Int J Clin Exp Pathol 2018;11(9):4346-4351
www.ijcep.com /ISSN:1936-2625/IJCEP0081996

Original Article

Primary renal synovial sarcoma: two cases and review of the literature

Zheng Cao, Hai-Zhen Lu, Xiao-Li Feng

Department of Pathology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Received July 2, 2018; Accepted July 27, 2018; Epub September 1, 2018; Published September 15, 2018

Abstract: Objective: To investigate the clinicopathological features, treatment, and prognosis of primary renal synovial sarcoma. Method: Retrospectively collected and analyzed clinical and pathological data of two cases of patients with renal primary synovial sarcoma, and reviewed domestic and foreign related literature. Results: The first patient was admitted for progressive enlargement of a left renal mass, then she underwent a radical resection of left kidney and adrenal gland, and the final diagnosis was primary renal synovial sarcoma. However, the tumor progressed with multiple nodules in the left peritoneal retroperitoneal space and abdominal wall 3 months later. The second patient was hospitalized for a left lung mass and left renal mass after 3 months. She received left nephrectomy and left lower lobectomy. The final diagnosis was primary renal synovial sarcoma with extensive metastasis in both lungs and pelvic and abdominal cavity. The patient underwent chemotherapy and targeted therapy after operation, and died because of tumor burden after 23 months. Conclusion: Primary renal synovial sarcoma is a rare soft tissue tumor in the kidney with a poor prognosis. An accurate diagnosis needs consideration of the morphology, immunohistochemistry, and SYT-SSX gene results. Clinically, radical nephrectomy is the main strategy, and adjuvant ifosfamide-based chemotherapy after operation has benefits.

Keywords: Synovial sarcoma, SYT-SSX, kidney

Introduction

Synovial sarcoma (SS) is an aggressive malignant tumor which has a poor prognosis. Primary renal synovial sarcoma (PRSS) is a rare tumor, first described by Faria et al in 1999 [1], and there are less than 50 cases were reported in the literature. We collected two cases of primary renal synovial sarcoma diagnosed by the department of pathology in National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital and these are reported as follows.

Case report 1

A seventy-four-year old woman presented with a left renal mass for 9 years. Nine years ago, abdominal computerized tomography (CT) revealed a 2.0 cm, well-defined mass. Because the patient had no hematuria, urinary pain or other discomfort, the mass was assumed to be benign and needed follow-up. Recently, the patient was admitted for the progressive enlargement of the left renal mass. Abdominal MRI detected a marked enhancing, huge lobular soft tissue mass in the left kidney; the mass pushed the tail of the pancreas and the maximum diameter was 17.8 cm (**Figure 1A**, **1B**). The renal dynamic imaging showed that the left kidney had nearly no function. Physical examination showed a firm mass in the left kidney, without tenderness and percussion pain. According to the clinical and radiological presentation, radical resection of left kidney and adrenal gland was performed. Intraoperatively, the shape of left kidney was abnormal and the mass involved almost the whole kidney (**Figure 1C**). On gross inspection, a solid mass, measuring 18 × 15 × 10 cm, occupied the whole left kidney; the cut surface was whitish to grey-yellow, with focal calcification and hemorrhagic necrosis (**Figure 1D**). There were multiple cysts between 0.3-1 cm in the peripheral kidney. Also, there was a partial nephric duct, whose

