

Primary Synovial Sarcoma of the Kidney: A Case Report and Literature Review

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Received : October 9, 2008
Accepted : January 6, 2009

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Synovial sarcoma is a rare renal neoplasm that is not easy to diagnose unless SYT-SSX fusion transcripts are identified. We report here on a case of primary renal synovial sarcoma in a 35-year-old woman. A mass was discovered by accident in the lower part of the right kidney when ultrasonography was performed, and it was removed via radical nephrectomy. Grossly, the tumor was a homogeneously tan-brown soft mass that measured $4.5 \times 3.2 \times 3.0$ cm, and it was encircled by a well-defined cystic space. The lesion exhibited hypercellularity of the oval or short spindle cells that were arranged in various solid sheets or intersecting fascicles. Immunohistochemically, the tumor showed diffuse positivity for vimentin, bcl-2 and CD99, and it showed focal positivity for epithelial membrane antigen. The SYT-SSX fusion transcripts were detected by reverse transcription-polymerase chain reaction (RT-PCR). Synovial sarcoma should be considered in the differential diagnosis when a spindle cell neoplasm is encountered in the kidney.

Key Words : Synovial sarcoma; Kidney; SYT-SSX fusion protein

Primary renal synovial sarcoma (PRSS) is a rarely seen spindle cell neoplasm that's characterized by the specific translocation $t(X;18)(p11.2;q11)$. To date, 26 cases of genetically confirmed PRSS have been reported in the English literature, but none has yet been reported in the Korean literature.¹⁻¹⁸ It is not easy to diagnose a renal synovial sarcoma due to the paucity of specific immunohistochemical markers and/or ultrastructural features, and perhaps this is due to the rarity of this kidney tumor. It is necessary to making the differential diagnoses from the more common renal spindle cell tumors, including adult blastemal/primitive stromal Wilms tumors, mixed epithelial and stromal tumors, undifferentiated or sarcomatoid carcinoma, and primitive neuroectodermal tumors. Moreover, to arrive at a diagnosis of PRSS, the possibilities of distant metastasis and a secondary extension of a retroperitoneal synovial sarcoma to the kidney must be ruled out.

We present here a case of monophasic PRSS in a 35-year-old woman, and the SYT-SSX fusion transcript was detected through nested reverse transcription-polymerase chain reaction (RT-PCR) analysis with using the formalin-fixed and paraffin-embedded tumor tissue. We describe the gross and histopathologic findings of the case, several important aspects of the differential diagnoses

are discussed and the characteristics of genetically confirmed PRSS are summarized.

CASE REPORT

A 35-year-old woman with a right renal mass that was incidentally found during a periodic ultrasonographic examination was admitted to our urology clinic. There were no related complaints such as pain, tenderness, hematuria or a palpable mass. She had a history of near total thyroidectomy at another hospital for papillary carcinoma 2 years previously, and a history of right salpingectomy for a tubal pregnancy 10 months previously. She had been on regular follow-up and was taking synthroid medication since the thyroidectomy. CT and magnetic resonance imaging revealed a 7 cm sized cavitary lesion that contained a slightly enhanced protruding solid mass measuring about 3.8 cm in diameter at the lower pole of the right kidney, and there were multiple tiny calcifications in the cystic wall (Fig. 1A). The possibility of cystic renal cell carcinoma confined to the kidney (clinical stage I) was preferentially suggested, and so radical nephrectomy of the right kidney was done via laparoscopy.

