

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

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Key Words

Renal synovial cell sarcoma · Renal spindle cell tumor · *SYT-SSX* gene fusion · *SYT* gene rearrangement · Transducin-like enhancer of split 1

Abstract

Synovial cell sarcoma (SCS) of the kidney is a rare tumor entity with a poor prognosis. Morphologic and immunohistochemical characteristics may overlap with other more common neoplasms of the kidney. Therefore, the diagnosis of primary renal SCS not only requires the exclusion of similar tumor types, but also a confirmation of *SYT-SSX* gene fusion using molecular techniques. The treatment comprises radical surgery, and, depending on age and health status, adjuvant chemotherapy in selected patients. Here, we present an elderly SCS patient in whom straightforward radical surgical treatment resulted in a sustained complete remission; it allowed us to perform a literature survey focusing on current diagnostic tools for SCS.

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Introduction

Synovial cell sarcoma (SCS) of the kidney is a rare tumor entity first described in 1999 and published in 2000 by Argani et al. [1, 2]. To date, no more than 50 cases have been described in the literature. It mostly affects young people (median age 35 years). Differential diagnosis mainly includes renal sarcomatoid carcinoma, metastatic sarcoma, solitary fibrous tumor of the kidney and retroperitoneal sarcoma involving the kidney. SCS is a malignant mesenchymal tumor which typically affects proximal limbs of young adults, but it can also

involve other sites (head and neck, heart, duodenum, lung, mediastinum, abdominal wall, kidney and prostate) [3]. Histologically, SCS is subclassified into monophasic (spindle cells) or biphasic (spindle cell component mixed with plump epithelioid cells) as well as poorly differentiated types. At the molecular level, SCS is characterized by a *SYT-SSX* gene fusion caused by the rearrangement between the p11.2 and q11.2 portions of chromosomes X and 18, respectively, i.e. t(X;18)(p11.2;q11.2) [4] and rare variants.

Here, we report the case of a 76-year-old woman who was diagnosed and treated at our institution.

Case Report

A 76-year-old woman was referred to our hospital because of macrohematuria and right flank pain. The medical history revealed a slight mitral regurgitation as well as a substituted hypothyroidism due to a total thyroidectomy performed because of a benign pathology 40 years earlier. The patient was a nonsmoker and had no history of exposure to chemicals. Blood tests revealed no signs of systemic inflammation or renal insufficiency, only a moderate anemia was noticeable. We performed a cystoscopy, which brought no evidence of bladder pathology, but we noticed active bleeding from the right ureteral orifice. Sonography and an abdominal CT scan showed a hypodense mass with slow contrast enhancement, 80 mm in diameter and located in the upper pole of the right kidney and involving the pyelon. There was no evidence of metastases (fig. 1). Suspecting an urothelial carcinoma of the right pyelon, we performed a retroperitoneoscopic nephro-ureterectomy.

Macroscopic pathological evaluation revealed a right kidney weighing 300 g and measuring 12 × 6 × 5 cm. The upper pole tumor showed a greyish, partly hemorrhagic cut surface and a firm consistency. It measured 8 × 5 × 5 cm and showed a macroscopic infiltration of the renal parenchyma as well as a pedunculated growth into the pyelon, almost completely filling out the latter. Histological analysis revealed a monotonous tumor composed of spindle-shaped cells. There was prominent mitotic activity and a microscopic vascular invasion (fig. 2). Resection margins were tumor free. Immunohistochemical analysis demonstrated positivity for Bcl-2, CD99, transducin-like enhancer of split 1 (TLE1), vimentin and focal positivity for cytokeratin (CK) 7. The other applied markers such as S100, HMB45, SMA, actin, CD34, desmin, CK22 and CK19 remained negative. The immunohistochemical pattern was typical for SCS. As the tumor revealed no epithelial component, it was classified as monophasic SCS. A definitive diagnosis was achieved by the confirmation of a *SYT* gene rearrangement using a *SYT* dual color break apart probe-based (Z-2097-50; Zytovision, Bremerhaven, Germany) FISH test (fig. 3).

The postoperative follow-up was uncomplicated. The interdisciplinary tumor board decided not to perform adjuvant chemotherapy mainly because of the patient's age. Twenty months after surgery, the patient feels well and shows no clinical or radiological signs of recurrence.