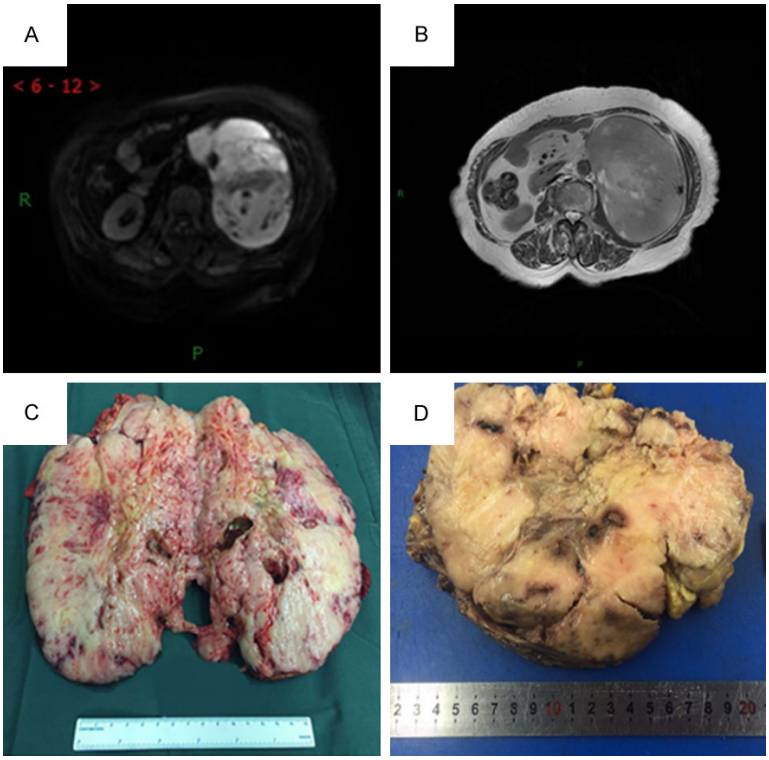

Figure 1. A, B. Abdominal MRI: a huge mass occupied left kidney; C. Fresh specimen after operation; D. 10% formalin fixed specimens.

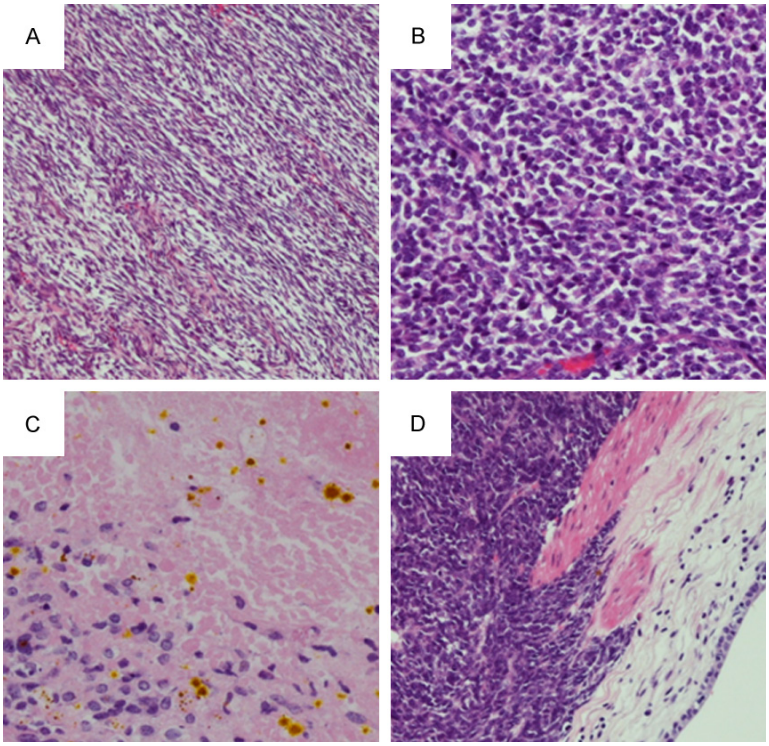

Figure 2. A. Area of spindle cells (× 200); B. Area of epithelial cells (× 200); C. Hemorrhagic necrosis of tumor; D. Tumor cells invaded muscularis of renal pelvis.

outer surface was surrounded by tumor.

Microscopy: The neoplastic cells presented epithelial and spindle-cell components (**Figure 2**). The spindle-cells were arranged in intersecting fascicles. These cells were uniform spindle with ovoid, bland but hyperchromatic nuclei, and the mitosis was common. The epithelial cells were arranged in solid nests or cords; cells were round or oval with larger size. Tumor invaded the muscularis of renal pelvis and ureter. Immunohistochemical staining findings: AE1/AE3, vimentin and caldesmon were positive. bcl-2 and CD99 were focally positive. Desmin, SMA, S-100, PAX-8 and CD10 were negative (**Figure 3**). SYT-SSX gene fusion of tumor was detected by fluorescence in situ hybridization (FISH) (**Figure 4**), Combined with the microscopic morphology, immunohistochemistry findings, and FISH results, the final diagnosis of primary renal synovial sarcoma was achieved. She underwent two cycles of chemotherapy after operation.

However, Abdominal CT scan detected the tumor progressed with multiple nodules in the left peritoneum, retroperitoneal space, and abdominal wall, and the disease-free survival (DSF) was 3 months. Up to now, this patient is still alive with regular chemotherapy and targeted therapy.

