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ПРИКАЗ БОЛЕСНИКА / CASE REPORT
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Rapidly Progressive Course of Primary Renal Synovial Sarcoma – Case Report

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SUMMARY

Introduction Primary kidney sarcoma, especially synovial sarcoma (SS), is a very rare neoplasm. Preoperative signs and symptoms are very similar to renal cell carcinoma, therefore, the proper diagnosis is very difficult and usually made after nephrectomy. This is a case report of primary renal SS.

Case Outline A 38-year-old man presented with a history of fever and hematuria, and right flank pain 3 weeks ago. Abdominal computerized tomography revealed a heterogeneous well-marginated soft tissue mass arising in the lower part of the right kidney. Right nephrectomy was performed. A cystic tumor of 120x85 mm in size with soft solid growth, and with the extensive areas of hemorrhage and necrosis was seen on gross examination. Histopathology revealed a neoplasm composed of solid monomorphic sheets of spindle cells. Immunohistochemistry showed tumor cells strongly positive for BCL2, CD99, CD56 and vimentin, and focally positive for epithelial membrane antigen (EMA). The histological diagnosis of primary renal SS was based on morphology and immunohistochemistry. FISH analysis and RT-PCR was carried out on formalin-fixed paraffin-embedded tissue sections. The molecular analysis demonstrated translocation of SYT gene on chromosome 18 and SSX2 gene on chromosome X. The findings were consistent with diagnosis of SS.

Conclusion Our case shows that histopathological diagnosis of primary kidney SS, although difficult, is possible to be made on the basis of morphological and immunohistochemical analysis. However, this diagnosis should be corroborated by molecular techniques confirming SYT-SSX translocation on chromosome 18 and chromosome X. Here we present visceral monophasic SS with aggressive clinical course and poor outcome.

Keywords: primary renal synovial sarcoma; SYT-SSX2; RT-PCR

INTRODUCTION

Primary renal synovial sarcoma (SS) is a rare tumor, first described by Faria et al in 1999 [1]. SS is a clinically, morphologically and genetically well defined entity. Although SS may occur at any unusual site, their predominant localization is in para-articular regions of the extremities in about 80% of cases. Since SS accounts for 5–10% of adult soft tissue sarcomas and primary renal sarcomas account for 1% of malignant renal tumors, it is quite clear why diagnosis of primary renal SS can be difficult [2, 3, 4]. Diagnostic dilemma of primary renal SS becomes evident because the growth is usually presented clinically as renal cell carcinoma and morphologically it is not simple to differentiate it from metastatic sarcoma, sarcomatoid renal cell carcinoma or other primary renal sarcomas. Fortunately, molecular pathological methods can solve diagnostic problems [5, 6].

CASE REPORT

A 38-year-old man presented with a history of fever and hematuria, and right flank pain 3 weeks ago. On examination, a tender mass was palpable in his right flank. Abdominal computerized tomography (CT) revealed presence of heterogeneous, well-marginated mass arising in the lower part of the right kidney, sized 12×9 cm (Figure 1A). Abdominal MR imaging detected well circumscribed tumor, sized 120×85 mm, in the right kidney caudally, which was prominent to the perirenal retroperitoneal space, adherent to the psoas muscles without any infiltration of them. Tumor mass was non-homogenous and partially necrotic. Gerota's fascia was tended and edematous but not infiltrated. There was no intra abdominal lymphadenopathy or intra abdominal metastasis. According to the clinical and radiological presentation, laparotomy and radical right nephroureterectomy were performed. No extracapsular extension was noticed during operation.

