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Original Article

Renal myopericytoma: a clinicopathologic study of six cases and review of the literature

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Abstract: To evaluate the morphologic features, immunohistochemical profiles, and biological behavior of renal myopericytoma. Six cases of renal myopericytoma are retrospectively retrieved and analyzed by H&E and immunohistochemical staining. Clinically, patient's age ranged from 33 to 70 years (median, 56 years). Male to female ratio was 5:1. Five of the six patients were asymptomatic of the urinary tract, the remained one presented with abdomen pain. Grossly, all six tumors were solitary masses with sizes ranging from 1.8 to 7.3 cm of maximum diameter (mean, 4.4 cm). Five tumors were described as well-circumscribed, and 1 case was showed as ill-defined. Histologically, in all cases, numerous thin-walled vessels and a perivascular arrangement of ovoid, spindled or round myoid tumor cells were seen. However, a broad morphologic spectrum ranging from fibroma-like (3 cases), glomangiopericytoma-like (3 cases), angioleiomyoma-like (2 cases), glomoid- like (2 cases), and myofibroma-like (2 cases) components were observed. In addition, 1 neoplasm with immature cellular features and another infiltrating myopericytoma were found. A coexisting papillary adenoma was detected in 1 case. Nuclear atypia was seen in 2 cases. Immunohistochemically, SMA, caldesmon, and MSA were positive in all 6 cases, whereas CD34 and desmin was partial positive in 1 case, respectively. Ki67 index was aproximately 5% in 1 case but less than 2% in the others. All patients are free of disease by follow-up ranging from 14 to 66 months (mean, 38.7 months).

Keywords: Myopericytoma, perivascular myoid cell tumor, infiltrating, uncertain malignant potential, papillary adenoma, kidney

Introduction

Myopericytoma is an unusual benign neoplasm and shows a perivascular concentric multilayering of ovoid- to spindle-shaped cells with a myoid appearance and immunophenotype [1, 2], which typically originating from the skin and superficial soft tissues of distal extremities, trunk, and head and neck regions [3-5]. Rarely, these tumors have been reported to occur in visceral sites [6-13]. Most myopericytomas behave in a benign style; however, rare cases of malignant myopericytoma arising in both superficial soft tissue and visceral locations have been described [14]. In the kidney, to our knowledge, only 4 cases of myopericytoma have been documented in the English literature since the first such tumor was described by Lau SK et al in 2010 [15-18]. Because of its rarity, the morphologic features, immunohistochemical profiles, and biological behavior of this tumor have not been entirely understood. Herein, we report the clinicopathologic features of 6 cases of renal myopericytoma which, to the best knowledge of us, is the largest series of these rare tumors reported in the kidney in the literature.

Materials and methods

Six cases of renal myopericytoma were identified in a search of the archive files of the author's institutions for the years 2000 to 2014, one of the cases (case no. 6) has already been published in detail [18]. Available clinical information was recorded, including patient age, clinical presentation, type of procedure, and follow-up data. Macroscopic findings were obtained from surgical pathology reports. Four-micrometer-thick, 4% buffered formalin-fixed,

Table 1. Clinicopathologic features of 6 cases of renal myopericytoma

Case (no.)	1	2	3	4	5	6
Age/Sex	56/F	33/M	46/M	70/M	69/M	59/M
Symptoms	Pain on the right side of the abdomen	Asymptomatic	Asymptomatic	Asymptomatic	Asymptomatic	Asymptomatic
Location	Right, lower pole, bulging from the capsule	Left, middle pole	Left, lower pole	Left, middle pole	Right, middle pole	Left, middle pole
Gross findings	1.8 × 1.6 × 1.2 cm, well circumscribed	4.5 × 4.5 × 4.0 cm, well circumscribed	7.3 × 6.3 × 6.0 cm, well-circumscribed	4.8 × 4.3 × 4.0 cm, infiltrative border	4.2 × 3.0 × 2.8 cm, well-circumscribed	3.6 × 2.8 × 2.7 cm, well-circumscribed
Histological findings	TI, AL, IM	TI ,GP, FR	TI, FR, AL	TI, GP, AL, GM, CH	TI	TI, GP, GM
Cellular pleomorphism	No	No	No	Rarely found	No	Rarely found
Mitotic figures	No	No	No	No	No	No
Necrosis	No	No	No	No	No	No
Vascular invasion	No	No	No	No	No	No
Stroma	Hyalinized	Myxomatous, loose, edematous, hyalinized	Hyalinized, inflammatory infiltrate	Loose, edematous, hyalinized	Myxomatous, loose, edematous, inflammatory infiltrate, hemorrhage	Loose, edematous, hyalinized
Immunhis tochemical results	VM+, SMA+, Caldemon+, MSA+, Desmin-, CD34-, Ki-67+ <2%	VM+, SMA+, Caldemon+, MSA+, Desmin-, CD34-, Ki-67+ <1%	VM+, SMA+, Caldemon+, MSA partial+, Desmin-, CD34-, Ki-67+ <2%	VM+, SMA+, Caldemon+, MSA partial+, Desmin-, CD34 partial+, Ki-67+ 5%	VM+, SMA+, Caldemon+, Desmin-, MSA+, CD34-, Ki-67+ <1%	VM+, SMA+, Calde mon+, MSA l+, Desmin patchy+, CD34-, Ki-67+ <1%
Treatment	PN	RN	RN	RN	RN	RN
Coexistence	No	No	No	papillary adenoma	No	No
FU (mo)	ANED (66)	ANED (64)	ANED (46)	ANED (16)	ANED (14)	ANED (26)

F indicates female; M, male; TI, a distinct perivascular and concentric growth of ovoid to spindle-shaped cells showing catherine wheel features or a typical spinning off from the vessel walls; AL, angioleiomyoma appearance; IM, immature cellular features; GP, glomangiopericytomatous appearance; FR, fibroma-like appearance; GM, glomoid features; CH, cavernous haemangioma appearance; PN, partial nephrectomy; RN, radical nephrectomy; FU, follow-up; ANED, no evidence of disease. *All 6 cases of renal myopericytoma showed CK-, EMA-, PAX8-, CD10-, CD31-, F8-, CD117-, S-100-, HMB-45-, MelanA-, ALK-, CGA-, SYN-, cathepsin K-, ER-, PR-, EBV-.