Discussion

SCS is the fourth most common sarcoma, which primarily develops in the limbs of young individuals. SCS originating from the kidney is extremely rare and its histogenesis is uncertain. Less than 50 cases have been described in the literature to date. This rare renal tumor typically affects younger patients of both genders, with a slight predominance in males. To

our knowledge, the presented case has the highest age at time of diagnosis (76 years) described so far. There are no specific clinical or imaging characteristics for SCS: clinical symptoms and CT images do not differ from other malignant renal tumors.

For the pathologist, it may be difficult to differentiate SCS from other, more common forms of sarcomatoid tumors originating in the kidney, especially sarcomatoid renal cell carcinoma, metastatic sarcoma, solitary fibrous tumors and retroperitoneal sarcomas involving the kidney. This particularly applies to monophasic SCS, which are more commonly observable in the kidney than biphasic ones. Renal SCS are typically positive for Bcl-2, CD99, CD56, vimentin and focally for epithelial membrane antigen. However, this pattern can also be seen in other tumor types (primitive neuroectodermal tumors and malignant peripheral nerve sheath tumors) [5, 6]. A promising, more specific marker for SCS, like in the present case, appears to be TLE1 (fig. 4), the expression of which is strongly predictive of *SYT* gene rearrangement according to large studies [8, 9], but still needs molecular confirmation according to data from smaller studies [10].

Therefore, definitive diagnosis of a renal SCS requires confirmation of rearrangement involving the *SYT* gene by either reverse transcriptase polymerase chain reaction or applying FISH testing with properly designed probes. This feature seems to be specific for renal SCS [4, 7].

The treatment certainly includes radical surgical resection. However, the clinical benefit of adjuvant chemotherapy for SCS is still controversial. Initial studies, mostly based on anthracycline-only chemotherapy, did not show an improved survival [11, 12]. Later studies included anthracycline- and ifosfamide-based chemotherapy and revealed a small gain in survival, which could not be reproduced in a subsequent, large clinical trial [13]. Thus, no consensus has been achieved yet and the debate is still ongoing, with the chemotherapeutic management of sarcomas varying between institutions and countries. So far, there is no convincing evidence on survival benefits with respect to chemotherapy, which may be due to the heterogeneous inclusion of different histological subtypes in studies as well as the evolution in the quality of treatment and the selection criteria of patients for adjuvant systemic therapy. Therefore, recent studies recommend the use of adjuvant chemotherapy only for younger patients and/or larger tumors where clinical advantages could rather be expected [14].

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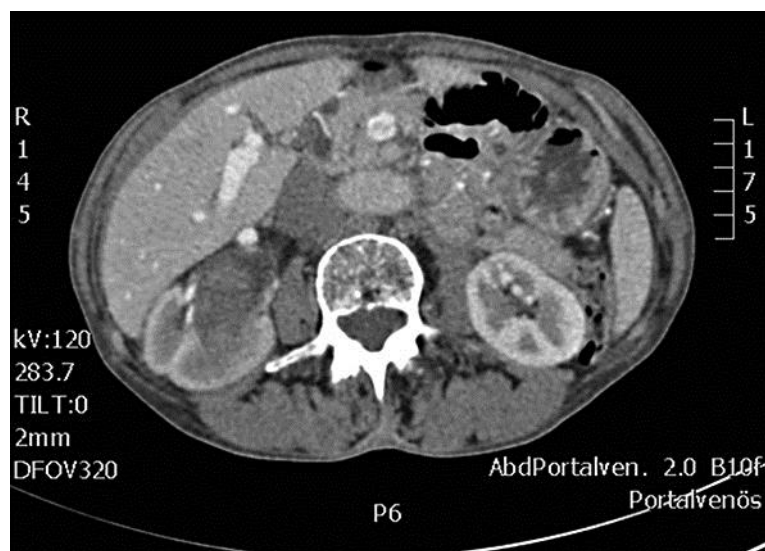


Fig. 1. Computed tomography, portal venous phase: tumor of about 5cm in diameter filling out the right pyelon and showing slow contrast enhancement.