On gross examination, a cystic tumor, measuring 120×90×85 mm, originated from the lower pole of the right kidney. Cut surface of greyish-white soft solid growth, with the extensive areas of hemorrhage and necrosis was seen (Figure 2). Histopathology revealed a neoplasm composed of solid cellular monomorphic sheets consisting of fascicles of spindle cells (Figure 3), with the areas of necrosis and hemorrhage. Neovascularization was extensive and no epithelial differentiation was present. There was a moderate pleomorphism and mi-

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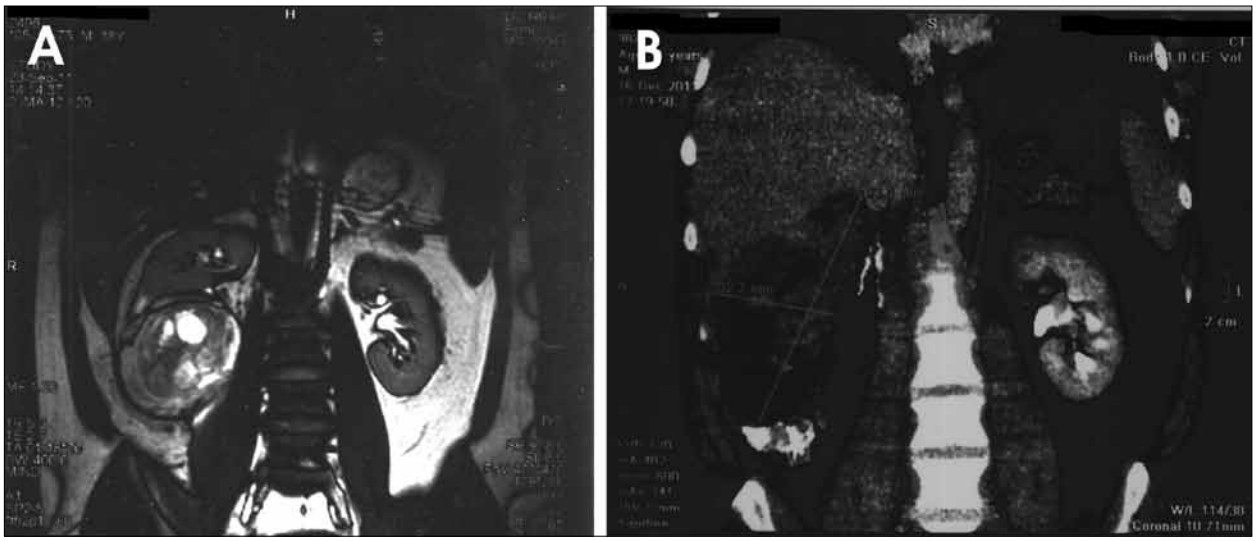

Figure 1. Abdominal CT: A) well marginated cystic mass in the lower pole of the right kidney; B) two months after nephrectomy

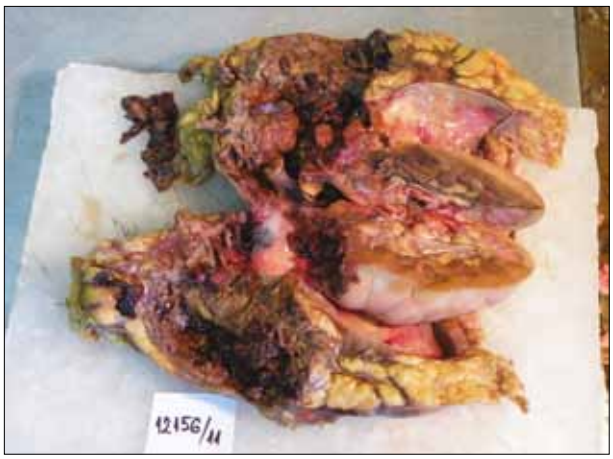

Figure 2. Gross appearance of cut surface: well defined cystic space in the lower pole of the kidney with hemorrhage and necrosis

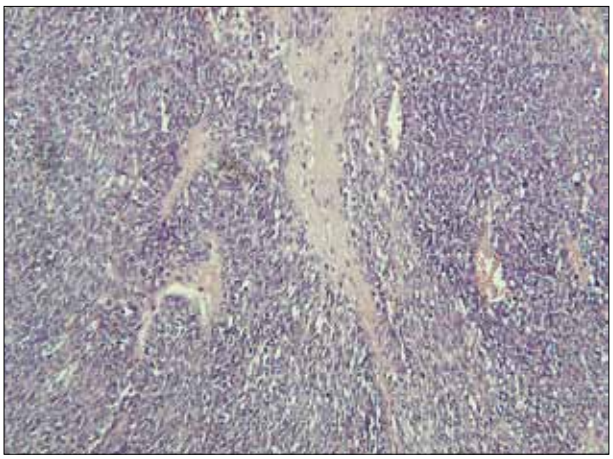

Figure 3. Solid sheets of spindle cells with frequent mitosis and abundant neovascularization (H&E, ×40)