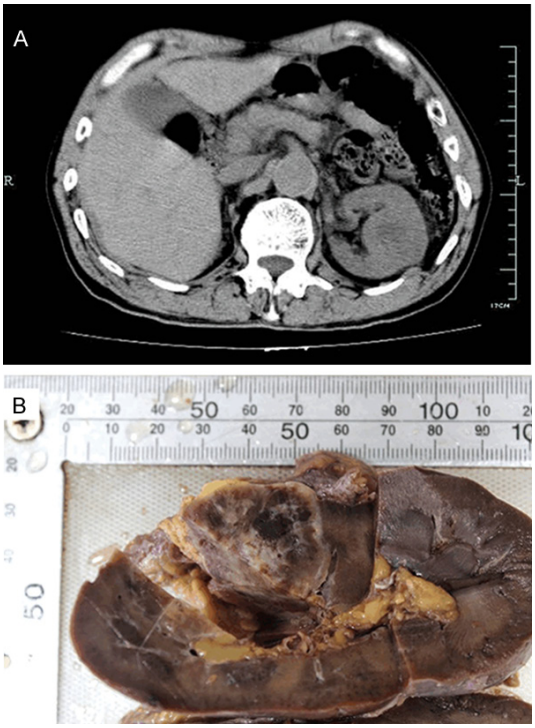

Figure 1. Computed tomography reveals a well-circumscribed and heterogeneous mass in the left mid-kidney of case no. 2 (A). Macroscopic examination shows a 4.8 × 4.3 × 4.0 cm, solid, rubbery and gray-tan mass with gray white fibrotic centrally in case no. 4 (B).

paraffin-embedded sections of all cases were stained with hematoxylin and eosin (H&E) for routine microscopic examination. Upon microscopic examination, we recorded the following morphologic patterns in each tumor including: tumor borders, growth patterns, nuclear atypia, mitotic activities, necrosis, and vascular invasion. Nuclear atypia was defined as greater than 3-fold variation in nuclear size. Immunohistochemical analysis of all cases was performed using the avidin-biotin complex immunoperoxidase technique with a panel of commercially available primary antibodies to the following antigens: cytokeratins (AE1/AE3, 1:50, DAKO), epithelial membrane antigen (EMA, Mc 5, 1:400, Biogenex), PAX-8 (Polyclonal, 1:1000, DAKO), CD10 (56C6, 1:100, DAKO), vimentin (V9, DAKO, 1:3000), smooth muscle actin (SMA, 1A4, 1:150, DAKO, Carpinteria,CA), caldesmon (h-CD, 1:200, DAKO), muscle specific actin (MSA, HHF35, 1:150, DAKO), desmin (D33, 1:200, DAKO), S100 protein (4C4.9, 1:1000, DAKO), HMB-45 (HMB-45, 1:100, DAKO), Melan-A (A103, 1:200, DAKO), CD34 (QBEnd/10, 1:400, DAKO), CD31 (JC/70a, 1:400, DAKO), factor VIII-related antigen (F8, Polyclonal, 1:1000, DAKO), c-kit (CD117, YR145, 1:600, DAKO), anaplastic lymphoma kinase (ALK, 5A4, 1:50, 1EICA), cathepsin K (3F9, 1:150, Abcam), synaptophysin (SYN, polyclonal, 1:200, DAKO), chromogranin (CGA, LK2H10, 1:1000, Roche), estrogen receptors (ER, 1D5, 1:150, DAKO), progesterone receptors (PR, PgR 636, 1:200, DAKO), Epstein-Barr virus (EBV, LMP-1, CS.1-4, DAKO), and Ki67 (MIB-1, 1:300, DAKO), CK7 (OV-TL 12/30, 1:200, DAKO), renal cell carcinoma (RCC, 66.4C2, 1:50, Invitrogen), P63 (4A4, 1:400, DAKO), and AMACR (P504s, 1:100, LabVision). Appropriate positive and negative controls were used in each case.

Results

Clinical features

Clinical and pathologic informations of the 6 cases of myopericytoma of the kideny are summarized in **Table 1**. There were 5 male and 1 female patients. The mean age at initial examination was 56 years (range, 33-70 years). Five patients were asymptomatic of the urinary tract, and their tumors were discovered incidentally on routine physical examination. One patient presented with right abdominal pain. Four of the tumors were located in the left kidney and 2 in the right kidney. Five patients were treated with radical nephrectomy and 1 with partial nephrectomy. Patients were followed up for 14 to 66 months (mean, 38.7 months), and no tumors recurred or metastasized.

Pathologic findings

Grossly, all the tumors were solitary masses with sizes ranging from 1.8 to 7.3 cm (mean, 4.4 cm). Five tumors were described as well-circumscribed (**Figure 1A**, **1B**), and 1 case (case no. 4) was showed as ill-defined in some areas. The cut surface was solid, rubbery and gray-tan, yellow or red-brown in color (**Figure 1B**). Hemorrhage was identified in all cases and was extensive in one tumor. Necrosis was not found in any case, nor was tumor invasion of the renal vein, perirenal fat, or renal pelvic fat.

Low-magnification microscopic examination showed 5 lesions had a well circumscribed margin and were encapsulated by a layer of a