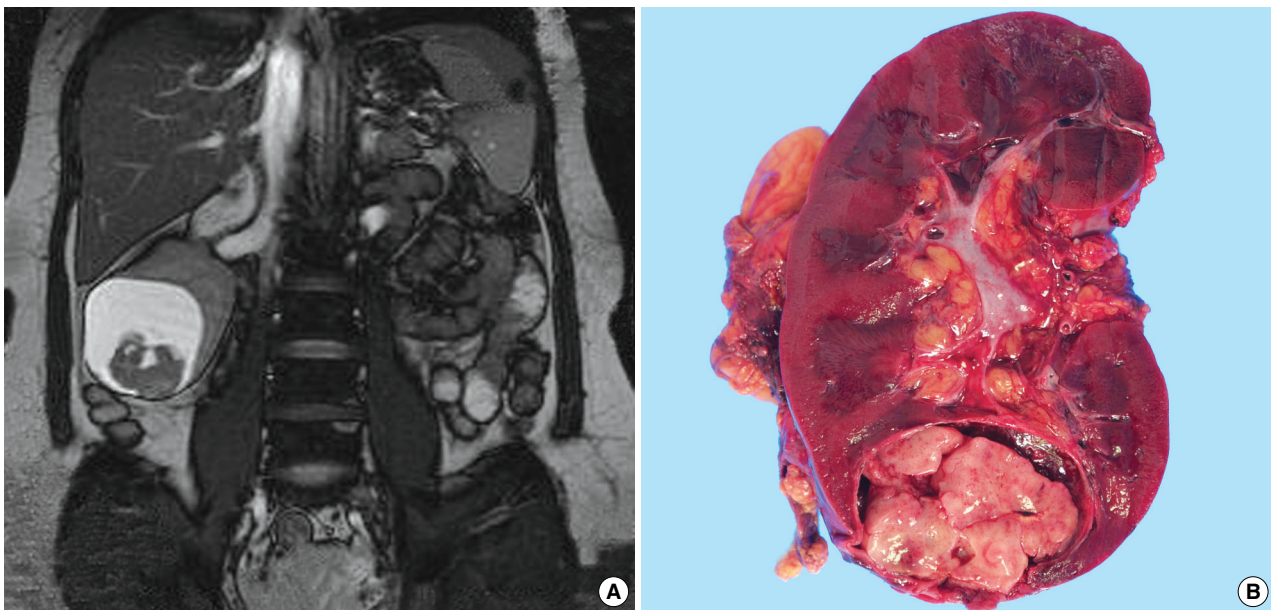


Fig. 1. (A) The MRI image shows a cystic cavity containing a protruding and slightly enhancing solid mass at the lower pole of the right kidney and this mass measured about 3.8 cm at the largest diameter. (B) Grossly, the tumor was soft, tan-brown in color and encircled by a cystic cavity.

Grossly, the tumor was soft and homogeneously tan-brown, it measured $4.5 \times 3.2 \times 3.0$ cm, it was encircled by a well-defined cystic space and it was detached from the cystic wall during artificial aspiration of the cystic fluid (Fig. 1B). The mass was not connected to the pelvocaliceal tracts. The remaining renal parenchyma was unremarkable, except for mild congestion. Microscopically, the tumor was composed of solid sheets of spindle cells that showed a vague fascicular pattern (Fig. 2A). The tumor cells mostly had spindle or ovoid shapes, eosinophilic cytoplasm, and a high nuclear/cytoplasmic ratio (Fig. 2B), and the cells focally showed clear or rhabdoid cytoplasm. They also displayed moderate nuclear atypia and 3 to 5 mitoses per 10 high-power fields. Areas of necrosis and hemosiderin-laden or foamy macrophages were also observed focally (Fig. 2C). There was no epithelial lining in the cyst, and the cystic wall was infiltrated by tumor cells that were identical to those of the solid mass (Fig. 2D).

Immunohistochemically, the tumor was focally positive for EMA (1:200, Novocastra, Newcastle, UK) and calretinin (1:25, Zymed, South San Francisco, CA, USA), and diffusely positive for vimentin (1:50, Novocastra), CD99 (1:200, DiNoA, Seoul, Korea) and bcl-2 (1:25, Novocastra) (Fig. 3). The tumor cells were negative for cytokeratin (1:50, Novocastra), S100 protein (1:200, Novocastra), CD34 (1:25, Novocastra), smooth muscle actin (SMA, 1:50, Novocastra) and HMB45 (1:40, Signet Pathology Systems, Dedham, MA, USA).

