Primary Synovial Sarcoma of the Kidney with Unusual Recurrence: Ureteral Stump Recurrence after Radical Nephrectomy

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We present a case report of a 38-year-old woman with a 6.3x4.0cm left renal mass that was detected on computed tomography (CT). A laparoscopic radical nephrectomy was performed, and the morphological and immunohistochemical findings were compatible with a diagnosis of primary renal synovial sarcoma. Reverse transcription-polymerase chain reaction showed the weak SYT-SSX1 and the strong SYT-SSX2 fusion gene transcripts. She complained of gross hematuria during the follow-up, and a CT scan showed a 4cm sized enhancing mass lesion along the distal ureter and ureterovesical junction. The ureteral stump and bladder cuff were removed, and we confirmed a recurrence on the ureteral stump. **(Korean J Urol Oncol 2014;12:89-94)**

Key Words: Kidney, Synovial sarcoma, Ureteral stump

Primary renal synovial sarcomas (PRSS) is an extremely rare renal neoplasm that was first described in 2000 by Kim et al.[1] and Argani et al.[2] who distinguished it from a subset of embryonic kidney sarcomas. Fewer than 70 cases of primary synovial sarcoma of the kidney have been reported.[3] An accurate diagnosis of PRSS is difficult because of its rarity and its similar presentation to other renal tumors. Therefore, patients typically undergo radical nephrectomy. The presence of a unique chromosomal translocation, t(X;18)(p11.2;q11.2), which results from fusion of the SS18 gene (previously known as the SYT gene) on chromosome 18 with an SSX-family gene (SSX1, SSX2, or SSX4) on chromosome X, as detected by reverse transcriptase polymerase reaction (RT-PCR) and fluorescence *in situ* hybridization, is the main diagnostic hallmark of this tumor.[4,5] Moreover, microscopic features and positive immunohistochemistry results for selected markers play a major role in the diagnosis.

The clinical course of PRSS is unclear due to the limited number of cases. Tumors usually present as large masses and recurrence more frequently affects the lungs. Local recurrence occurs (renal fossa, abdominal lymph node, and adrenal glands), although liver and bone metastases have also been described.[3] Herein, we describe a case of PRSS with recurrence on the ureteral stump after radical nephrectomy and summarize the clinical course of PRSS by reviewing the relevant Korean literature.

CASE REPORT

A 38-year-old woman presented with left flank pain for more than 2 months. The medical history and physical examination were noncontributory, and there was no microscopic hematuria on the urinalysis. A computed tomography (CT) scan revealed

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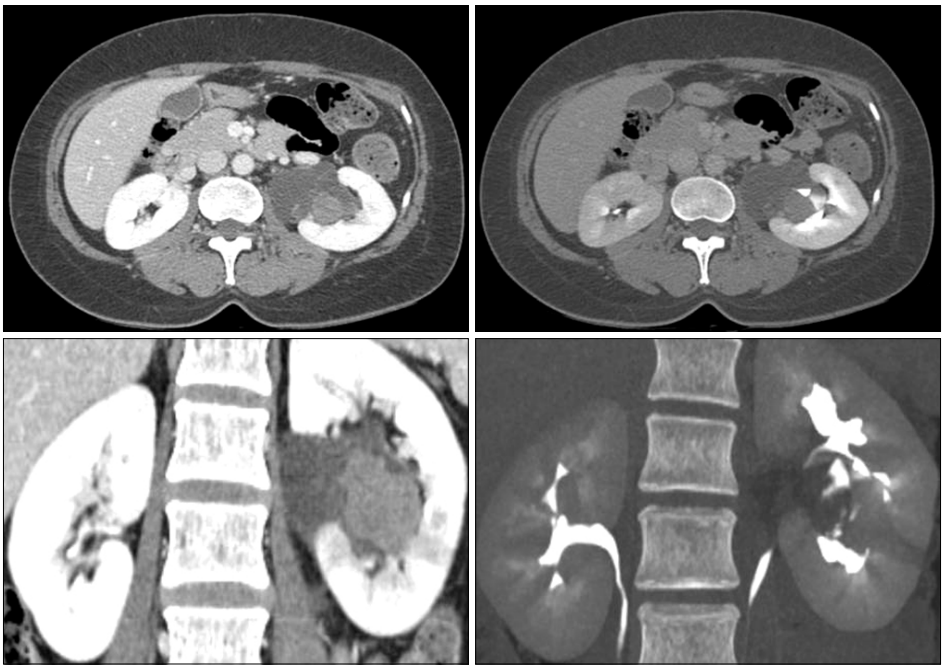