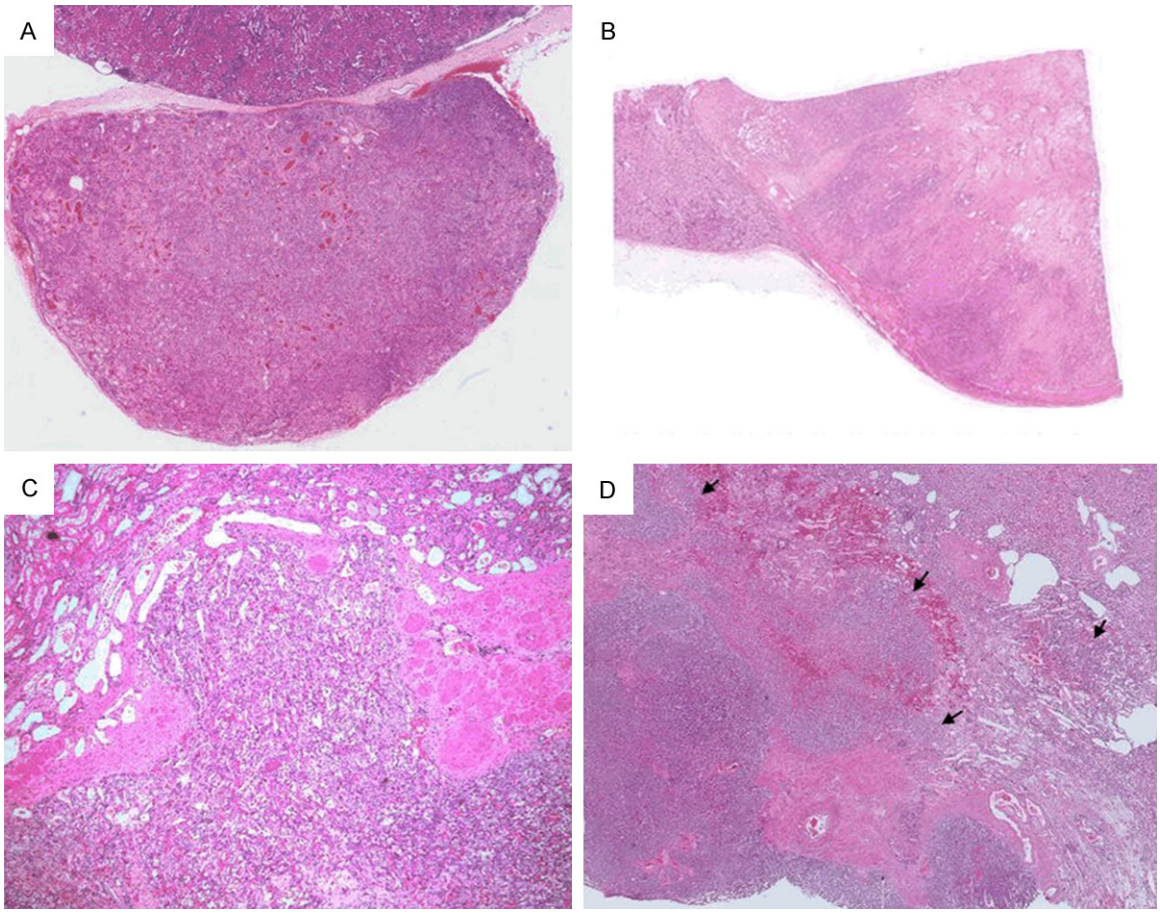

Figure 2. Low-magnification microscopic examination shows a well-defined margin encapsulated by a fibrous capsule in case no. 1 (A) and no. 6 (B), and the tumor of case no. 1 is bulging from the renal contour (A). Focal mushroom-like projections into the adjacent renal parenchyma (C) and multiple sites of involvement invasion into the adjacent renal parenchyma (D) are observed in case no. 4.

smooth muscle fibers or a fibrous capsule (**Figure 2A**, **2B**), but 1 tumor (case no. 4) had an infiltrative border with mushroom-like projection and multiple sites of involvement invasion into the adjacent renal parenchyma (**Figure 2C**, **2D**). Histologically, all neoplasms contained numerous thin-wall blood vessels and were composed of ovoid, spindled, and/or round myoid tumor cells with an abundant cytoplasm, evenly distributed chromatin, and spindled or round nuclei. Characteristically, a distinct perivascular and concentric growth of neoplastic cells showing catherine wheel features or a typical spinning off from the vessel walls was seen in all the six cases (**Figure 3A**, **3B**). However, a broad morphologic variation was also noted in the analyzed neoplasms. In 3 cases (case nos. 2, 4 and 6), areas demonstrated a glomangiopericytoma-type growth pattern, characterized by dilated branching thin-walled vessels surrounded by evenly distributed spindled neoplastic cells (**Figure 4A**, **4B**). Three lesions (case nos. 2, 3, and 6) demonstrated fibroma-like areas composed of bland myoid cells and set in a prominent collagenous stroma (**Figure 5A**). Two cases (case nos. 1 and 4) showed a more prominent fascicular or whorled arrangement of smooth muscle-like cells resembling angioleiomyoma in some areas (**Figure 5B**). Two tumors (case nos. 4 and 6) exhibited partial glomoid features with round/epithelioid tumor cells containing ample pale to lightly eosinophilic cytoplasm, distinct cell borders, prominent intracytoplasmic vacuoles, and round uniform nuclei (**Figure 5C**, **5D**). In addition, case nos. 2 and 3, similar to the morphologic features of myofibroma, were arranged around thin-walled vascular structures and no biphasic growth was present (**Figure 6A**), case no. 4 manifested numerous

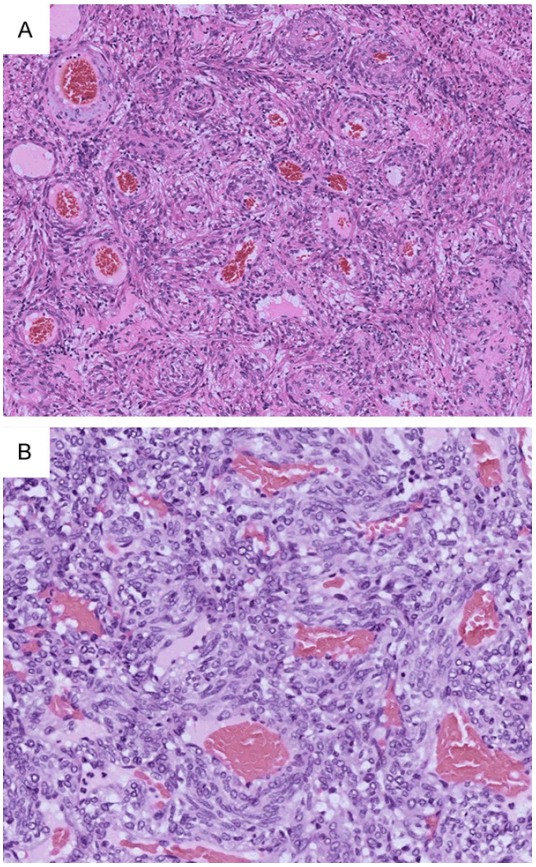

Figure 3. Histological examination of renal myopericytoma: numerous blood vessels surrounded concentrically by uniform spindle-shaped cells (A) and the presence of numerous thin-wall blood vessels accompanied by a perivascular proliferation of oval- to spindle-shaped cells (B) are seen.

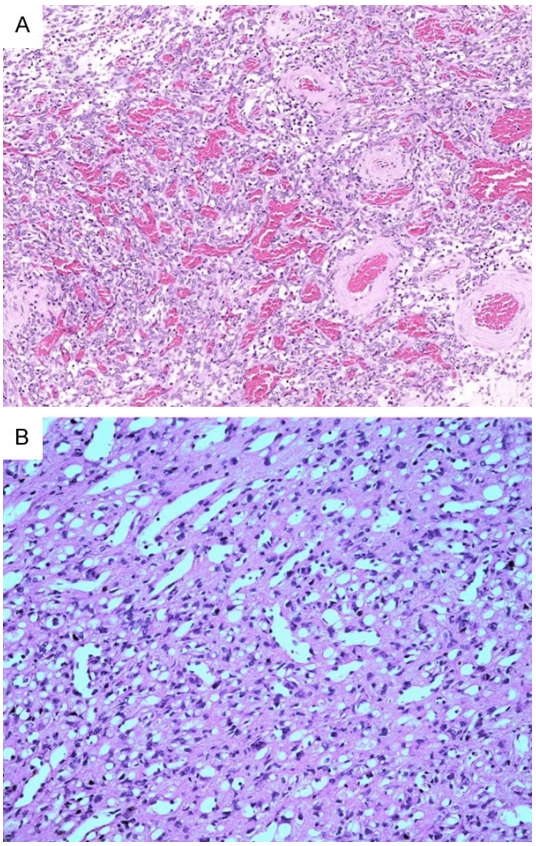

Figure 4. Hemangiopericytoma-like areas characterized by numerous gaping and branching, thin-walled vessels and surrounded concentrically by myoid tumor cells is found in case no. 4 (A) and no. 6 (B). Foci of hyalinization of vessel walls are also noted in case no. 4 (A).