The tumor cells with clear cytoplasm were weakly positive for

PAS, but they were negative for Alcian blue at pH 2.5 and Sudan black B. Ultrastructurally, the tumor cells showed a few organelles and some intermediate filaments (Fig. 4A). Desmosomes or tight junctions were not identified.

Nested RT-PCR analysis with using the RNA extracted from the formalin-fixed, paraffin-embedded tissue was performed as previously described.¹⁹ The primer sequences were as follows: SYT1, 5'-GGATATAGACCAACACAGCCTGGA-3'; SYT2, 5'-CAGCAGAGGCCTTATGGATATGAC-3'; and SSX, 5'-GGGCCAGATGCTTCTGACACT-3'. SYT-SSX fusion transcripts resulting from the specific translocation t(X;18)(p11.2;q11) were detected (Fig. 4B).

Postoperatively, the patient received no adjuvant chemotherapy and she has shown no evidence of local recurrence for six months after the surgery.

DISCUSSION

Primary renal sarcomas are rare; leiomyosarcomas account for 50-60% of all of them, followed by liposarcoma, rhabdomyosarcoma, and fibrosarcoma.² Although synovial sarcoma (SS) is a tumor of an unknown histogenesis, this neoplasm is a clinically and pathologically well-defined entity that occurs predominantly in the para-articular, deep soft tissue of the extremities. Histologically, it is subclassified into the biphasic and monopha-

