ABSTRACT

Background: Primary kidney sarcomas are rare neoplasms. Pre-operative signs and symptoms are non-specific, thus making early diagnosis of this condition difficult. The presenting features are similar to other common renal tumors.

Material and Methods: Two cases of primary renal synovial sarcoma were diagnosed based on histopathology and immunohistochemistry (IHC). Fusion gene product analysis was also done for one patient.

Results: Both patients underwent radical nephrectomy. The morphology and IHC of the tumors were consistent with primary synovial sarcoma of the kidney. One of the patients received adjuvant chemotherapy and is on regular follow-up since two years. The second patient was lost to follow-up.

Conclusion: These tumors should be correctly diagnosed because the line of treatment is distinct from primary renal cell carcinoma. Chemotherapy has a role in managing these patients.

Key Words: Synovial sarcoma – kidney – RT-PCR – SYT-SSX – t (X;18) translocation – Fusion gene.

INTRODUCTION

Primary renal cell sarcomas are rare tumors; primary renal synovial sarcomas even more so. The presenting features are similar to other common renal tumors. If the histopathology of the resected mass is suggestive of synovial sarcoma, appropriate immunohistochemical, genetic and molecular tests must be performed to reach a firm diagnosis. Chemotherapy may have a role in kidney sarcomas, in contrast to renal cell carcinoma where biotherapy with interferon, interleukin, and newer targeted molecules are used.

We report here two cases of primary synovial sarcoma of kidney.

Case 1:

A 50-year-old female presented to our tertiary-care cancer institute with a 6-week history of right flank pain, discolored urine, and a mass in the abdomen. On examination, a tender mass was palpable in her right flank. Computerized tomography scan of the abdomen revealed a large retroperitoneal heterogeneous mass involving the right kidney and infiltrating the psoas muscle (Fig. 1). There was no intra abdominal lymphadenopathy or intra abdominal metastasis.

Ultrasound-guided fine needle aspiration cytology (FNAC) of the renal mass was suggestive of a malignant small cell neoplasm. The patient then developed severe abdominal pain, and underwent an emergency laparotomy and radical right nephrectomy.

Grossly, the surgical specimen was an encapsulated mass measuring $7 \times 3.2 \times 5.1$ cm (Fig. 2). Histopathological examination revealed a malignant spindle cell neoplasm consisting of short spindle and ovoid cells with areas of necrosis and hemorrhage. A hemangiopericytoma-like pattern was noted (Fig. 3). Capsular invasion was also seen. The right adrenal gland, ureter and renal vein were not involved, and the regional lymph nodes were reactive.
Immunohistochemistry (IHC) revealed that the tumor cells were strongly positive for BCL2 and CD99, focally positive for epithelial membrane antigen (EMA), and negative for smooth muscle actin (SMA), cytokeratin (CK), HMB45, and LCA. The morphology and IHC of the tumor was thus consistent with primary synovial sarcoma of the kidney.

A reverse transcriptase polymerase chain reaction (RT-PCR) for SYT-SSX fusion gene transcripts using ribonucleic acid extracted from formalin-fixed, paraffin-embedded tumor tissue was performed. PCR was performed using primers specific for SYT and SSX2 genes. The primers were generated upstream and downstream of the translocation breakpoint. Products were run in a polyacrylamide gel. Techgene 24 well Thermal Cycler was used for PCR. A band was noted at 331bp position that corresponded with the positive control. Thus, the molecular analysis revealed a translocation of the SYT gene on chromosome 18 and SSX2 gene on chromosome X, and the findings were consistent with a diagnosis of synovial sarcoma.

Her post-operative recovery was uneventful. She received 6 cycles of adjuvant therapy with ifosfamide and adriamycin. At present she is asymptomatic and on regular follow-up since 2 years.

Case 2:

A 45-year-old male presented to our institute with a 3-month history of flank pain and episodes of gross hematuria. Computed tomography scan revealed a mass in the inferior pole of the left kidney, without intra-abdominal lymphadenopathy or metastasis. Ultrasound-guided FNAC of the renal mass was suggestive of a malignant spindle cell neoplasm. He underwent a left nephrectomy. A mass measuring 3.5 × 2.5 × 1.5cm was present at the inferior pole of the kidney. On cut section, the mass was brown, with poorly defined borders. There was hemorrhage and necrosis, as well as extension into the peri-renal fat. There was no visible invasion into the renal vein or artery.