dilated vascular channels with thin walls between septa composed of few neoplastic cells, somewhat simulating cavernous haemangioma (**Figure 6B**), and case no. 1 was composed of immature, ovoid, and plump spindled tumor cells showing a prominent perivascular growth pattern (**Figure 6C**). Mild nuclear atypia with large irregular and hyperchromatic nuclei was focally seen in case no. 4 (**Figures 5C**, **6D**), and symplastic-type atypia showing nuclear enlargement, pleomorphism, binucleation, and intranuclear cytoplasmic invaginations were present in case no. 6 (**Figures 5D**, **7A**). Vascular invasion was not evident in all 6 cases. Prominent degenerative stromal changes such as stromal fibrosis, hyalinization, mucoid, or edema were seen in all cases (**Figures 5B**, **7B**). Foci of hyalinization of thin-wall bloods were noted in case nos. 4 and 6 (**Figure 4A**). In addition, inflammatory infiltrate, consisting primarily of mature plasma cells and lymphocytes, was identified in case nos. 3 and 5 (**Figures 5A**, **7C**), and obviously remote hemorrhage was noted in case no. 5 (**Figure 7C**). Case no. 4 was characterized by an infiltrative growth and scattered mild cytologic atypia. These features, by current definition, would suggest malignant behavior. However, the rarity of such an entity in the kidney and the other benign morphology (no necrosis or mitotic activity) highlights the need for caution and a diagnosis in a continuum between benignity and malignancy, so we diagnosed the tumor as an infiltrating myopericytoma or myopericytoma of uncertain malignant potential. In addition, a coexisted papillary adenoma (measuring 0.25 cm in maximum diameter), lined by epithelioid cells with small dark nuclei and scant cytoplasm, was also detected in the periphery of myopericytoma in case no. 4 (**Figure 7B**, **7D**).

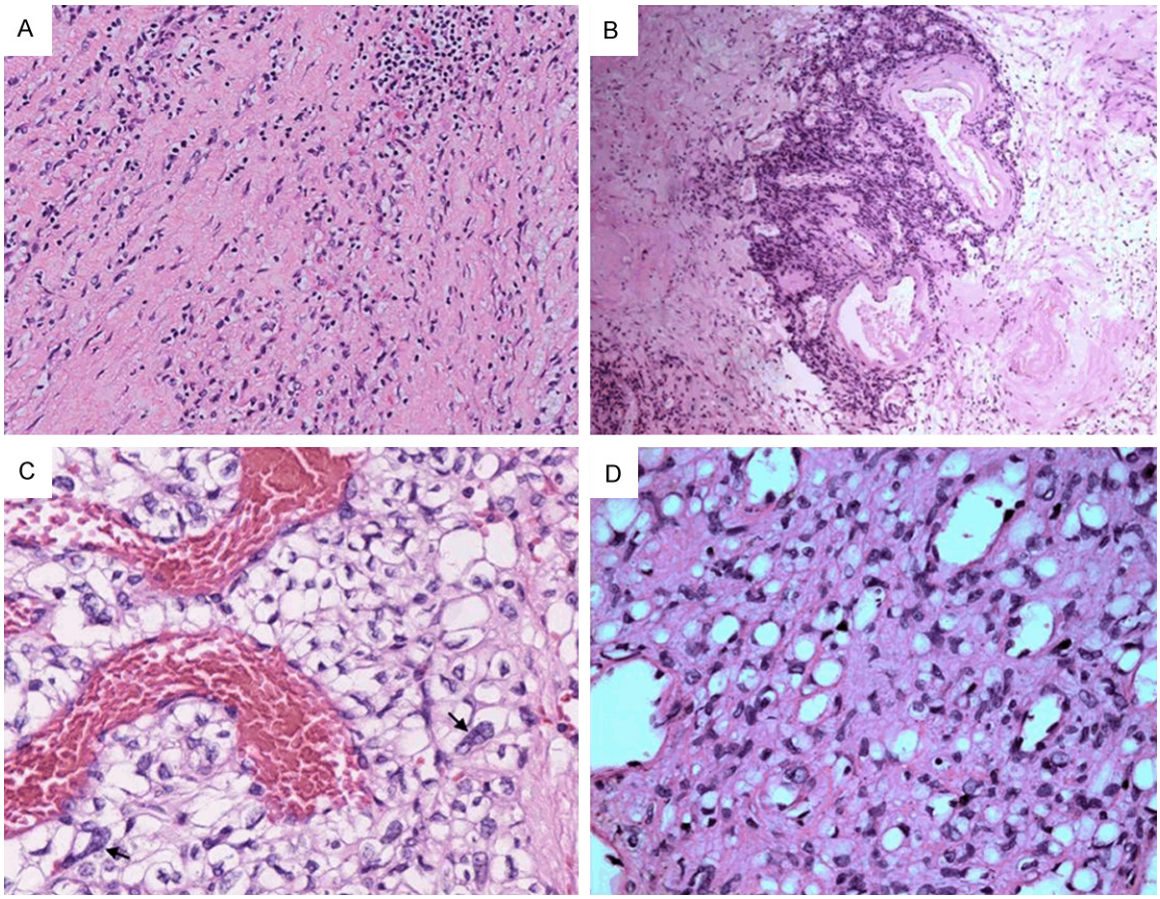

Figure 5. The fibroma-like areas composed of bland myoid cells and set in a prominent collagenous stroma, and inflammatory infiltrate are identified in case no. 3 (A). Angioleiomyoma-like areas composed predominantly of elongated spindled tumor cells and characterized by a concentric perivascular growth, and prominent degenerative stromal changes are noted in case no. 4 (B). The glomus-like cells with ample pale to lightly eosinophilic cytoplasm, distinct cell borders, and prominent intracytoplasmic vacuoles are observed in case no. 4 (C) and no. 6 (D). Large irregular and hyperchromatic nuclei are rarely found in case no. 4 (C) (arrows).

Immunohistochemical findings

The immunohistochemical results are summarized in **Table 1**. Tumor cells in all cases were diffusely and strongly positive for vimentin, SMA (**Figure 8A**) and caldesmon (**Figure 8B**). MSA (**Figure 8C**) was positive in the ovoid- to spindled-shaped cells of 6 cases, but negative in the epithelioid glomus-like cells of case no. 4. In contrast, CD34 was partially coexpressed in the glomus-like cells of case no. 4 but negative in the tumor cells of other 5 cases (**Figure 8D**). Desmin was patchy, weak positive in case no. 6 (**Figure 8E**). Ki67 proliferative index was <2%, <1%, <2%, 5%, <1%, and <1% in case nos.1, 2, 3, 4, 5, and 6, respectively. Antibodies to CD31 and F8 labeled the endothelial cells of the numerous variably-sized vascular channels but not the tumor cells. Keratin AE3/AE4, EMA, PAX-8, CD10, S100 protein, HMB-45, Melan-A, CD117, ALK, cathepsin K, SYN, CGA, ER, PR, and EBV were negative in all cases tested. In addition, papillary adenoma in case no. 4 was positive for keratin AE1/AE3, EMA, CK7 (**Figure 8F**), PAX-8, and AMACR, but negative for CD10, RCC, or P63.

