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The Value of Immunohistochemistry in Diagnosing Primary Renal Synovial Sarcoma: A Case Report and Literature Review

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Primary synovial sarcoma of the kidney is rare and difficult to diagnose with 100% accuracy without the use of up-to-date histopathologic methods. Immunohistochemical procedures are well established and are continuously expanding and improving. Currently, these methods are successful in up to 90% of tumor identification. The remaining cases will ultimately benefit by combining immunohistochemistry with tumor-specific genetic marker identifiers, the latter of which are increasing in availability for tumor diagnosis. The principal immunohistochemical methods enlisted in establishing a diagnosis of primary renal synovial sarcoma are summarized.

Key words: Renal synovial sarcoma – Immunohistochemistry – Diagnosis

Primary synovial sarcoma of the kidney, a rare type of soft-tissue sarcoma, is extremely rare.[1–3] It is currently difficult to make an accurate clinical diagnosis, even through the application of multiple imaging modalities. Since the appearance of synovial sarcoma is histomorphologically similar to adult Wilms' tumor, malignant primitive neuroectodermal tumor (MPNET) and other renal sarcoma, it is usually misdiagnosed initially. While pathologic confirmation always requires specific molecular/genetic testing, this usually has additional costs, time, and special equipment needs, thereby limiting its use in clinical practice.[4–6] Immunohistochemical staining, while helpful in identification, cannot make an accurate diagnosis alone due to a lack of highly sensitive and specific markers.[7,8] Herein we describe one case of primary renal synovial sarcoma that was treated at our institution and summarize the immunohistochemical findings of renal synovial sarcoma through reviewing the relevant literature. We hope that this will provide additional information for improving immunohistochemical diagnosis of renal synovial sarcoma.

Case Report

A 31-year-old male presented to the hospital citing 2 days of gross hematuria without pain. Blood

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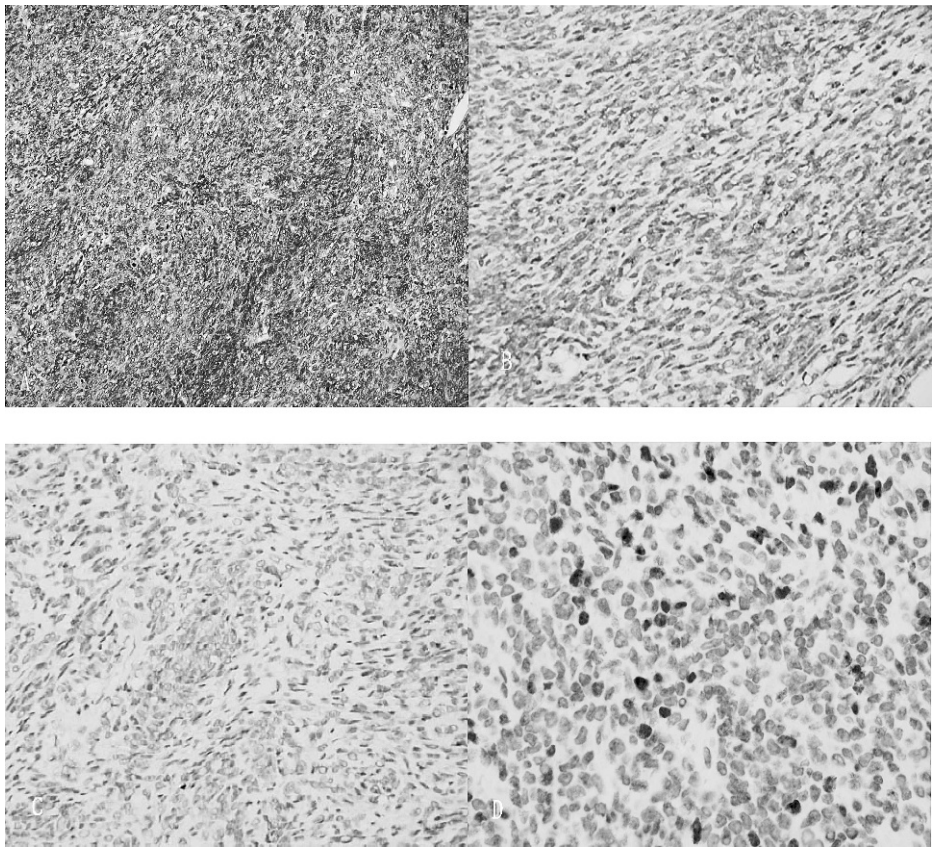

Fig. 1 Primary renal synovial sarcoma. (A) H&E stained (×20) tumor cross-section revealing tumor composed of short spindle cells arranged in intersecting fascicles and epithelial component; biphasic spindle cell sarcoma was identified. (B) Expression of CD99 (×20). (C) Focal positivity of tumor cells for EMA (×20). (D) Expression of Ki-67 (×40) (about 40%–50% positivity).

hemogram and biochemistry data were within normal limits. An enhanced computed tomography (CT) scan of the abdomen and pelvis demonstrated a 7.1-cm × 6.8-cm enhancing mass occupying the inferior pole of the right kidney. Renal cell carcinoma was suspected preoperatively, and the patient underwent a right-sided radical nephrectomy. No gross invasion of the adjacent structures nor regional lymphadenopathy or venous thrombus were found during the operation.

