Schwannoma of the Kidney

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Schwannomas of the kidney are rare, with only a few reported cases. We report three additional cases with immunohistochemical analysis. All three tumors were from females (aged 27, 35, and 59 years) and ranged from 4.8 to 8 cm in diameter. All of the patients underwent nephrectomy. The tumors were totally or partially encapsulated; two were in the hilum and one was centered in the renal cortex. All tumors were diffusely positive for S100 protein. Two were positive for neuron-specific enolase. Immunostaining for neurofilament, HMB45, microphtalmia transcription factor, smooth muscle actin, CD34, cytokeratin AE1/3, cytokeratin 7, and CD10 were negative. Follow-up data were available for two patients; neither had tumor recurrence or metastasis. In conclusion, renal schwannoma is rare, usually arises centrally, impinging on the hilum or the pelvis, and is cured by resection. Sarcomatoid carcinoma and other spindle cell tumors should be considered in the differential diagnosis.

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Schwannomas are uncommon tumors that originate from the neural sheath and are most common in the head and neck, extremities, and posterior mediastinum. Although 3% of schwannomas occur in the retroperitoneum, involvement of visceral organs is extremely uncommon.¹ Schwannomas are rare in the kidneys, and only 19 cases have been reported.^{2–16} We report herein the clinicopathologic features of three additional cases of renal schwannoma.

Materials and methods

Clinical findings, operative data, and patient follow-up were obtained from medical records. Immunohistochemical preparations were performed on formalin-fixed, paraffin-embedded tissue in all cases. The antibodies, clones, dilutions, antigen retrieval methods, and vendors are listed in Table 1. Appropriate positive and negative controls for each antibody were run concurrently.

Results

Clinical findings are summarized in Table 2. The patients were all women and were 27, 35, and 59 years old. None showed any sign of neurofibromatosis type 1. Clinical presentations included abdominal pain and nausea in one case; the other two patients were asymptomatic. Imaging revealed a renal mass suspicious for renal cell carcinoma in each case. Subsequently, two patients underwent radical nephrectomy and one had a laparoscopic nephrectomy. Short-term (4 and 8 months) follow-up data were available from two patients. Both were alive without recurrence or metastasis.

Macroscopically, case 1 showed a 4.8 × 4.2 × 4.2 cm well-circumscribed lobulated nodular lesion located in the hilum, compressing the renal pelvis, and distorting the surrounding vasculature. Its cut surface was gray–tan to yellow and fibrotic. Case 2 showed an 8.5 × 5.5 × 5 cm well-circumscribed, red–brown fibrous mass centered in the renal cortex in the middle and lower pole of the kidney. Its cut surface appeared myxomatous and fibrous. Case 3 showed a 7 × 4.8 × 4 cm multicystic, encapsulated, focally gelatinous-appearing mass involving the hilum of the kidney.

Histologically, all three tumors were encapsulated and showed characteristic features of schwannoma. In cases 1 and 3, the tumor was composed mainly of spindle cells with a loose textured pattern (Antoni B) and with microcyst formation, and some cellular

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Table 1 Antibody panel used in this study

<i>Antibody/molecule</i>	<i>Clone</i>	<i>Dilution</i>	<i>Antigen retrieval</i>	<i>Source (city/state)</i>
S100	Polyclonal	1:100	Dako pH 6.0 citrate	Dako (Carpenteria, CA, USA)
NSE	BBS/NC/V1-H14	Prediluted	Dako pH 6.0 citrate	NeoMarker (Fremont, CA, USA)
Neurofilament	2F11	1:500	EDTA pH 8.0	Cell Marque (Rocklin, CA, USA)
HMB45	HMB-45	1:30	Dako pH 6.0 citrate	Dako (Carpenteria, CA, USA)
MiTf	D5	1:100	Dako pH 6.0 citrate	Dako (Carpenteria, CA, USA)
SMA	1A4	Prediluted	None	Dako (Carpenteria, CA, USA)
CK AE1/3	AE1/AE3	1:80	Dako pH 6.0 citrate	Dako (Carpenteria, CA, USA)
CK 7	OV-TL 12/30	Prediluted	Proteinase K	Dako (Carpenteria, CA, USA)
CD34	QBEND	Prediluted	Dako pH 6.0 citrate	Dako (Carpenteria, CA, USA)
CD10	56C6	Prediluted	Borg pH 9.0	Cell Marque (Rocklin, CA, USA)

CK, cytokeratin; NSE, neuron-specific enolase; SMA, smooth muscle actin.

areas with Verocay bodies (Antoni A). In case 2, the tumor showed extensive hyaline change in a predominantly Antoni B pattern composed of pleomorphic cells with smudged-appearing chromatin, consistent with degenerative changes. Vascular sclerosis, hemorrhage, and hemosiderin deposits were observed in case 3. Isolated or scattered nuclear atypia was present in cases 2 and 3. Rare mitotic figures were detected in case 1. Necrosis was not observed (Figure 1).