Discussion

Myopericytoma is an uncommon but increasingly recognized mesenchymal neoplasm and is one of the members of the perivascular tumors family, which includes myofibroma, angioleiomyoma, glomus tumor, myopericytoma, and lesions with hybrid features (such as glomangiopericytoma) as defined in the latest edition of *World Health Organization (WHO)* classification of tumors of soft tissue and bone [1]. Histologically, these tumors are characterized by a concentric, perivascular arrangement

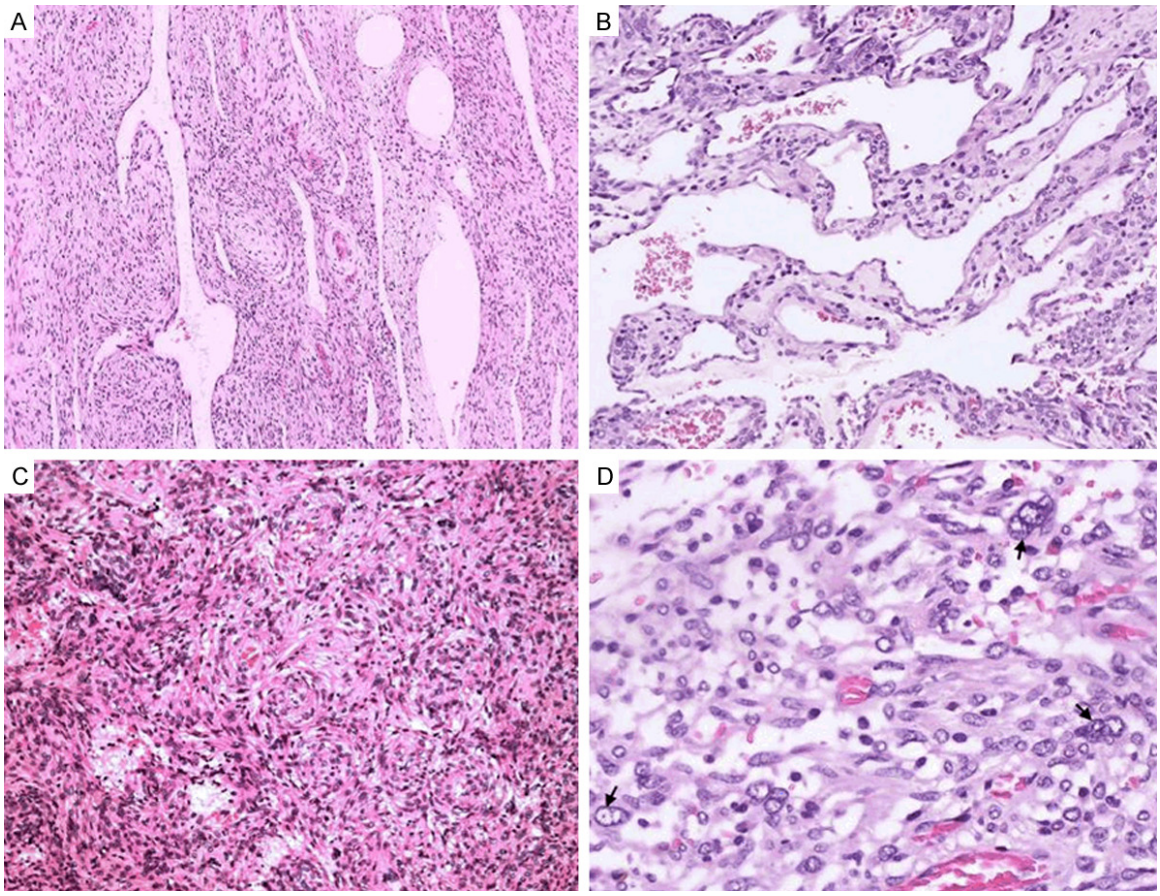

Figure 6. The lesion of myofibroma-like is arranged around thin-walled vascular structures and no biphasic growth is present in case no. 2 (A). The areas show numerous dilated vascular channels with thin walls between septa composed of few neoplastic cells, simulating cavernous haemangioma in case no. 4 (B). The area is composed of immature, ovoid, and plump spindled tumor cells showing a prominent perivascular growth in case no. 1 (C). Large irregular and hyperchromatic nuclei of ovoid to spindled tumor cells are seen in case no. 4 (D) (arrows).

of plump to spindle-shaped myoid cells with bland, round or ovoid nuclei. Myopericytomas can arise at any age, however, most are seen in adults with a male predominance [1-5]. Myopericytomas are typically found in the skin and superficial soft tissues, most commonly in the extremities or occasionally in the head and neck or trunk [1-3]. Rarely, these tumors have been reported to occur in other sites, including the oral or nasal region [6-8], the external auditory canal [8], thorax and lung [9, 10], heart [11], brain [12], and gastrointestinal tract [13]. Although myopericytoma generally is a benign, slow-growing, painless, and solitary tumor, multiple nodular lesions in a single or multiple anatomic locations have been occasionally described [5, 10]. The size of myopericytoma is usually less than 2 cm in superficial soft tissue but larger tumor size has been reported in the visceral locations [5, 15-17].

Myopericytoma arising in kidney is exceedingly rare with only 4 (1 case is our case no. 6 [18]) such cases have been reported in the English literature, the clinicopathological features of which are summarized in **Table 2** [15-18]. Our study of 6 cases is, to the best of our knowledge, the largest series reported in the literature until now. Clinically, these tumors occurred in middle to aged men (ages ranged from 33 to 70 years, median: 56 years, male to female ratio was 5:1), and the majority of patients (5 of 6 cases) were asymptomatic of the urinary tract and were discovered by examination of other unrelated reasons, these features are similar to the previous reported [15-17].

Grossly, the masses of our cases were solitary and solid, most of them were larger (mean, 4.4 cm) than those arising from superficial locations (usually <2.0 cm in diameter) [1]. The cut