Case report 2

A forty-nine year old female was hospitalized for cough and hemoptysis without obvious inducement, CT scanning showed a lobular, sharply

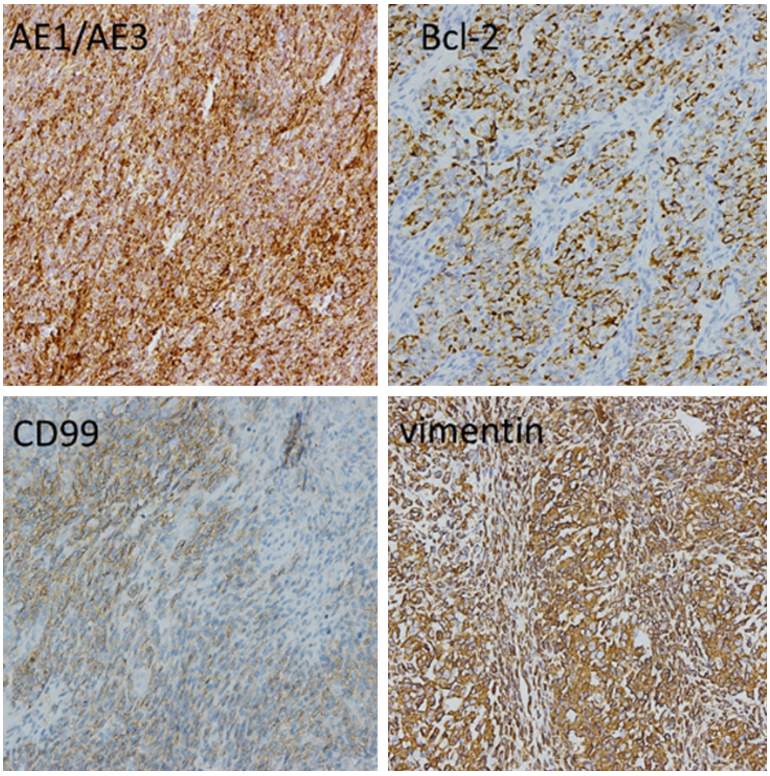

Figure 3. Tumor cells show positivity for AE1/AE3, vimentin, and are focally positive for CD99, and Bcl-2.

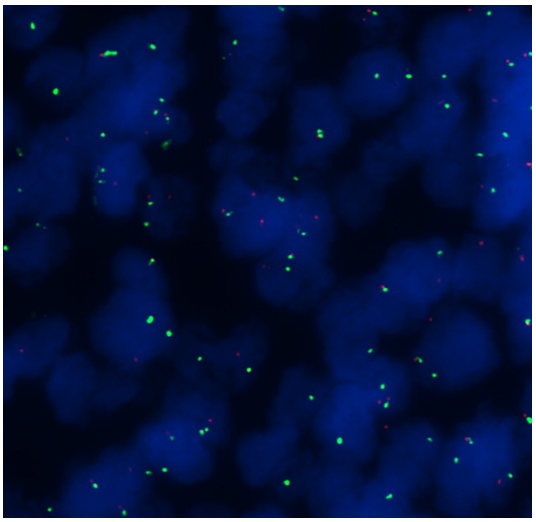

Figure 4. SYT-SSX gene arrangement detected by FISH.

defined, measuring 6.5 × 5 × 6.1 cm mass in the superior segment of lower lobe of left lung. She underwent left lower lobectomy. The post-operation PET-CT examination 3 months later showed a markedly enlarged left kidney and left pelvic mass, with uneven density and unclear border. She underwent radical left nephrectomy after 5 cycles of chemotherapy and 6 cycles of biological treatment in other hospital. The histopathologic features of left lung, left kidney and left pelvic tumor were similar. Microscopic examination showed the tumors composed of spindle cells and epithelial cells (**Figure 5A**). Epithelial cells with dark stained big nucleoli were arranged in sheets, and cells were round or oval. Focally, some spindle-cells were arranged intersecting fascicles and with obvious mitotic (**Figure 5B-D**). Immunohistochemical staining revealed Bcl-2, CD99, vimentin and CD56 were positive, and cytokeratin AE1/AE3 was focally positive (**Figure 6**). Molecular analysis showed the presence of SYT-SSX gene fusion. Combined with histopathological morphology, immunohistochemical results, and molecular results, synovial sarcoma was made. In consideration of common location of the synovial sarcoma, the final diagnosis was renal primary synovial sarcoma with extensive metastasis in bilateral lungs, pelvic and peritoneal cavity. The patient received 2 cycles of anthracycline-based chemotherapy and target drug Eratinib. However, she gradually developed fever and abdominal distention. Because the patient was in the state of tumor consumption and poor general status, there was no definitive and effective treatment after multicourse therapy. The patient died with an overall survival of 23 months.