Histopathological examination revealed a malignant spindle cell neoplasm consisting of short spindle and ovoid cells with areas of necrosis and hemorrhage. There was moderate pleomorphism of the cells (Fig. 4), and a mitotic rate of 12/10 high power fields in the most cellular areas. IHC revealed that the tumor cells were focally positive for EMA, positive for BCL2 and CD99 (Fig. 5); and negative for SMA, CK, HMB 45, and LCA. Correlating the IHC findings with morphology, a diagnosis of primary renal SS was made. Unfortunately, the patient was lost to follow-up and further molecular analysis could not be performed.
DISCUSSION

Sarcomas originating in the kidneys of adults are rare. Histological types of renal sarcomas include leiomyosarcoma, rhabdomyosarcoma, angiosarcoma, haemangiopericytoma, liposarcoma, chondrosarcoma, and osteosarcoma [1].

Synovial sarcoma usually occurs in children and young adults adjacent to extremity joints and tendons. This tumor has been reported to occur in unusual sites like head and neck, heart, lung, peritoneum and prostate [2]. Two histological types of synovial sarcoma have been classically described. One is the monophasic type, where only either spindle cells or epithelial cells are seen; the former is more common. The other is the biphasic type, in which both epithelial-like as well as spindle cell populations can be identified [2]. A third variant, known as poorly differentiated synovial sarcoma characterized by predominantly round or short-spindled cell morphology, has also been described [3]. This rare type of synovial sarcoma has been known to have a poor prognosis. Recent gene expression profile studies have shown that it has a distinct biology [4].

Lewis et al. performed a multivariate analysis of prognostic factors in 112 patients with primary localized synovial sarcoma of the extremity, and found that tumor size greater than 5cm and the presence of bone or neurovascular invasion were independent adverse predictors of distant recurrence as well as mortality [8]. In their study, the 5 year local-recurrence, distant-recurrence, and mortality rates were 12%, 39%, and 25%, respectively. Kreig et al. recently reported a multicentre retrospective analysis of 62 patients who were followed up for a median of 7.7 years for dead patients and 17.2 years for living patients [6]. The 5-year, 10-year, and 15-year survival were 74.2%, 61.2%, and 46.5%, respectively. Local recurrence occurred after a mean of 3.6 years, and metastases after a mean of 5.7 years. Adverse prognostic factors in this cohort included larger tumor size, metastases at time of diagnosis, high grade histology, disease location in the trunk, and inadequate initial surgery.

Primary renal synovial sarcoma is exceedingly rare and was initially described as recently as 1999 [7]. About 40 cases have been reported in the literature so far [8].

In adults, the most important differential diagnoses include renal cell carcinoma, sarcomatoid carcinoma, adult primitive neuroectodermal tumor (PNET), adult Wilms' tumor, and fibrosarcoma. IHC markers are useful in clarifying the differential diagnosis of spindle cell malignancies. The diagnosis of synovial sarcoma can be suggested by the pattern of IHC markers (positive CK, EMA, BCL-2, and CD99). Wang et al. recently reported a series of 4 cases of primary renal sarcomas [9]. IHC analysis revealed positivity for vimentin (4/4), Bcl-2 (4/4), CD99 (4/4), CD56 (3/4), and focally for EMA (3/4) and cytokeratin (3/4).

Currently available IHC markers, although highly suggestive, are not specific enough to make a firm diagnosis. A characteristic and
consistent translocation, \( t(X;18)\) (p11; q11), is seen in the majority of patients with synovial sarcomas \cite{10}. Conventional cytogenetics (using chromosomal banding studies) or molecular techniques can be used to identify this translocation and clinch the diagnosis of synovial sarcoma. Additional molecular tests have recently become available for confirmation of the diagnosis of synovial sarcoma. These include the detection of characteristic specific fusion gene products. The SSX gene (at Xp11) and the SYT gene (at 18q11) are juxtaposed as a result of the \( t(X;18)\) translocation. The resulting chimeric SYT-SSX transcript is a molecular marker of this neoplasm \cite{11}. Crew et al. have demonstrated that there are in fact two homologous genes at the X chromosome (SSX1 and SSX2) which may fuse with SYT \cite{12}. Five genes (SSX1 to 5) have been so far identified in the Xp11 region in synovial sarcoma \cite{13,14}. Biphasic synovial cell sarcoma is usually associated with SYT-SSX1, while monophasic synovial cell sarcoma may be associated with either transcript \cite{15}. The former has a higher rate of proliferation and some reports (but not all) have suggested a poorer outcome \cite{16}.

Positron emission tomography (PET) may reveal high maximum standardized uptake value (SUVmax) in the primary tumor and nodal metastases \cite{17,18}. However, the role of nuclear imaging in this setting is evolving, and as yet remains undefined.

There is no standard treatment strategy for synovial sarcoma. In many published cases, surgery followed by ifosfamide-and/or adriamycin-based chemotherapy have been used \cite{19}.

The take-home message is that, despite its rarity and non-specific presentation, clinicians should consider synovial cell sarcoma in the differential diagnosis of renal masses, especially when histopathology is non-diagnostic. Since morphological differentiation from other tumors may be difficult, other diagnostic modalities like IHC, cytogenetics, and advanced molecular analyses need to be employed.

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