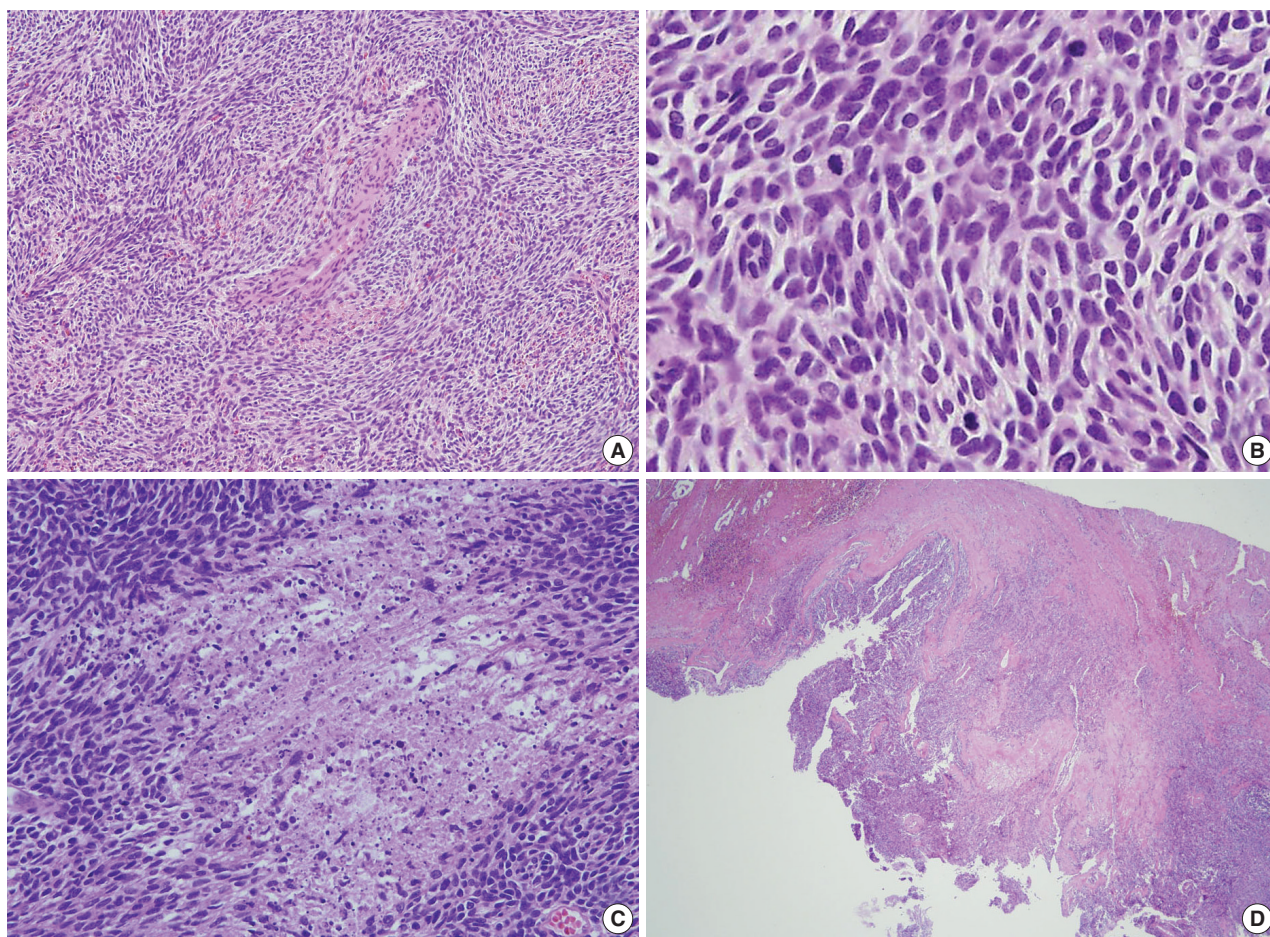


Fig. 2. (A) The solid sheets of spindle cells show a vague fascicular pattern. (B) The tumor cells are mostly shown to have a spindle or ovoid shape and a high N/C ratio, moderate nuclear atypia and 3 to 5 mitoses/10 HPF. (C) Focal necrosis is also observed. (D) The cystic wall is focally infiltrated by tumor cells that were identical to those cells of the solid mass.

sis types, and it is also subclassified into the poorly differentiated variants. As the molecular diagnostic methods expand, reports of PRSS appear to be increasing since the first description in 2000,² and many of the previously described embryonal sarcomas of the kidney are now recognized to be PRSS.^{2,3}

To date, 26 genetically confirmed PRSS cases have been reported in the English medical literature.¹⁻¹⁸ The patients they occurred in were between 17 and 71 years of age (average 39) without a sex predilection. The patients complained of flank or abdominal pain and/or gross hematuria. One patient had a palpable mass, and three patients were asymptomatic like our case. Most of these neoplasms were interpreted by the radiologic findings as being renal cell carcinomas. Grossly, they varied from case to case, but they were generally well-defined, irregular large masses between 5 and 20 cm in diameter. Extensions to the perirenal soft tissue and/or the renal hilum were present in 11 cases,^{2,3,12-17} to the adrenal glands and the liver in one¹² and to the inferior

vena cava in two,² and the mass had ruptured into the abdominal cavity in one case.² Grossly identifiable smooth-walled cysts were identified in eight cases.^{2,5,9,12,17} The present case also showed a solid tumor encircled by a pseudocyst that was perhaps the result of degenerative change. The cystic change might provide an impression of benign tumors such as a mixed epithelial and stromal tumor. The histological subtypes were monophasic in 14 cases,^{2,4,6,9,10,13,14,16,18} poorly differentiated in seven cases,^{3,11,12,15} biphasic in four cases^{5,8,17} and not ascertained in one case.⁷

The immunohistochemical summary of these neoplasms was as follows: positivity for cytokeratin (AE1/AE3 or Cam5.2) in 10/22 cases, positivity for EMA in 8/17 cases, positivity for vimentin in 16/17 cases, positivity for CD99 in 9/19 cases, positivity for CD56 in 9/10 cases, positivity for synaptophysin in 1/2 cases, positivity for neuron specific enolase in 2/2 cases, positivity for WT-1 in 2/3 cases and positivity for bcl-2 in 8/8 cases. There was no immunoreaction to the antibodies to CD34 (0/8),