Fig. 1. Computed tomography (CT) scan of the abdomen shows a large heterogeneous and well defined mass measuring 6.3x4.0cm. Axial and coronal contrast-enhanced CT image reveals a solid cystic mass growing in the left renal pelvis containing a 3.2x3.2cm heterogeneous enhancing solid portion and suspicious renal parenchymal invasion with several wedge shaped densities. Axial and coronal CT image at the excretory phase shows deviating and mass effect to the left urinary tract rather than dilatation and no contrast passage delay or disturbance on the left urinary tract.

a 6.3x4.0cm sized solid and cystic component arising from the left kidney centered near the renal hilum with anteroposterior extension abutting the psoas muscle posteriorly (Fig. 1) but no invasive features and no evidence of lymphadenopathy or intra-abdominal metastasis were found. She underwent laparoscopic radical nephrectomy after we confirmed no mass invasion to the renal pelvis and calyx by ureterorenoscopic examination.

A macroscopic examination revealed a cyst lesion in the kidney containing a solid, fragmented mass measuring 5x4x3cm, and the mass appeared to infiltrate the renal parenchyma. A microscopic examination of the tumor revealed monomorphic spindle cell proliferation taking the form of short intersecting fascicles or solid sheets with high mitotic activity (26mitoses/10high power fields). The tumor had an infiltrative growth pattern into the surrounding renal pelvis, ureter, and sinus fat without necrosis (Fig. 2A). Immunohistochemical staining showed diffuse, strong expression of B-cell lymphoma/leukemia-2 (Bcl-2), cluster of differentiation 99, epithelial membrane antigen (EMA), and vimentin in the tumor cells, whereas staining for cluster of differentiation 34 (CD34) and cytokeratin (CK) were negative. RT-PCR to detect SYT-SSX fusion transcripts produced by the chromosomal translocation t(X;18) (p11.2;q11.2) was carried out as described previously.[6] Both the weak SYT-SSX1 and the strong SYT-SSX2 fusion gene transcripts were detected (Fig. 2B).

After surgical and medical oncology consultations, it was decided to treat the patient with adjuvant radiation therapy at the surgical bed with 5,000cGy (200cGyx25 fractions) (Fig. 3). Six months after surgery and 2 months after radiation therapy, the patient complained of gross hematuria. An abdominal CT scan was performed to evaluate the hematuria. About a 4cm enhancing mass lesion was found along the left distal ureter and ureterovesical junction, and the mass lesion was a recurrence of synovial sarcoma as shown by a cystoscopic biopsy (Fig. 4). The ureteral stump and bladder cuff were removed, and the patient received VAC (vincristine, total dose of 2 mg, adriamycin 70mg/m^2 and cyclophosphamide 600mg/m^2) and IE (followed after 21 days by ifosfamide, 1.8g/m^2 infused over 1h, daily for 5 consecutive days, with mesnauroprotection, plus etoposide at 500mg/m^2 infused over 2h on the first day) chemotherapy. The patient had no evidence of recurrence or malignancy at the 6-month follow-up visit, which was confirmed by abdominal CT.