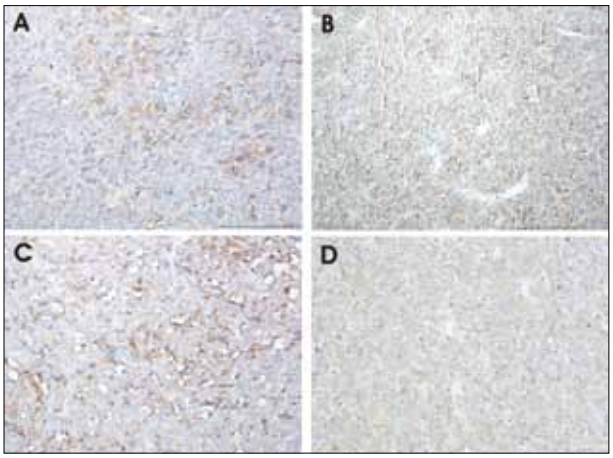

Figure 4. Immunohistochemistry of the tumor: A) about half of the tumor cells strongly expressed vimentin (magnification ×400); B) diffuse staining of almost all tumor cells with anti-CD56 antibody (×200); C) strong membranous staining of CD99 on majority of tumor cells (×400); D) all tumor cells expressed BCL-2 (×400)

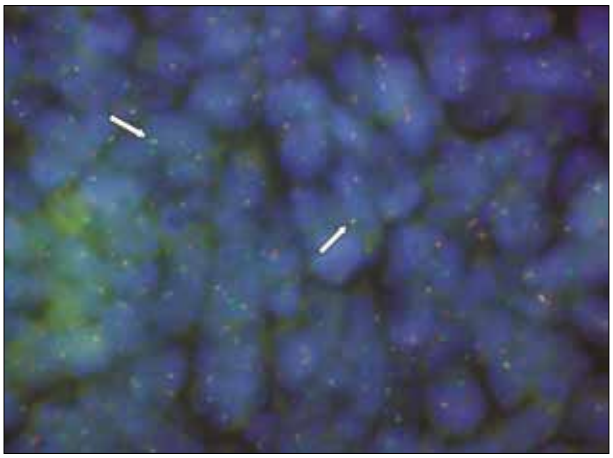

Figure 5. Image FISH analysis: Presence of 18q11.2 translocation hybridized with the LSI SS18 Dual Colour Break Apart Probe, yellow fusion signal (arrows), while one orange and one green signal pattern represent an absence of translocation in cells.

Table 1. Primers used for RT-PCR

Primer name	Primer sequence (5′ to 3′)	Fusion transcript	Prod size (bp)
SYT SSX1-REV2	AGA CCA ACA CAG CCT GGA CCA C ACA CTC CCT TCG AAT CAT TTT CG	T(X;18)(p11;q11) (Xp11.23)	110
SYT SSX2-REV2	AGA CCA ACA CAG CCT GGA CCA C GCA CTT CCT CCG AAT CAT TTC	T(X;18)(p11;q11) (Xp11.21)	110
SYT SSX-REV (SSX1/2 consensus)	AGA CCA ACA CAG CCT GGA CCA C TCC TCT GCT GGC TTC TTG	SYT-SSX Consensus	87

totic rate 8/10 high power magnification field. The tumor was relatively good margined from renal parenchyma and perirenal fat tissue. Immunohistochemistry showed tumor cells that were strongly positive for BCL2, CD99, CD56 and vimentin, and focally positive for epithelial membrane antigen (EMA) (Figure 4). They were negative for smooth muscle actin (SMA), CD10, desmin, CD34, TTF_1, CK19. The histological diagnosis of primary monophasic SS of the kidney was based on morphology and immunohistochemistry. The patient was recommended by pathologist for chemiotherapy. Since the operator was not aware of the possibility that malignant cystic renal mass could be SS, the patient did not receive any therapy. In the meantime, the paraffin blocks were sent for molecular biological confirmation of PH diagnosis.