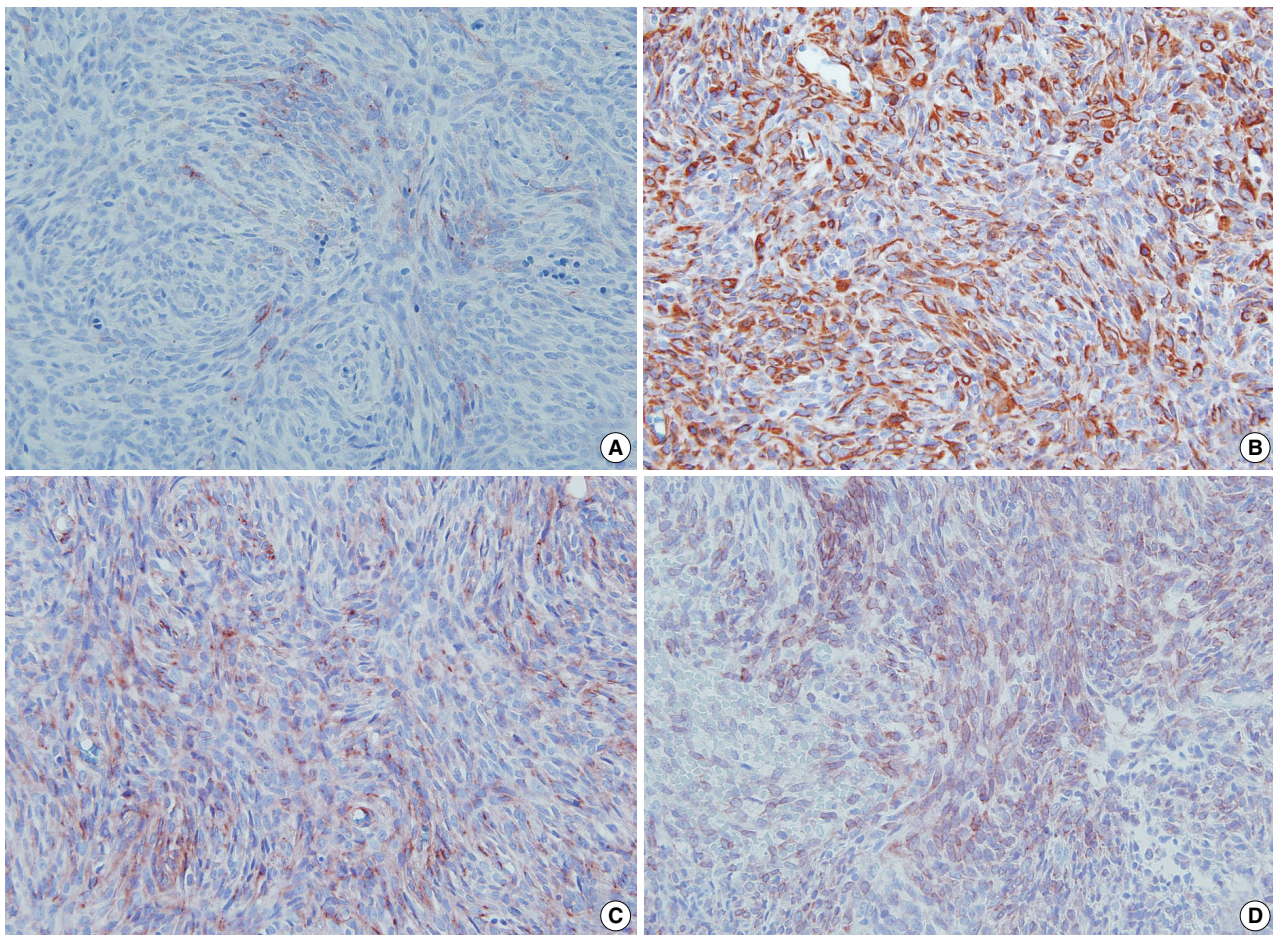


Fig. 3. The tumor cells are focally positive for EMA (A) and they were diffusely positive for vimentin (B), CD99 (C) and bcl-2 (D).