In each tumor, the neoplastic cells showed strong and diffuse immunoreactivity for S100 protein. Neuron-specific enolase was expressed in about 90% of the cells in cases 2 and 3 and in 10% of the cells in case 1. CD34 was expressed only in the endothelial cells. All other immunohistochemical reactions (neurofilament protein, cytokeratins (CK7 and AE 1/3), HMB45, microphthalmia transcription factor, smooth muscle actin, and CD10) were negative.

Discussion

Schwannomas consist of a nearly pure population of cells showing schwannian differentiation, and arise eccentrically from the surface of their nerve of origin. The main nerves of the kidney consist of sympathetic and parasympathetic fibers that accompany the renal artery entering in the renal hilum. This could explain the more frequent location of schwannomas at the renal hilum. Schwannoma rarely arises from the kidneys with only 19 cases reported (Table 2).^{2–16} Clinical presentations include abdominal or flank pain (12 cases),^{2,4–6,8,10,11,13} microhematuria (2 cases),^{3,15} or fever (4 cases).^{4,6,10,11} Sometimes patients are asymptomatic and the finding is incidental.^{2,12,14,16} No patient has been reported to show any sign of neurofibromatosis type 1. All patients are adults and the mean age at diagnosis is 51 years (range, 18–84 years). The male-to-female ratio is 1:1.2. The mass is often located centrally in the kidney, impinging on the hilum and renal pelvis. Less commonly, the tumors appear to arise from the renal cortex or capsule. Two

previously reported cases (9%) were diagnosed as ‘malignant schwannomas’ and those patients died with metastases 3 and 15 months after the diagnosis.^{9,11} These cases probably represent malignant peripheral nerve sheath tumor since rarely does malignancy truly arise in a benign schwannoma.

The histologic appearance of schwannoma of the kidney is similar to that seen in other organs and includes the range of different morphologic patterns described in schwannomas. The classic schwannoma is characterized by a mixture of Antoni A and Antoni B patterns as seen in cases 1 and 3.¹⁷ Microcystic degeneration with hemorrhage and hemosiderin deposits associated with cells showing bizarre hyperchromatic nuclei are common degenerative features of large schwannomas usually seen in retroperitoneum.¹⁸ The tumor in case 2 showed the features of the so-called ancient schwannoma. Ancient schwannomas are not considered as a distinct subtype of schwannoma, but rather longstanding tumors with degenerative nuclear and architectural changes. They do not seem to differ clinically from conventional schwannomas.¹⁹ Cellular schwannoma is exclusively composed of spindle cells in the Antoni A pattern without Verocay bodies,^{17,20} a pattern described in four of the reported renal schwannomas.^{2,8}

Differential diagnostic considerations include low-grade malignant peripheral nerve sheath tumor, renal angiomyolipoma, sarcomatoid carcinoma, synovial sarcoma, solitary fibrous tumor, leiomyoma, low-grade leiomyosarcoma, rhabdomyosarcoma, and angiosarcoma. The distinctive clinical, histologic, and immunohistochemical findings usually permit a definitive diagnosis.

S100 protein family is the largest subgroup of the EF-hand proteins, which consists of several members that display amino-acid sequence homology ranging from 25 to 65%. S100 protein has been studied in the spectrum of epithelial tumors of the kidney and has been proposed to be a useful tool in the differential diagnosis among renal cell neoplasms, particularly in the differential diagnosis of chromophobe renal cell carcinoma vs renal oncocytoma.²⁰ Among renal tumors, S100 protein is

Table 2 Clinicopathologic findings of three cases of renal schwannoma and review of the literature