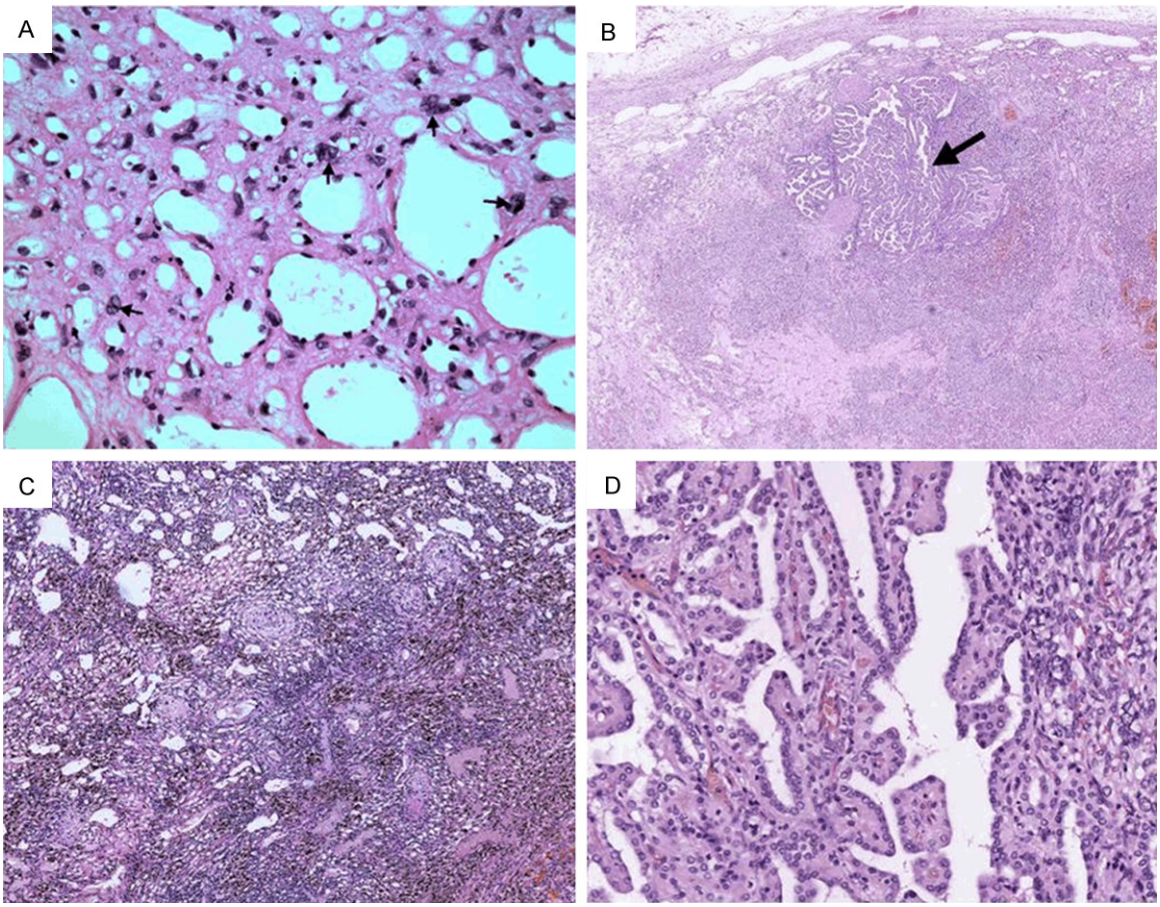

Figure 7. Symplastic-type atypia is easily seen in case no. 6 (A) (arrows). Papillary adenoma is shown in the periphery of renal myopericytoma (arrows), and the degenerative intervening stroma (left side) is seen in case no. 4 (B). Inflammatory infiltrate and obviously remote hemorrhage are identified in case no. 5 (C). Papillary adenoma is composed of epithelioid cells with small dark nuclei and scant cytoplasm in case no. 4 (D).

surfaces of these tumors were various in color. By low-power light microscope, although a well circumscribed margin was observed in most of our cases, similar to the previous 3 cases reported [15-17], however, an infiltrative border with mushroom-like projection and multiple sites of involvement invasion into the adjacent renal parenchyma was noted in 1 case. Histologically, renal myopericytoma showed a wide range of growth patterns. All tumors were composed of a concentric proliferation of oval- or spindle-shaped cells around numerous vascular channels at least in certain areas. Three cases contained numerous gaping and branching, thin-walled glomangiopericytoma-like blood vessels, and 2 cases composed partially of angioleiomyoma-like cells with elongated eosinophilic shape in some areas, similar to the case of Lau SK et al has reported [15]. In addition, 3 cases showed partial fibroma-like areas (characterized by a low cellularity and composed of bland myoid cells and set in a prominent collagenous stroma), 2 cases showed myofibroma-like areas (arranged around thin-walled vascular structures and no biphasic growth was present), 2 cases possessed glomoid-like features (made up of nests of small, uniform, round cells with well-defined cell membranes, and grouped non-concentrically around capillary sized vessels), and 1 case appeared at least focal immature cellular features, respectively. The morphologic features of the latter 4 have not been mentioned in the previous reports, which imply that our cases broaden the morphologic spectrum of renal myopericytoma. Nuclear atypia was focally observed in 2 of six cases but no necrosis or mitotic figures were identified.

Immunohistochemical analysis of 6 cases of renal myopericytoma showed that the tumors