Fluorescence in situ hybridization (FISH) analysis was carried out on formalin-fixed paraffin-embedded tissue sections using the SS18 (18q11.2) Dual Colour Break-Apart Probe (Abbott). Evidence of translocation involving the SS18 locus was detected (Figure 5). The majority of nuclei displayed one set of fused signals and one set of split signals. A total of 500 nuclei from all areas of the tissue section were scored. Additionally, a reverse transcriptase polymerase chain reaction (RT-PCR) for SYT-SSX fusion gene transcripts using ribonucleic acid extracted from formalin-fixed paraffin-embedded tissue was performed using the primers given in Table 1. The primer 'B-actin' (274 bp) was used as a 'housekeeping' primer to show good RNA quality. A number of control samples were used

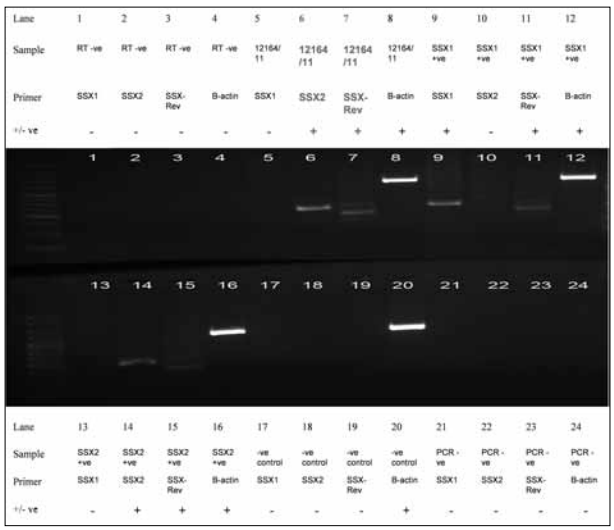

Figure 6. Electrophoresis gel showing the PCR transcripts. Tissue probes of renal tumor are on positions 5, 6 and 7: SSX2 was positive by PCR and reverse-PCR (positions 6 and 7), but negative for SSX1 (position 5). All other positions are different positive or negative controls.

(RT-ve: No RNA template added to reverse transcription reaction; PCR-ve: No cDNA template added to PCR reaction; positive controls for both SSX1 and SSX 2 transcripts; negative control to ensure transcript specificity) to ensure sample specificity and rule out false positivity as a result of contamination. The RT-PCR revealed a translocation of SYT gene on chromosome 18 and SSX2 gene on chromosome X but lack of SS18-SSX1 translocation (Figure 6). The findings were consistent with diagnosis of monophasic SS.

Two months later, when diagnosis was verified, CT scanning revealed traumatic worsening of the lesion. Diffuse spread of the tumor into retroperitoneal space on both sides was discovered (Figure 1B). The patient underwent second laparotomy. Grossly, by intraoperative observation, one could see an abundant widespread tumor mass infiltrating the retroperitoneal space on both sides and adhering to the vena cava inferior. Shortly afterwards, that is, three months after the first hospitalization, the patient died.

DISCUSSION

SS could be present in unexpected sites, such as thoracic and abdominal wall, head and neck region, retroperitoneum, as well as visceral organs such as lung, prostate and kidney [7, 8]. Previously, these tumors were diagnosed as embryonal sarcoma of the kidney or adult Wilms tumor but they subsequently revealed presence of the t(X;18)(p11.2:q11.2) translocation that is specific for SS [2].

To the best of our knowledge, 64 cases of primary renal SS have been reported up to now upon reviewing 11 years of medical literature [9, 10, 11]. We presented here a young man at age of 38 years with primary renal SS. According to published data, our patient was a typical case. Clinical and imaging characteristics of this tumor were similar to other renal tumors, particularly to the renal cell carcinoma (RCC). Cystic formation which is very characteristic for SS, and was present in described patient's tumor, could be commonly seen in RCC, too. Clinical diagnosis is not possible [12, 13].