DISCUSSION

Synovial sarcoma accounts for approximately 10% of all soft tissue sarcomas.[7] It is a clinically and histologically well-defined entity that occurs predominantly in the para-articular, deep soft tissues of the extremities in adolescents and young adults 25-40 years old. However, it has also been found at vari-

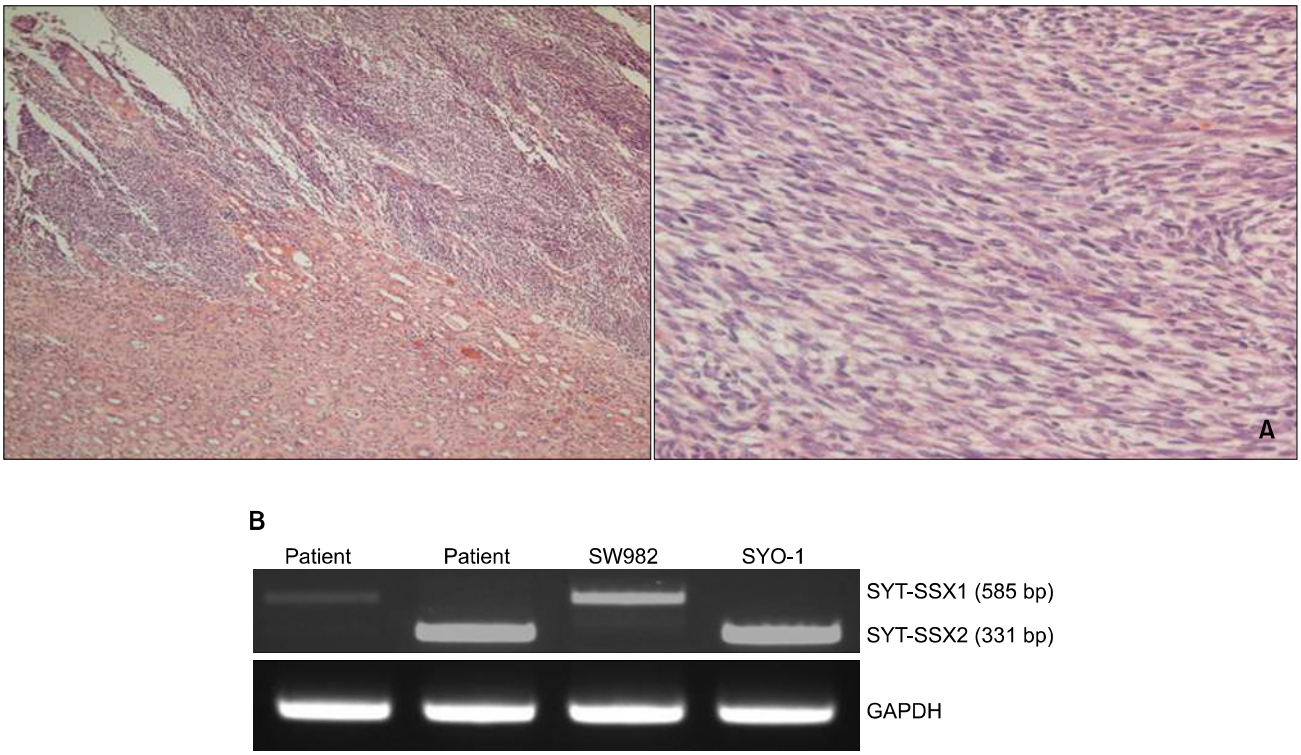

Fig. 2. Photomicrograph of histological specimen and expression levels of SYT-SSXs (SYT-SSX1 and SYT-SSX2) in synovial sarcoma tissues and cell lines. (A) Circumscribed cellular lesion composed of fascicles of plump spindle cells with hyperchromatic elongated nuclei and indistinct cytoplasm. These cells involve the renal pelvis with extension to the renal cortex (hematoxylin and eosin stain [H&E], x100). Tumor cells show high mitotic activity (26 mitoses/10 high power fields), (H&E, x400). (B) SYT-SSX expression was analyzed by reverse transcription polymerase chain reaction performed for 30 cycles using SYT-SSX1 or SYT-SSX2-specific primers. The GAPDH gene was used as the positive control. The SYO-1 and SW982 synovial sarcoma cell lines were obtained from Prof. Seo (Sungkyunkwan University, Seoul, Korea).