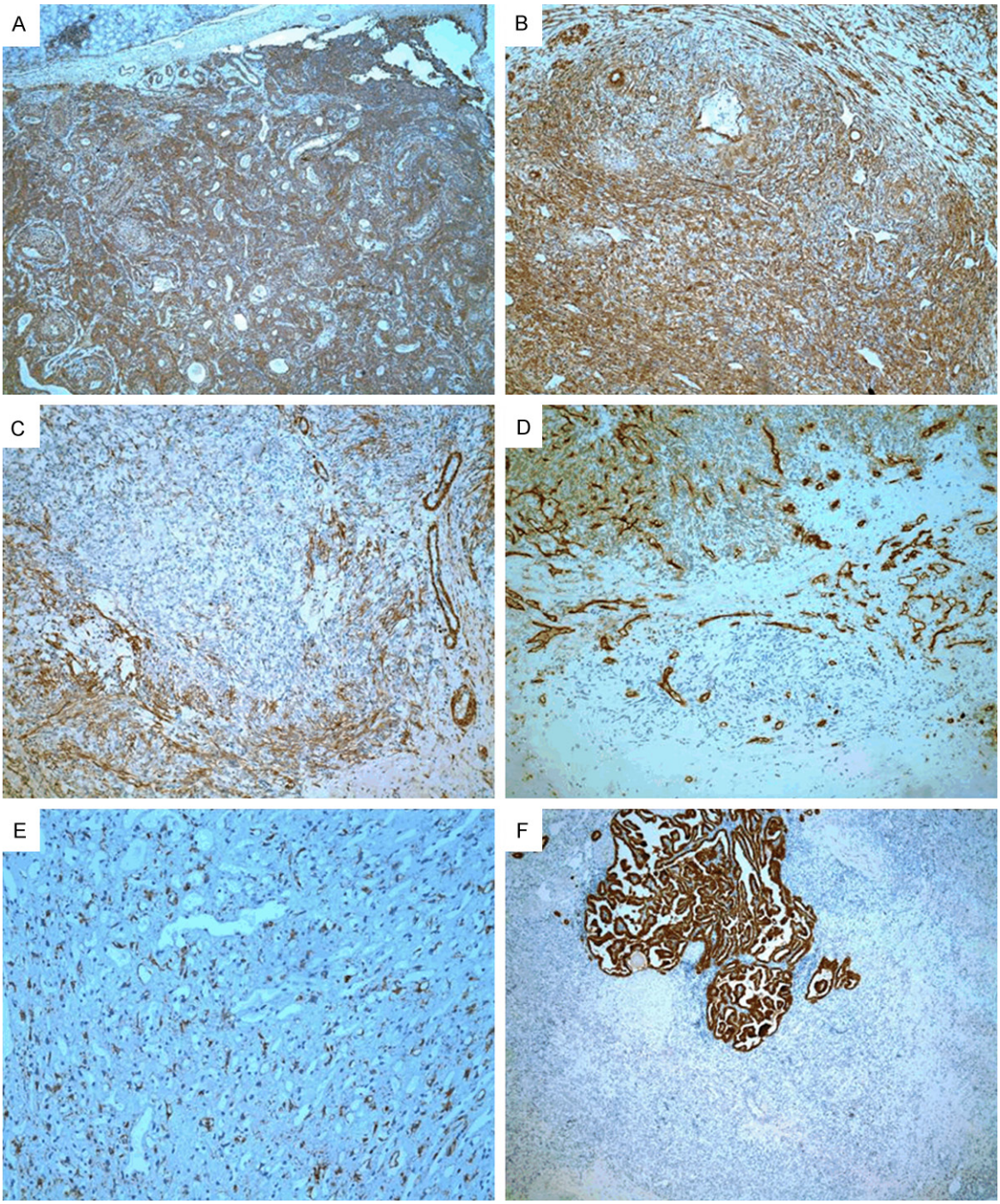

Figure 8. Immunohistochemical examination of renal myopericytoma: SMA (A) and caldesmon (B) are diffuse and strong positive in neoplastic cells in case no. 1 and no. 5. MSA is positive in the ovoid-to spindled-shaped cells, but negative in the glomus-like cells in case no. 4 (C). CD34 is partial positive in the glomus-like cells but negative in the ovoid-to spindled-shaped cells in case no. 4 (D). Desmin is patchy, weak positive in case no. 6 (E). CK7 is positive in epithelioid cells of papillary adenoma but negative in the cells of myopericytoma in case no. 4 (F).

were diffusely or predominantly positive for SMA, caldesmon, and MSA which are generally thought to be characteristic for myopericytoma. CD34 was partially reactive in the glomus tumor-like areas of 1 case, similar to the 2 cases that have been reported [15, 16], and desmin was only focal and weak positivity in 1 case, which was generally negative in myoperi-

Table 2. Clinicopathologic features of the previously reported 3 cases with renal myopericytoma

Case	Lau SK	Dhingra S	Zhang Z
Age/Sex	59/M	40/F	39/M
Clinical findings	respiratory tract symptoms, hemoptysis	pain on the left side of the abdomen and frequent urination	a painless and palpable mass in the left abdomen
Location	Left, upper pole	Left	Left, upper pole
Gross findings	3.0-cm,well circumscribed	3.8 × 3.0 × 3.0 cm, well-demarcated	20 × 13 × 10 cm, well-circumscribed
Histological findings	TI, AL, GP, PG	TI	TI
Cellular ple-omorphism	no	no	rarely found
MI	inconspicuous	no	rarely found
Necrosis	no	no	some areas
VI	no	unknown	unknown
Stroma	edematous, hyalinized	myxomatous, loose, edematous	unknown
Immunhis tochemical results	SMA+, CD34+, BCL2+, collagen IV+, CK-, EMA-, des-, S100-, HMB-45-, Melan-A-, CD31-, CGA-, SYN-	SMM-HC+, SMA+, MSA+, CD34 partial+, S-100-, HMB-45-, Melan-A-, EBV-, Ki-67+ <5%	SMA+, CD10+, CD34-, BCL2-, CK-, CD99-, HMB-45-, S-100-, Melan-A-, Ki-67+ <1%
Treatment	PN	PN	RN
Coexistence	no	no	no
FU (mo)	ANED (8)	ANED (24)	ANED (20)

F indicates female; M, male; TI, the presence of numerous vessels accompanied by a perivascular proliferation of plump oval to spindle-shaped cells; AL, angioleiomyoma appearance; GP, glomangiopericytomatous appearance; PG, paraganglioma appearance; MI, mitotic figures; VI, vascular invasion; PN, partial nephrectomy; RN, radical nephrectomy; FU, follow-up; ANED, no evidence of disease.

cytoma. Ki67 proliferation index was less than 2% in 5 cases but was approximately 5% in 1 case of the infiltrative myopericytoma. Sex hormone receptor (ER and PR) and EBV were negative in all 6 cases, which is in consistent with the result of rare cases reported [13].

Mesenchymal tumors of the kidney are greatly outnumbered by epithelial neoplasms, such as renal cell carcinomas. Therefore, diagnosis of mesenchymal neoplasms occurring in the kidney often poses a differential diagnostic challenge [19, 20]. In the tumors in this study, discrimination from an epithelial neoplasm was largely not a dilemma due to the prominent perivascular myoid components. However, those exhibit glomus tumor-like epithelioid morphology and nuclear atypia the possibility of an epithelial neoplasm might be considered. Fortunately, the immunohistochemical profiles of these cells (negative for epthelial markers) readily facilitate resolving this challenge.

Other differential diagnoses for renal myopericytomas include other members of the perivascular tumors. Glomus tumor is an uncommon, benign perivascular neoplasm that rarely occurs in the kidney [21, 22] and renal pelvis [23]. It is composed of a mixture of glomus cells, blood vessels and smooth muscle cells in various proportions. Depending on the prevalent component, tumors have been subdivided into solid glomus tumor, glomangioma, and glomangiomyoma. The solid subtype is the most common, characterized by nests of small, cuboidal to rounded epithelioid cells surrounding small blood vessels [3]. The hemangiopericytoma-like vasculature and concentric distribution of spindle-shaped tumor cells around vessels characteristic of myopericytoma are typically not present in glomus tumor; however, like the 2 tumors reported here, cases of myopericytoma with a cellular glomus cell-like component have been reported [1, 5, 16]. These hybrid cases have sometimes been designated as “glomangiopericytoma” [1]. Since both glomus tumor and myopericytoma exhibit similar immunophenotypic features (SMA+, caldesmon +, desmin-, CD34-), the distinction between myopericytoma with a glomus tumor-like component and a glomus tumor may be somewhat arbitrary. Another member of the perivascular myoid cell tumor group is angioleiomyoma, which is likewise composed of well-differen tiated smooth muscle cells arranged around many intervening vascular channels and shows

SMA, caldesmon, and desmin coexpression in the neoplasic cells. Angioleiomyomas have been classified into three histologic variants based on the vascular component: solid, venous, and cavernous [1]. Although 2 cases in our study contained angioleiomyoma-like appearances, a prominent concentric perivascular arrangement of neoplastic cells and negative for desmin were against the diagnosis of classical angioleiomyoma. Myofibroma is another member of the category of perivascular myoid cell tumors, histologically characterized by a biphasic growth of immature-appearing, plump spindled tumor cells associated with numerous thin-walled, branching solitary fibrous tumor-like vessels associated with more mature, spindled tumor cells with abundant eosinophilic cytoplasm, arranged in bundles and whorls. In addition, the tumor cells of myofibroma are positive for SMA but are usually negative for caldesmon [1, 2, 5]. Our 2 cases with myofibroma-like features lacked the biphasic growth pattern and immunoreactivity for caldesmon, which are helpful features in the distinction of myopericytoma from myofibroma. Indeed, in the latest WHO classification of tumors of soft tissue, myopericytoma and myofibroma are listed under the same heading and the latter appears as a histologic variant of the former [1]. Although glomus tumor, angioleiomyoma, myofibroma, and myopericytoma are currently classified as distinct entities, the presence of hybrid cases with overlapping morphological and immunohistochemical features emphasizes the existence of a continuous spectrum of perivascular myoid tumors [1]. Given the close relationship of these lesions, it has been suggested that a tumor be designated as myopericytoma or other members of the perivascular tumors depending on the predominant growth pattern.