Discussion

Brief introduction

SS is a kind of soft tissue tumor, which displays a variable degree of epithelial differentiation. Most tumors arise in the proximity of large joints or tendon tissues of the lower or upper extremities. Unusual sites of involvement include kidney, lung, bone, head, and abdominal wall. It can occur in all age groups, but more

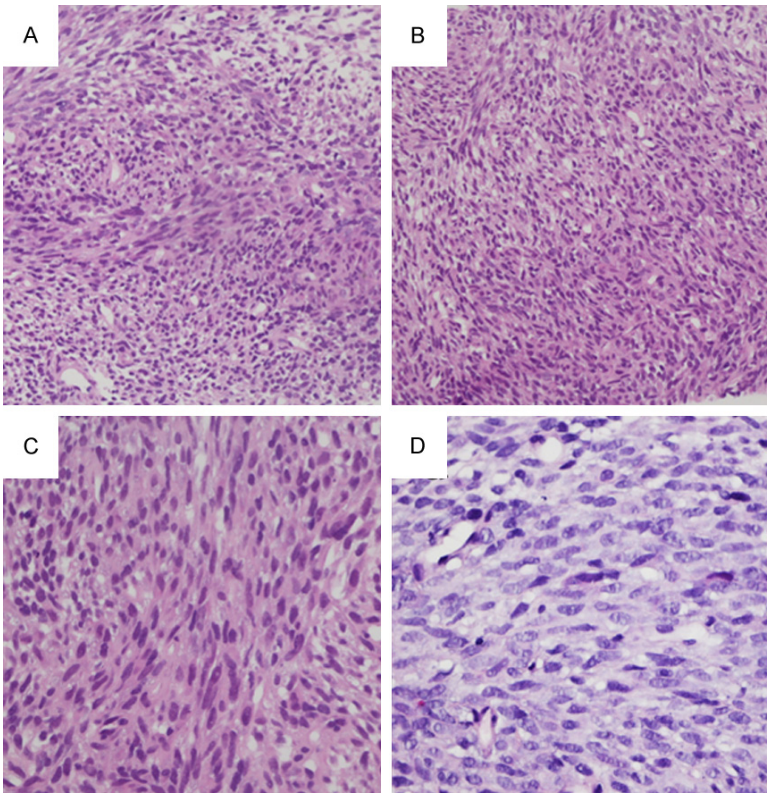

Figure 5. A. A transitional region of spindle cells and epithelial cells (× 200); B-D. Short spindle cells (× 200, × 400).

