pattern which are rarely seen in fibrosarcomas.[8] Due to the hemangiopericytomatous vascular arrangements and higher incidence than synovial sarcoma of the intra-abdominal cavity,[9] it is mandatory to make a differential diagnosis of MSS from hemangiopericytoma. It should be noted, however, the MSS has the "hemangiopericytomatous vascular arrangement" throughout the entire neoplasm. In addition, the MSS generally has a greater cellularity with a higher nuclear to cytoplasmic ratio, more mitotic figures and straighter cell alignments.[10] Finally, the expression of CD34 is absent in cases of synovial sarcoma but it is typically seen in most cases of hemangiopericytoma.[10] A differential diagnosis of MPNST should be made from MSS based on the differences in chemosensitivity between the two sarcomas.[8] A differential diagnosis between the two tumors can be made not only with an ancillary test using a combination of S-100 protein and CD99 but also based on distinct nuclear findings such as wavy contour on microscopic examination. The GIST should also be considered in the diagnosis, although it can be

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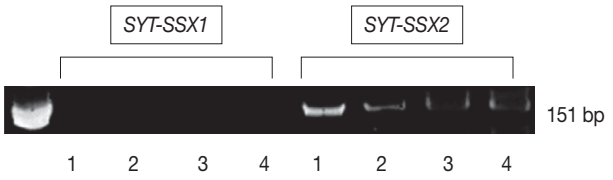

Fig. 3. Analysis of the t(X;18) translocation using the reverse transcriptase-polymerase chain reaction (RT-PCR) is performed to confirm the diagnosis of synovial sarcoma. The RT-PCR reveals a *SYT-SSX2* fusion transcript (151 bp) (left, DNA ladder; 1, the current case; 2-4, positive control [2, 4, monophasic synovial sarcoma; 3, biphasic synovial sarcoma]).

distinguished from the MSS based on some distinctive histologic and immunohistochemical findings.[8,11] GISTs are almost always positive for CD34 or CD117, whereas synovial sarcoma is negative for both markers.[12]

According to Begueret *et al.*,[7] however, unusual immunohistochemical results might occur in the intrathoracic MSS. These authors reported that CD34, S-100 protein and CD117 were expressed in 4-8% of MSS on the immunohistochemistry.[7] In addition, TLE1 was also expressed in a number of tumors when it has been considered as specific markers for synovial sarcoma.[13] Therefore, the molecular detection of the *SYT-SSX* fusion gene transcripts is necessary along with immunohistochemistry. Coindre *et al.*[14] conducted a prospective study to investigate the utility of molecular testing in 204 patients with synovial sarcoma and concluded that it was very useful in detecting the MSS that occurred in uncommon or unexpected sites including the retroperitoneum and lung. We have therefore performed the RT-PCR to detect the *SYT-SSX* fusion gene transcript and thereby detected it in the current case. The t(X;18)(p11.2;q11.2) translocation is found in about 90% of synovial sarcomas and it is considered a pathogenic factor of this tumor.[15] Two different types of breakpoints on chromosome X have been reported to correspond to the chimeric genes *SYT-SSX1* and *SYT-SSX2*.[16] Nearly all monophasic tumors bear the *SYT-SSX2* fusion, as shown in the current case.[8] Because the primary MSS of the mesentery is an extremely rare condition, it can be misdiagnosed as another type of spindle cell tumor. It is mandatory to recognize the occurrence of monophasic synovial sarcoma of the mesentery based on the morphological and genetic characteristics, which may help in making a correct diagnosis.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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