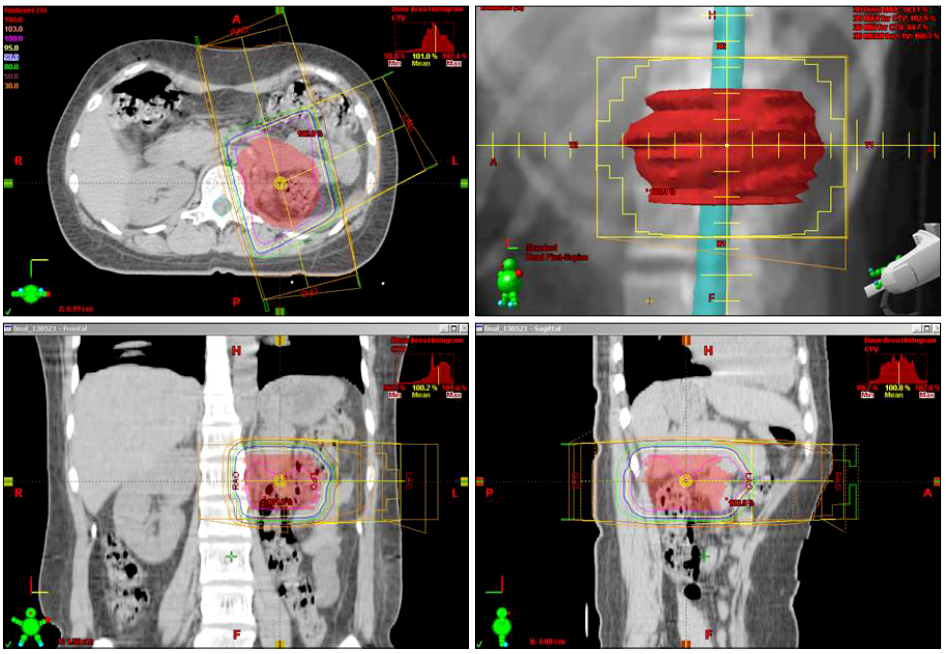

Fig. 3. Adjuvant radiation therapy at surgical bed after radical nephrectomy.