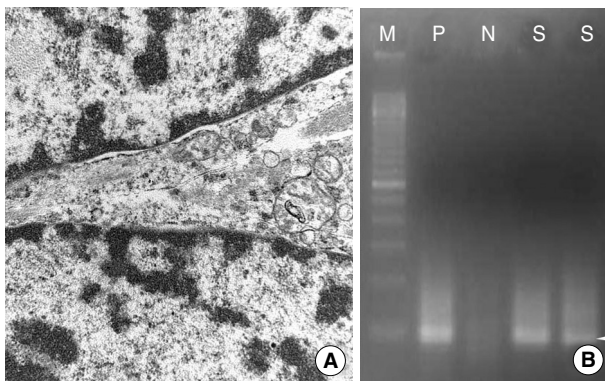


Fig. 4. (A) Ultrastructurally, a few organelles and some quantity of intermediate filaments are present. Desmosomes or tight junctions are not identified. (B) SYT-SSX fusion transcripts are detected through RT-PCR analysis using the SYT-SSX primer (92 bp). M, molecular marker; P, positive control; N, negative control; S, present case.

desmin (0/21), SMA (0/22), S-100 protein (0/16), CD10 (0/1), or CD15 (0/1). The present case showed positivity for vimentin, CD99, bcl-2, EMA and calretinin, and negativity for cytokeratin,

S-100 protein, CD34, SMA, and HMB45, which is like some of the previously reported immunoprofiles.

Monophasic PRSS should be differentiated from the following tumors; mixed epithelial and stromal tumor with an exclusively stromal component, adult blastema/primitive stromal Wilms' tumor, fibrosarcoma, leiomyosarcoma, malignant peripheral nerve sheath tumor, hemangiopericytoma, solitary fibrous tumor, primitive neuroectodermal tumor, sarcomatoid renal cell carcinoma and extension of a primary retroperitoneal sarcoma and metastasis.

The mixed epithelial and stromal tumor can be distinguished from PRSS by their bland features and the presence of an epithelial element. Hemangiopericytoma and solitary fibrous tumor are immunohistochemically different from PRSS in their CD34 positivity and cytokeratin negativity. Although EMA and CD56 are positive for both PRSS and MPNST, the tumor cells in MPNST are rarely positive for CD99, which is frequently expressed in PRSS. However, many other malignant tumors may be difficult to differentiate from PRSS as the histological or immunohisto-

chemical findings can overlap. Molecular studies, such as on *SYT-SSX* and the abnormalities involving *WT1* and *EWS-FLI1*, are important tools for making the differential diagnosis.

Synovial sarcoma is cytogenetically characterized by the translocation t(X;18)(p11.2;q11) that generates a fusion between the *SYT* gene on chromosome 18 and one member of the *SSX* family gene (*SSX1*;*SSX2*;*SSX4*) on chromosome X. This translocation was recognized 20 years ago in soft tissue synovial sarcoma,¹⁹ and RT-PCR method has been widely used to detect the fusion transcript.²⁰ Argani *et al.*² demonstrated that monophasic or poorly differentiated PRSS was more frequently associated with *SYT-SSX2*, while the biphasic PRSS was more commonly associated with *SYT-SSX1*. Our case of monophasic PRSS was confirmed to harbor *SYT-SSX*, but the differentiation between *SSX2* and *SSX1* was not possible with the primer we used.

In summary, PRSS is not easy to diagnose until *SYT-SSX* fusion transcripts are identified because of the lack of specific immunohistochemical markers and/or ultrastructural features, and perhaps because of its rarity. So we did not refer to a previous case report of renal SS in the Korean medical literature that was without genetic studies.

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