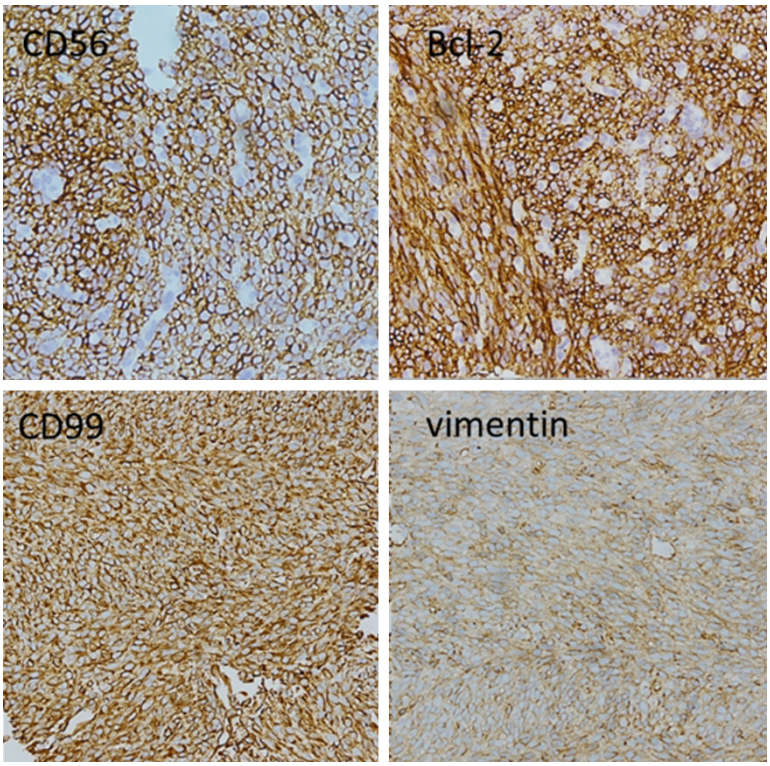

Figure 6. Tumor cells show positivity for CD56, CD99, bcl-2, and vimentin.

than half of patients are teenagers and young adults [2]. SS is characterized by the chromosomal translocations of t (X; 18) (P11; q11), which are present in >95% of all cases. This translocation leads to the fusion of the SYT gene on chromosome 18 and the SSX gene of the X chromosome [3]. The diagnosis of PRSS is a challenge because it is difficult to differentiate from other spindle-cell tumors such as renal clear cell carcinoma with sarcomatoid differentiation, fibrosarcoma, angiomyolipoma, malignant peripheral nerve sheath tumors, and primitive neuroectodermal tumor [4].

Primary renal synovial sarcoma (PRSS) is rare, accounting for 1-3% of all malignant renal tumors. It often occurs in unilateral kidney especially in left kidney, and the incidence of male to female is 1.7:1 [5]. Clinically it usually presents with hematuria, lumbago, and imaging finding usually shows a “triple signal” pattern on T2WI in four cases [6], but radiological and clinicopathological features of PRSS are not specific, so it is difficult to diagnose before operation. The diagnosis of PRSS depends on the postoperative histopathologic and immunohistochemistry features, especially molecular genetic results.

Clinicopathological features

Grossly, mean diameter of the tumor is 18.6 cm, ranging 3-21 cm. In some cases, areas of necrosis, hemorrhage, and cyst formation can be seen [7]. Histologically, tumor cells present epithelial and

spindle-cell components, it contains three subtypes: monophasic, biphasic and poorly differentiated according to cell compositions [8]. Poorly-differentiated SS is composed of sheets of round or spindled cells showing severe nuclear atypia and high mitotic activity, and the prognosis is very poor. In biphasic SS, the epithelial cells usually are cuboidal or columnar and have ovoid vesicular nuclei, and are arranged in solid nests or cords. The spindle cells are relatively uniform with sparse cytoplasm and arranged in intersecting fascicles [9]. The majority of SS are positive for Bcl-2, CD99, CD56, vimentin, and focally positive for EMA, and negative for desmin, WT-1, and S-100 [10], but these markers are not specific. Studies show that TLE1 is a promising and helpful marker for the diagnosis of synovial sarcoma [11, 12], but it is not specific for SS, and also occurs in other similar tumors.

Molecular genetics

95% of cases have chromosomal transposition of t (X; 18) (p11; q11). The translocation leads to the fusion of the SYT gene on chromosome 18 and the SSX1 gene (about 2/3 cases, usually biphasic SS), SSX2 (about 1/3 cases, only monophasic SS), or the SSX4 (rare cases) on chromosome X [13]. The detection of gene fusion by break-apart FISH or RT-PCR has an important value in the diagnosis of synovial sarcoma [14].

Clinical treatment and prognosis

There are no unified and standardized strategies at present since rare cases have been reported. Radical nephrectomy is the main strategy, and adjuvant ifosfamide-based chemotherapy after operation has some good effect [15]. Primary renal synovial sarcoma is an aggressive soft tissue tumor, and in a retrospective study of 64 cases of primary renal synovial sarcoma reported by Roberto Iacovelli [16], the mean survival time was 48 months, and the prognosis of the patients with metastasis was very poor, with average survival time only about 6 months.