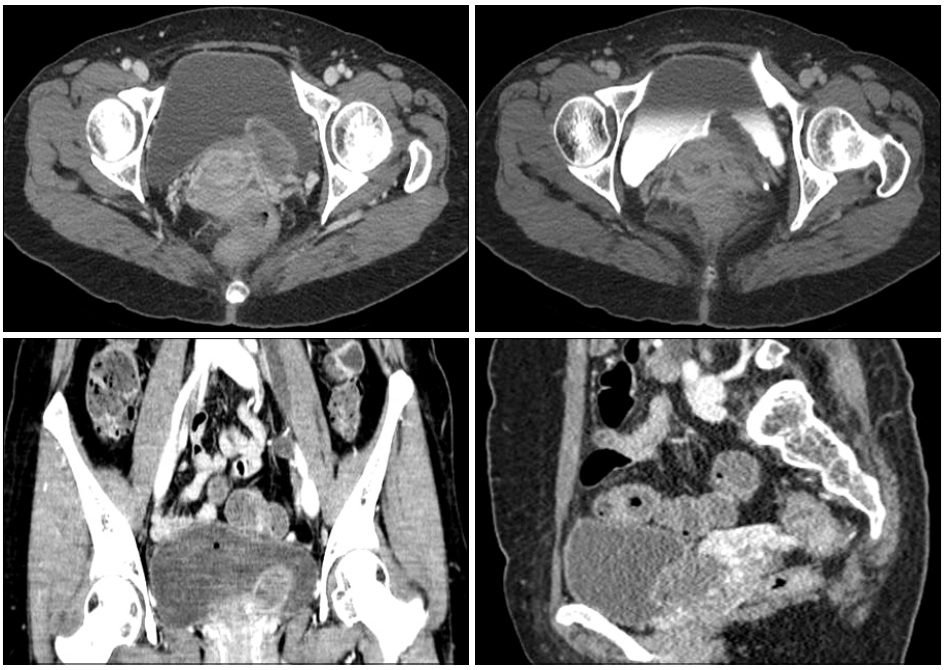

Fig. 4. Follow-up computed tomography (CT) scan of the bladder shows 4cm mass along the distal ureter and bladder cuff. Axial and coronal contrast-enhanced CT images show the mass enhanced lesion along the left distal ureter and uretetovesical junction. Axial and coronal CT image at the excretory phase shows ureteral mass protruding into the bladder as filling defect.

ous other sites unrelated to joints/synovial tissues and has been described recently in the kidney.

PRSS are usually large, often ten, and rubbery with cystic and necrotic areas. PRSS are histologically categorized into biphasic, monophasic, and poorly differentiated variants.[1,8] Although the biphasic type is easily recognized because it has both epithelial cell and spindle cell components, the monophasic or poorly differentiated variants can be difficult to distinguish from other mesenchymal neoplasms. The poorly differentiated type of synovial sarcoma is composed of sheets of undifferentiated round cells with hyperchromatic high-grade nuclei and scant cytoplasm. The monophasic variant of synovial sarcoma is more common and has a better prognosis than the biphasic variant.[9] A mitotically active, monomorphic highly cellular neoplasm composed of plump spindle cells with indistinct cell border growing in short intersecting fascicles is seen microscopically. The tumor cells are strongly immunoreactive for vimentin and show focal positive immunostaining for the epithelial markers EMA and CK.[10] These tumors are also positive for bcl-2, but are nonimmunoreactive for desmin, smooth muscle actin, S-100, and CD34.[10] In the present case, necrotic spindle cell sarcoma of the kidney was seen. Our patient had monophasic PRSS, and the immunohistochemical findings were similar to those of previous reports.

A biphasic synovial sarcoma typically expresses the SYT-SSX1 fusion transcript, whereas monophasic synovial sarcoma or poor differentiated synovial sarcoma are more associated with the SYT-SSX2 transcript. SYT-SSX1 is significantly associated with poor metastasis-free survival and a higher tumor load.[11] An individual synovial sarcoma is generally believed to carry only a single type of SYT-SSX fusion, but the weak SYT-SSX1 and the strong SYT-SSX2 fusion gene transcripts were co-expressed in our case. Yang et al.[12] demonstrated that co-expression of SYT-SSX1 and SYT-SSX2 was seen in 10% of cases (12/121) and it may be possible that a transition through deletional remodeling occurred in a tumor cell carrying one type of SYT-SSX fusion, leading to a population of cells with the other type of fusion.

These tumors need to be distinguished from sarcomatoid renal cell carcinoma, cellular mesoblastic nephroma, fibrosarcoma, malignant peripheral nerve sheath tumor, sarcomatoid transformation of multilocular cystic nephroma, hemangiopericytoma, and other sarcomas involving the kidney.[2,4] Immunostaining and cytogenetic analyses are helpful.