The postoperative pathologic examination showed biphasic spindle cell sarcoma with the following immunohistochemical findings: B-cell lymphoma/leukaemia-2gene (Bcl-2) and Cluster of differentiation 99 (CD 99) were positive, epithelial membrane antigen (EMA) was focally positive and Ki-67 was in the range of 40% to 50%; phosphoenolpyruvate carboxykinase (PCK), leucocyte common antigen (LCA), desmin, Wilms' tumor-1 (WT-1), cytokeratin-7 (CK7), cytokeratin-20 (CK20), Cluster of differentiation 10 (CD 10), Cluster of differentiation 34 (CD 34), and S100 were negative. Fluorescence *in situ* hybridization (FISH) to detect the SYT-SSX fusion transcript produced by the t(X;18) using RNA extracted from the paraffin blocks was carried out in the case; the case was positive for SSX18 group translocation. Upon combining the results, it was considered a synovial sarcoma. Hematoxylin and eosin staining of the tumor cross-section is shown in Fig. 1.

Discussion

Primary renal synovial sarcoma (RSS) is rare; there are currently no standard therapies or clinical guidelines because of the limited number of reported cases.[9] Making an accurate diagnosis is always a problem, since renal synovial sarcoma is usually confused with other soft-tissue sarcomas under the microscope. The current diagnostic gold standard for synovial sarcoma is demonstration of the t(X;18)(p11.2,q11.2) translocation using reverse transcriptase polymerase chain reaction (RT-PCR), involving fusion of the SYT (Synonyms: SS18-synovial

Table 1 Immunohistochemical results in primary renal synovial sarcomas

Case No.	Component	Immunohistochemical results
1		WT-1, CD56, Bcl-2, vimentin+, CD99 focally+; S100, desmin, chromogranin, CD45, cytokeratin cocktail, cytokeratin, AE1/AE3, EMA−
2		Bcl-2,vimentin+; CK, EMA, MIC2−
3		EMA focally+; CK, SMA, desmin, CD34, CD31, MyoD1−
4		Bcl-2, vimentin+; MIC2, NSE, MyoD1, desmin−
5		Bcl-2, MIC2, calponin+; CK, EMA, SMA, S100−
6		Bcl-2+; MIC2, EMA, desmin, S100, WT-1 myoglobin−
7		Bcl-2, calponin, vimentin+; S100, MIC2, CK, CD34−
8		Bcl-2, vimentin+; S100, WT-1, HMB45−
9		S100, AE1/AE3, CD45−
10		Vimentin, MSA, AE1/AE3, EMA, CD99, desmin−
11		Vimentin+; MSA, AE1/AE3, EMA, desmin, S100, Cam5.2−
12		Bcl-2, CD99+, EMA focally+, Ki-67 (40%–50%)+; PCK, LCA, desmin, WT-1, CK7, CK20, CD10, CD34, S100−
13		Bcl-2, MIC2, vimentin, AE1/AE3+; S100, WT-1, SMA−
14		CK7, vimentin+, CD99 focally+; pancytokeratin, chromogranin, CK20−
15	Epithelial	Bcl-2 focally+, CK+, EMA+, vimentin+, CD99 focally+
	spindle	Vimentin+; Bcl-2,CK, EMA, CD99−
16	Epithelia	Bcl-2 focally+, CK+, EMA+, vimentin+, CD99 focally+; WT-1−
	spindle	EMA focally+, vimentin+; Bcl-2, CK, CD99, WT-1−
17		Vimentin, CD56, CD99+; cytokeratin, neurofilament, EMA focally+; S100, desmin, SMA−
18		Vimentin, CD56, CD99+; cytokeratin, neurofilament, EMA focally+; S100, desmin, SMA−
19		Vimentin, CD34, Bcl-2,CD99+
20		Bcl-2, CD99, CD56+; cytokeratin focally+; CD34, SMA−
21		Bcl-2, CD99, CD56+; CD34, SMA−
22		Bcl-2, CD99+; CD34, SMA−
23		Vimentin+, cytokeratin+, EMA focally+; CD34, factor VIII−
24		Vimentin+; EMA focally+; keratins, CD34, S100, desmin, SMA−
25		Vimentin, Bcl-2, CD99+; CD56, CK, EMA focally+; S100, desmin, CD34, actin, PR, ER, CD117−
26		Vimentin, Bcl-2, CD99+; CD56, CK, EMA focally+; S100, desmin, CD34, actin, PR, ER, CD117−
27		Vimentin, Bcl-2, CD99+; CD56, CK, EMA focally+; S100, desmin, CD34, actin, PR, ER, CD117−
28		Vimentin, Bcl-2, CD99+; S100, desmin, CD34, actin, PR, ER, CD117−
29		Vimentin, Bcl-2, EMA, pancytokeratin+; CD99/MIC2, desmin, actin HHF-35−