SS may develop at unusual sites including kidney. Histologically, it is subclassified into biphasic SS, monophasic SS and poorly differentiated SS. According to the literature, the most common type of primary renal SS is monophasic, what was the case here [14]. The diagnosis based on morphological and immunomorphological tumor profile is also very difficult. Thus, our diagnosis of monophasic primary renal SS, based on morphology: plump spindle cells arranged in solid compact sheets without epithelial cell component, with abundant neovascularisation, and

immunomorphology: BCL2, CD99, CD56, vimentin, and focally EMA positivity, was somehow daring [15, 16]. However, confirmation by genetic analysis took some time. Monophasic SS is often associated with the SS18-SSX2 translocation while biphasic SS is associated with the SS18-SSX1. In presented case, the SS18-SSX2 translocation was detected by FISH and RT-PCR techniques, and the diagnosis was verified [17, 18, 19].

Since primary renal SS is very rare neoplasm, no definite medical therapy has been established. Primary surgical resection of the tumor is positively the treatment of choice. However, as we could see in the present case, the prognosis is very poor when this treatment is alone. In principal, chemotherapy is recommended. Adjuvant therapy to radical nephrectomy mostly includes ifosfamide and doxorubicin. However, currently, there are no consistent data concerning the effect of chemotherapy on primary renal SS, which usually has aggressive behavior [20].

In spite of diagnostic challenge for pathologists, in the presented case the histopathological diagnosis of primary renal SS was based on gross appearance of the cystic tumor, morphology and immunohistochemistry. However, it took a long time in our case to confirm the diagnosis of monophasic SS by molecular analysis, which revealed a translocation of SYT gene on chromosome 18 and SSX2 gene on chromosome X. Since the disease may have rapid course with bad outcome, as it was here, the clinicians need to be aware of the existence of this rare entity, so that timely and appropriate therapy can be applied.

ACKNOWLEDGMENT

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Брзи развој примарног синовијалног саркома бубрега – приказ болесника

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КРАТАК САДРЖАЈ

Увод Примарни саркоми бубрега су веома ретки, а нарочито синовијални сарком (СС) бубрега. Преоперациони симптоми су врло слични осталим карциномима бубрега, те се права дијагноза поставља тек после хируршког лечења болесника, тј. нефректомије. Следи приказ болесника с примарним СС бубрега.

Приказ болесника Тридесетосмогодишњи мушкарац је око три недеље имао неодређене тегобе, малаксалост, повишену температуру, затезање у лумбалном пределу и хематурију. Компјутеризована томографија абдомена је показала хетерогену, релативно добро ограничену, делом цистичну туморску масу на доњем полу десног бубрега. Урађена је нефректомија десног бубрега. Макроскопски је уочен мекоткивни тумор цистичног изгледа величине 120×85 *mm* с опсежним пољима некрозе и крварења. Хистопатолошки налаз је показао да је реч о саркому који чине поља изражене неоваскуларизације са мономорфним фузиформним ћелијама. Имунохистохемијски туморске ћелије су биле строго позитивне на *BCL2*, *CD99*, *CD56* и виментин, а фокално позитивне на епителни мембрански антиген (*EMA*). На основу морфолошке слике и имунохистохемијске анализе тумора постављена је дијагноза примарног СС бубрега. *FISH* анализа и *RT-PCR* су такође урађени на исечцима ткива фиксираних у формалину и укалупљених у парафину. Молекуларне анализе ткива утврдиле су транслокацију гена *SYT* на хромозому 18 и гена *SSX2* на хромозому *X*. Тиме је дијагноза СС бубрега била потврђена.

Закључак Овај случај јасно илуструје да је хистопатолошка дијагноза примарног СС бубрега, иако тешка, могућа на основу морфолошких и имунохистохемијских анализа. Међутим, дијагноза се мора потврдити доказивањем транслокације гена *SYT* и *SSX* на хромозомима 18 и *X* молекуларним техникама. Овде је приказан мономорфни СС бубрега агресивног тока и брзог смртног исхода.

Кључне речи: примарни синовијални сарком бубрега; *SYT-SSX2*; *RT-PCR*

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