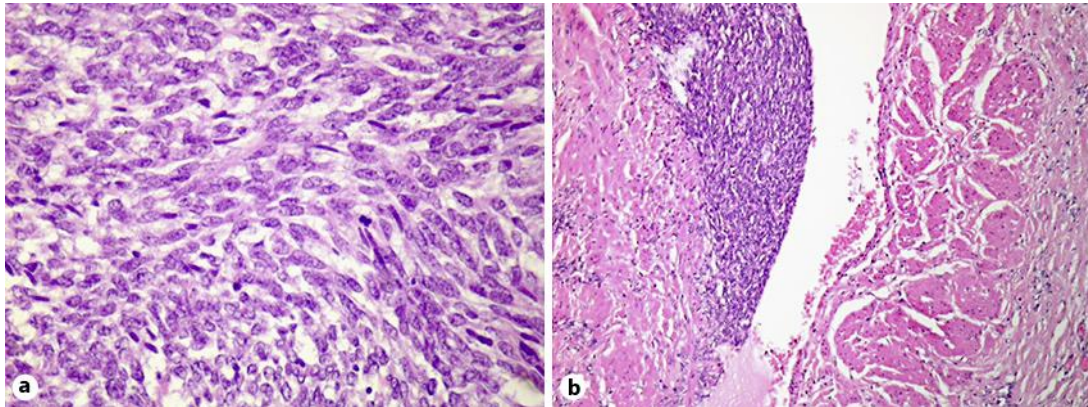


Fig. 2. a Typical fascicles of mitotically active spindle-shaped cells of monophasic synovial sarcoma. b Tumor cells invading into a blood vessel lumen.

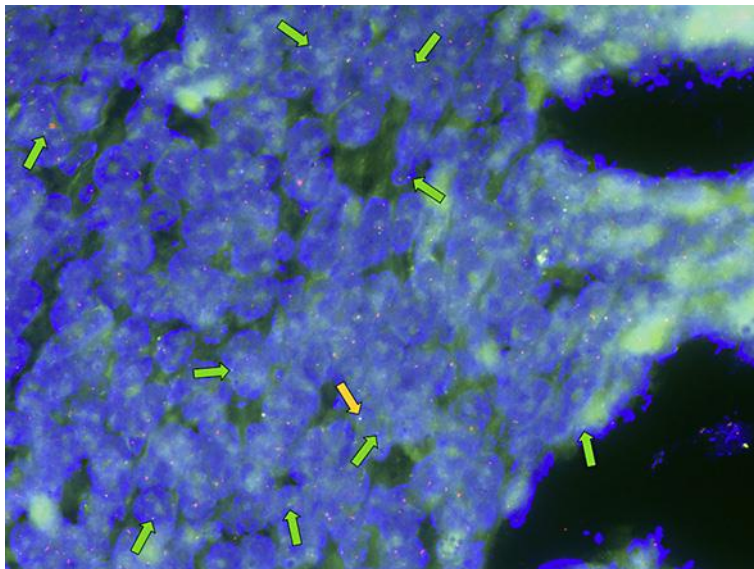


Fig. 3. FISH-testing revealing SYT gene rearrangement: some cells show a normal signal with yellow fusion signals (orange arrow), reflecting nonrearranged alleles. The majority of cells, however, show a pathological signal pattern with separated orange and green signals (green arrows) indicative of a rearrangement.

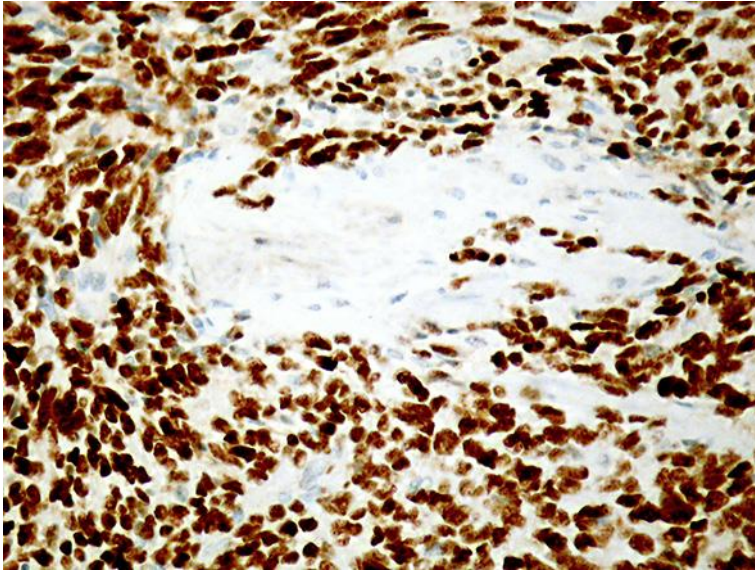


Fig. 4. TLE1 appears to be strongly predictive of a *SYT* gene rearrangement, and it is especially helpful in poorly differentiated synovial sarcomas where the expression of the protein may be even stronger.