Conclusion

Primary renal synovial sarcoma is a rare malignant tumor with poor prognosis, and the histopathologic and immunochemical stanning are not specific. The final diagnosis needs confirmation by molecular analysis, which reveals a SYT/SSX gene fusion. Radical resection is generally accepted as a main treatment, and adjuvant ifosfamide-based chemotherapy has some role. Besides, new therapy targeting SYT/SSX and multidisciplinary approach will be the research direction to improve prognosis.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xiao-Li Feng, Department of Pathology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 17, Panjiayuan Nanli, Beijing 100021, China. Tel: (0086)-10-87787507; E-mail: fengxl@hotmail.com

References

[1] Argani P, Faria PA, Epstein JI, Reuter VE, Perlman EJ, Beckwith JB, Ladanyi M. Primary renal synovial sarcoma: molecular and morphologic delineation of an entity previously included among embryonal sarcomas of the kidney. Am J Surg Pathol 2000; 24: 1087-96.

[2] Ud DN, Hopkins A, Memon A, Ahmad Z, Ahmed R. Calcifying/ossifying synovial sarcoma: a clinicopathologic and molecular study of 5 cases. Indian J Pathol Microbiol 2015; 58: 55-58.

[3] Ladanyi M, Antonescu CR, Leung DH, Woodruff JM, Kawai A, Healey JH, Brennan MF, Bridge JA, Neff JR, Barr FG, Goldsmith JD, Brooks JS, Goldblum JR, Ali SZ, Shipley J, Cooper CS, Fisher C, Skytting B, Larsson O. Impact of syt-ssx fusion type on the clinical behavior of synovial sarcoma: a multi-institutional retrospective study of 243 patients. Cancer Res 2002; 62: 135-40.

[4] Moorthy HK, Pillai BS, Varghese J. Primary renal synovial sarcoma: an oncologic surprise. Urol Case Rep 2014; 2: 152-153.

[5] Modi G, Madabhavi I, Panchal H, Anand A, Patel A, Parikh S, Revannasiddaiah S. Primary synovial sarcoma of kidney: a rare differential diagnosis of renomegaly. Case Rep Pathol 2014; 2014: 657497.

[6] Bakri A, Shinagare AB, Krajewski KM, Howard SA, Jagannathan JP, Hornick JL, Ramaiya NH. Synovial sarcoma: imaging features of common and uncommon primary sites, metastatic patterns, and treatment response. AJR Am J Roentgenol 2012; 199: W208-15.

[7] Majumder A, Dey S, Khandakar B, Medda S, Chandra Paul P. Primary renal synovial sarco-

ma: a rare tumor with an atypical presentation. Arch Iran Med 2014; 17: 726-8.
[8] Chandrasekaran D, Narayanaswamy K, Sundersingh S, Senniappan K, Raja A. Primary synovial sarcoma of the kidney with inferior vena caval thrombus. Indian J Surg Oncol 2016; 7: 345-8.
[9] Abbas M, Dämmrich ME, Braubach P, Meinardus A, Kramer MW, Merseburger AS, Herrmann TR, Grünwald V, Kreipe HH. Synovial sarcoma of the kidney in a young patient with a review of the literature. Rare Tumors 2014; 6: 5393.
[10] Yang L, Wang K, Hong L, Wang Y, Li X. The value of immunohistochemistry in diagnosing primary renal synovial sarcoma: a case report and literature review. Int Surg 2012; 97: 177-81.
[11] Foo WC, Cruise MW, Wick MR, Hornick JL. Immunohistochemical staining for TLE1 distinguishes synovial sarcoma from histologic mimics. Am J Clin Pathol 2011; 135: 839-44.
[12] Vedana M, Fuenfschilling M, Tzankov A, Zellweger T. Primary synovial cell sarcoma of the kidney: case report and review of the literature. Case Rep Oncol 2015; 8: 128-32.
[13] Pathrose G, John NT, Hariharan P. Renal synovial sarcoma in a young pregnant lady: a case report and clinico-pathological profile. J Clin Diagn Res 2017; 11: PD13-PD14.
[14] El Beaino M, Araujo DM, Lazar AJ, Lin PP. Synovial sarcoma: advances in diagnosis and treatment identification of new biologic targets to improve multimodal therapy. Ann Surg Oncol 2017; 24: 1-10.
[15] Wang Z, Zhong Z, Zhu L, Xiong W, Pan C, Wang X, Huang Z, Zhao X. Primary synovial sarcoma of the kidney: a case report. Oncol Lett 2015; 10: 3542-3544.
[16] Iacovelli R, Altavilla A, Ciardi A, Urbano F, Manai C, Gentile V, Cortesi E. Clinical and pathological features of primary renal synovial sarcoma: analysis of 64 cases from 11 years of medical literature. BJU Int 2012; 110: 1449-54.