As few cases of PRSS have been reported due to its extreme rarity, but no clear medical guidelines have been established. Surgery is considered first-line treatment for sarcomas to prevent local recurrence. However, recent studies indicate that surgery improves local control but confers no advantage in terms of disease-free, disease-specific, or overall survival.[3] Aggressive chemotherapy and/or radiation therapy in combination with surgery is now the treatment of choice for most patients, and local

Table 1. Clinical features of primary renal synovial sarcoma in Korea

	Sex/ age	Loca- tion	Maxi- mum size (cm)	Histological subtype	Immunohistochemical features		RT-PCR of SYT-SSXs	Treatment	Prognosis	Refe- rence
					Positive	Negative				
1	M/53	Rt	5.5	Poorly differentiated	Vimentin, CD99, CD56 CK, HMCK, LMCK, EMA, NF	S-100,CD34, desmin	SSX-2	RN	NA	1
2	M/47	Rt	5.0	Poorly differentiated	Vimentin, CD99, CD56 CK, HMCK, LMCK, EMA, NF	S-100,CD34, desmin	SSX-2	RN CTx	10 mon DOD	1
3	F/32	Lt	12.0	Monphasic	Vimentin	CK, EMA, s-100, CD 34	None checked	RN CTx	4 mon lung metz	13
4	F/35	Rt	20.0	Poorly differentiated	CD99, Bcl-2, CD56, CK	CD34, SMA, desmin, S-100	SSX-2	RN CTx, RTx	5 mon NED	14
5	F/27	Rt	8.5	Poorly differentiated	CD99, Bcl-2	CD56, CK, CD34, SMA, desmin, S-100	SSX-2	RN CTx, RTx	6 mon Vertebra metz	14
6	M/26	Rt	18.0	Poorly differentiated	CD99, Bcl-2, CD56	CK, CD34, SMA, desmin, S-100	SSX-2 SSX	RN	NA	14
7	F/35	Rt	4.5	Monophasic	CD99, Bcl-2, EMA, vimentin, calretinin	CK, CD34, S100, HMB45, SMA	SSX-1	RN	6 mon NED	15
Present case	F/37	Lt	6.3	Monophasic	CD99, Bcl-2, EMA, vimentin	CD34, CK	SSX-2	RN CTx, RTx	6 mon bladder & ureter metz	

Rt: right, Lt: left, CD: clusterof differentiation, CK: cytokeratin, HMCK: high molecular weight cytokeratin, LMCK: low molecular weight cytokeratin, EMA: epithelial membrane antigen, NF: neurofilament, Bcl: B-cell lymphoma/leukemia, RN: radical nephrectomy, CTx: chemotherapy, RTx: radiotherapy, NA: not available, DOD: died of disease, metz: metastasis, NED: no evidence of disease.

control rates of >80% have been achieved with a combination of wide local excision and radiation therapy for soft tissue sarcomas of the extremities.[9] Thus, we chose adjuvant radiotherapy.

Iacovelli et al.[3] described the clinical characteristic of PRSS collected from 61 patients. They reported that the risk of relapse for patients with non-metastatic disease at diagnosis was 36%. Of all relapsed patients, 29% were a local recurrence (renal fossa, abdominal lymph node, adrenal gland). However, ureteral stump invasion has not been reported, as in our patient, and it is very important to identify the PRSS characteristics. This finding means that we need to consider nephroureterectomy with excision of the bladder cuff if microscopic renal pelvic and ureteral invasion of PRSS are suspected, although we gained sufficiently safe ureteral margins from PRSS. Moreover, we must consider adjuvant systemic chemotherapy even if PRSS shows non-metastatic features and is resected completely. Synovial sarcoma may be sensitive to a high dose isophosphamide and adriamycin based regimen.[3]

Seven cases of PRSS have been reported in Korean patients aged 26-53 years (mean, 36.7 years) with four occurring in women.[1,13-15] Tumor sizes ranged from 4.5 to 20.0cm (mean, 10.5 cm). Tumors developed in the right kidney in six cases. A histological classification showed five poorly differentiated tumors and two with monophasic features. Detailed immunohistochemical staining features and results of SYT-SSX gene fusion are shown in Table 1. This is the first report of a rapidly recurrent renal synovial sarcoma at an unusual site such as the ureteral stump despite radical surgery and adjuvant radiotherapy; thus, nephroureterectomy with adjuvant therapy including radiation and systemic chemotherapy should be considered if PRSS is suspected to have invaded the renal pelvis or ureter.

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