No. 12 was treated in our hospital; others were found in the literature. Nos.15 and 16 were separately listed the immunohistochemical finding of epithelial cells and spindle cells in literature.

sarcoma translocation, chromosome 18) gene on chromosome 18 to either the SSX1 (synovial sarcoma, X breakpoint 1) or the SSX2 (synovial sarcoma, X breakpoint 2) gene on chromosome Xp11.[2,4,10,11] However, this method is limited in clinical practical work because of the cost, time, and availability of special equipment.[6] Thus, urologists and pathologists have been working to find a simple, quick diagnostic method for this disease. While immunohistochemical staining is helpful in diagnosis, it unfortunately is not as accurate as molecular/genetic testing. This is largely owing to the low and differing sensitivities and specificities of the currently available immunohistochemical markers including Bcl-2, EMA, and cytokeratins (CK).[12,13] A recent study reported that transducin-like enhancer protein 1 (TLE1) demonstrated a 92% positive predictive value and 100% negative predictive value. This is significantly better than other currently used immunohistochemical markers, and thus may preclude the need for more costly and time-consuming molecular testing in some cases. However, Kosemehmetoglu *et al* found TLE1 immunoreactivity in other mesenchymal tumors, showing that its presence is not specific for synovial sarcoma).[6] Can an immunohistochemical method ultimately replace molecular/genetic testing for the accurate diagnosis of RSS in the future? We summarized the immunohistochemical findings of renal synovial sarcomas after reviewing the literature[1–10,12–20] (Table 1), with a goal of better establishing a typical immunophenotype of the disease.

Through reviewing the literature, we found multiple immunohistochemical markers that have been investigated in cases of RSS. Markers such as Bcl-2, vimentin, CD99, EMA, CD56, S100, desmin, SMA, CD34, AE1/AE3, and WT-1 have all been tested for use in diagnosis of the cancer from paraffin-embedded sections. Table 1 clearly shows that staining for Bcl-2, an anti-apoptotic factor, and vimentin, a major cytoskeletal component of

mesenchymal cells, demonstrated significant positivity (20/20 and 20/21 cases, respectively). CD99 was detected in 15 of 17 cases, EMA in 12 of 16 cases, and Cluster of differentiation 56 (CD 56) in 8 of 8 cases, with several samples in the latter 2 studies displaying focal positivity. Stains for S-100, smooth muscle antibody (SMA), CK, CD34, CD31, HMB45, CD10, desmin, myogloblin, chromogranin, PCK, actin HHF-35, PR, ER, CD117, LCA, and MyoD1 were all found to be negative in RSS. S100 was negative in 16 of 16 cases, desmin in 15 of 15 cases, SMA in 9 of 9 cases, CD34 in 12 of 12 cases, and both AE1/AE3 (AE1/AE3) and WT-1 both were negative in 4 of 5 cases tested. When comparing RSS with adult Wilms' tumor and malignant neuroectodermal tumor, a couple of key differences can be observed. For example, WT-1 expression is always found in cases of adult Wilms' tumor but not in primary RSS.[15] Furthermore, MPNETs are typically positive for NSE and approximately 50% to 70% of tumors express S100, while primary renal synovial sarcomas are negative for both.[15,21]

In Table 1, it can be seen that several immunohistochemical markers are focally positive, such as EMA, CD99, CK, and others. When combined with cases Nos. 15 and 16 from Table 1, this suggests that focal staining may be associated with the type of histologic features of the tumor. Histologically, primary renal synovial sarcomas have 3 composition types: monomorphic spindle cells, poorly differentiated, and the biphasic form of spindle cells with epithelial cells.[12,15] These differences may then lead to different immunohistochemical findings, such as the focally positive cases. Further study is needed to determine whether combining the histologic and immunohistochemical results may improve the accuracy of primary RSS diagnosis.

Ultimately, due to the limited number of cases, it is difficult to determine whether immunohistochemical methods alone can result in the accurate diagnosis of primary RSS. We suggest that a combination of immunohistochemical procedures with genetic testing should be used in the diagnosis of RSS in clinical practice. Genetic testing remains the ultimate criterion for the diagnosis when an accurate diagnosis cannot be made using only the immunohistochemical method. However, we hope that this summary can provide clues to better establish a specific immunophenotype of primary renal synovial sarcoma for urologists and pathologists, and provide insight to help find more sensitive and specific markers for diagnosing this disease. Perhaps our findings, in combination with data collected from additional future cases, will lead to the development of a quick and accurate immunohistochemical method for diagnosing primary RSS.

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