Main author, year of publication	Age	Sex	Symptoms and signs	Side	Operation	Gross	Location	Diagnosis	Follow-up
Phillips, 1955	56	M	Generalized malaise, weight loss, fever, flank pain, mild anemia	L	Left nephrectomy	12-cm encapsulated tumor	Pelvis	Schwannoma	NA
Kuz'mina, 1962	33	F	Generalized malaise, weight loss, mild temperature, flank mass	R	Right nephrectomy	Encapsulated, rubbery, pale gray tumor	Capsule	Schwannoma	NA
Fein, 1965	51	F	Congenital malformation, hydronephrosis, fever, flank pain, pyuria, palpable mass	R	Right nephrectomy	6-cm well encapsulated mass	Pelvis	Schwannoma ^a	NED (~24-month follow-up)
Bair, 1978	56	M	Hypertension, microhematuria, hypertensive renal disease	R	Right nephrectomy	7-cm mass	Hilum	Schwannoma	NED (5-month follow-up)
Steers, 1985	50	F	Microhematuria, palpable mass	R	Tumorectomy	9-cm multicystic mass	Hilum	Schwannoma	NA
Somers, 1988	55	F	Incidental finding	L	Left nephrectomy	5.1-cm well-defined solid lobular mass	Intraparenchymal upper pole	Schwannoma	NED (18-month follow-up)
Kitagawa, 1990	51	M	Upper abdominal pain and high fever; painful swelling of the scrotum	L	Left nephrectomy	2.8-cm well-demarcated yellowish tumor,	Hilum	Schwannoma	NA
Ma, 1990	67	M	Epigastric pain	R	Right nephrectomy	8-cm well-encapsulated, firm, yellowish	Intraparenchymal and pelvis	Cellular schwannoma	NED (1-year follow-up)
Naslund, 1991	50	F	Mild abdominal discomfort, weight loss, anemia	L	Left nephrectomy	14-cm mass	Intraparenchymal upper pole	Malignant schwannoma	DOD after 15 months
Romics, 1992	52	M	Back and flank pain, recurrent fever, anemia, leukocytosis	R	Right nephrectomy; mesenteric metastasectomy	Large infiltrating mass with cystic necrotic degeneration	Capsule	Malignant schwannoma	DOD after 3 months
Ikedo, 1996	89	M	Abdominal pain	R	Right nephrectomy	NA	Pelvis	Schwannoma	NA
Singer, 1996	70	F	Asymptomatic, elevated CEA	L	Left nephrectomy,	6-cm well demarcated lobulated mass	Hilum	Schwannoma	NED (18-mo follow-up)
Alvarado-Cabrero, 2000	45	M	Flank and abdominal pain	L	Left nephrectomy	16-cm mass	Intraparenchymal	'Ancient' schwannoma	NED (5-year follow-up)
	40	F	Flank pain	L	Left nephrectomy	12.5-cm mass	Intraparenchymal	Cellular schwannoma	NED (1-year follow-up)
	84	M	Found during work-up of cystitis	R	Right nephrectomy	4-cm mass	Intraparenchymal	Cellular schwannoma	NED (4.5-year follow-up)
	18	F	Flank pain	R	Right nephrectomy	6.2-cm mass	Intraparenchymal	Cellular schwannoma	NED (3.5-year follow-up)
Tsurusaki, 2001	69	F	Incidental finding	L	Tumorectomy	White mass with necrosis	Capsule	Schwannoma	NA
Singh, 2005	40	M	Renal colicky pain, vomiting	L	Left nephrectomy	3-cm firm mass	Hilum	Schwannoma	NED (3-year follow-up)
	35	M	Flank pain, gross hematuria	R	Right nephrectomy	NA	Intraparenchymal and pelvis	Schwannoma	NED (2-year follow-up)
Gobbo, 2008: case 1	59	F	Asymptomatic	L	Left nephrectomy	4.8-cm lobulated mass	Hilum	Schwannoma	NA
Gobbo, 2008: case 2	27	F	Incidental finding during study for polycythemia	R	Right nephrectomy	8.5-cm myxomatous fibrous mass	Intraparenchymal mid-lower pole	'Ancient' schwannoma	NED (8-month follow-up)
Gobbo, 2008: case 3	35	F	Abdominal pain, nausea	L	Left nephrectomy	7-cm encapsulated microcystic mass	Hilum	Schwannoma	NED (4-month follow-up)

DOD, died of disease; F, female; L, left; M, male; NA, not available; NED, no evidence of disease; R, right.

^aThis case was diagnosed as low-grade malignant schwannoma.

Figure 1 Schwannoma of the kidney; (a) (case 1) the tumor is characterized by a mixture of Antoni A and Antoni B pattern; (b) (case 1) cellular area with Verocay bodies (Antoni A); (c) (case 2) the tumor showed extensive hyaline change; (d) (case 2) neoplastic cells showed a strong and diffuse immunoreactivity with S100 protein; (e) (case 3) the tumor was separated from the renal parenchyma by a well-formed fibrous capsule; (f) (case 3) mixture of Antoni A and Antoni B patterns in a renal schwannoma; (g) (case 3) schwannoma showing vascular sclerosis; (h) (case 3) Antoni B area showing vascular sclerosis and hemosiderin deposits.

expressed in oncocytoma, papillary renal cell carcinoma, and clear cell renal cell carcinoma, whereas they are negative in chromophobe renal cell carcinoma.²⁰ In the current study, all three cases of renal schwannoma were positive for S100 protein.

Schwannomas rarely undergo malignant change, most often in the form of either malignant peripheral nerve sheath tumor or angiosarcoma.^{21–23} Malignant peripheral nerve sheath tumor is occasionally composed of epithelioid cells with vesicular nuclei and prominent nucleoli.²⁴ Angiosarcoma is typically immunoreactive for endothelial markers, such as CD34.²² The presence of nuclear atypia or diffuse hypercellularity in a schwannoma may lead to an erroneous diagnosis of malignancy. It is critical to distinguish schwannoma of atypical or cellular type from malignant peripheral nerve sheath tumor. Unlike malignant peripheral nerve sheath tumors, schwannomas with degenerative nuclear atypia lack mitotic figures. Their large cells with pleomorphic nuclei and smudged chromatin are reminiscent of those seen in ancient schwannoma. Cellular schwannoma is distinguished from malignant peripheral nerve sheath tumor by the smaller cell size, infrequent mitotic figures and lack of significant cytologic atypia, nuclear pleomorphism, and necrosis. In the absence of definite cellular crowding, nuclear enlargement (≥ 3 times the size of ordinary schwannoma nuclei) and hyperchromasia, the finding of rare mitotic figures in a cellular schwannoma is not sufficient for a diagnosis of malignancy.

In summary, schwannoma rarely arises from the kidney, is usually located in the renal hilum or pelvis, and clinically behave in a benign fashion.

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