Also entered into the differential diagnosis of renal perivascular myoid cell tumors is hemangioma. In the urinary tract, hemangiomas are uncommon and include capillary and more commonly cavernous types [19, 20]. Anastomosing hemangioma, a recently described, unusual variant of capillary hemangioma, seems to be unique to the genitourinary system, with a particular proclivity for the kidney [24, 25]. This tumor is composed of variably sized, anastomosing blood vessels lined by a single layer of hobnail-shaped endothelial cells, set in a framework of fibrous stromal tissue. Although this supporting stroma may contain myoid-appearing spindle-shaped cells and show immunoreactivity for SMA, this pattern is typically not prominent, distinguishing anastomosing hemangioma from myopericytoma.

Angiomyolipoma is the prototypical member of the perivascular epithelioid cell tumor (PEComa) family and represents the most common mesenchymal tumor of the kidney [20]. Therefore angiomyolipoma, particularly when it adopts a predominant appearance of epithelioid and spindle-shaped myoid cells with a prominent vascular component, is likely to enter into the differential diagnosis of myopericytomas, especially in the kidney. Adequate sampling and careful examination usually reveals the classic triphasic morphology of angiomyolipoma (thick-walled vessels, smooth muscle, and mature fat). Histologically, the closely arranged, narrow thin-walled vasculature accompanied by concentric, perivascular arrangement of tumor cells in myopericytoma contrasts somewhat to the less prominent, branching, and frequently thick-walled vessels surrounded by radiating, perivascular distribution of epithelioid cells of PEComa. By immunohistochemistry, PEComa contrasts more sharply to myopericytoma by its coexpression of melanocytic and smooth muscle cell markers. In this study, we also found lack of reactivity for cathepsin K, a recently recognized marker of the PEComa family of tumors [26], to yield negative reactivity in these neoplasms, further supporting this discrimination.

Another common mesenchymal neoplasm with a hemangiopericytomatous vascular pattern is solitary fibrous tumor, which can rarely arise in the kidney [27]. In contrast to myopericytoma, solitary fibrous tumor is more cellular, has nondescript ovoid or spindle cells with variable fibrosis, and lacks the concentric perivascular growth of tumor cells; it typically expresses CD34, bcl-2, and CD99, with negative or only focal reactivity for SMA. In addition, 3 neoplasms in this series showed fibroma-like areas composed of bland myoid cells growing and set in a prominent collagenous stroma, but a perivascular arrangement of tumor cells and immunoreactivity for SMA, caldesmon, and MSA different from other types of hypocellular fibroma (i.e., sclerotic fibroma).

Inflammatory infiltrate consisting of plasma cells and lymphocytes was noted in our 2 cases, which may raise the differential diagnostic possibility of inflammatory myofibroblas-

tic tumor, for which the kidney is a relatively common site [28]. Inflammatory myofibroblastic tumor is characteristically composed of a fascicular or storiform arrangement of spindle-shaped cells, lacking a perivascular arrangement. It also differs immunohistochemically from myopericytoma in its expression of SMA, ALK, and less commonly desmin but not caldesmon.

A final consideration in the differential diagnosis of myopericytoma in the kidney is juxtaglomerular cell tumor, a rare renal cortical neoplasm often affecting young adults [29]. Depending on clinical findings including blood pressure and serum potassium level, clinical classification into typical, atypical, and non-functioning types of juxtaglomerular cell tumor has been proposed. These lesions have characteristic ultrastructural features, including numerous membrane-bound, sharply angulated rhomboid and polygonal granules that are immunoreactive with antibodies to renin [29]. Juxtaglomerular cell tumor can demonstrate a broad spectrum of morphology, including a hemangiopericytoma-like growth pattern, leading to overlap with myopericytoma. In fact, it has been suggested that juxtaglomerular cell tumor be considered in the differential diagnosis of any renal tumor with epithelioid cells but a negative cytokeratin immunostain [29]. In this scenario, further immunohistochemical evaluation can aid in distinguishing these two lesions; in contrast to myopericytoma, juxtaglomerular cell tumor usually shows positive reaction to CD117 and CD34 in addition to renin [29, 30].

Myopericytomas are generally considered benign with an indolent clinical course, and few reports have described malignant myopericytomas arising in both superficial soft tissue and visceral locations, with only 8 bonafide cases described in the literature [5, 11, 13, 14]. They are composed of uniform oval- to spindle-shaped myoid tumor cells that demonstrate a perivascular, concentric growth (resembling what is seen in benign myopericytoma), but with features of malignancy including deep-seated location, a brisk mitotic rate, cytologic and nuclear atypia, necrosis, an infiltrative growth pattern, and aggressive clinical behavior [1, 14]. Out of the 8 reported patients, at least 1 had recurrent disease, 6 patients developed metastases, and 3 died of disease within 1 year. The majority of tumors arose in the extremities-on the arm, thigh, lower leg, and foot, and the superior mediastinum, the neck, periampullary region, and the left atrium was involved in 1 case, respectively. To date, there are no malignant myopericytomas has been reported in the kidney. Although 1 tumor in this study has an infiltrative growth pattern with scattered mild nuclear atypia and relative high Ki67 proliferation index (>5%), it shows the other benign morphology (no necrosis or mitotic activity) and has no evidence of recurrence or metastases by follow-up of 16 months. These findings suggest that the most appropriate term for diagnosis of this case could be an infiltrating myopericytoma or an uncertain malignant potential myopericytoma, and it broadens the growth pattern or biological behavior of renal myopericytoma.

Interestingly, a small papillary adenoma is observed in the periphery of the infiltrating myopericytoma in this series. Although the presence of minute papillary adenoma adjacent to the myopericytomas raises a dilemma regarding its nature (reactive, preneoplastic, or neoplastic) and pathogenesis, it has been postulated that papillary adenoma may progress to papillary renal cell carcinoma because of high coexistence, histopathological similarity, and similar genetic alterations between the two entities [31], and this is the first report of an infiltrating myopericytoma coexisted with another epithelial renal tumor arising in the same kidney.

There is no standard treatment for renal myopericytoma with particularly rare cases, and complete surgical excision of the lesion may be the only potentially curative treatment. 6 of 9 (including our cases and 3 previous reported) patients had radical nephrectomy [17], and the other 3 had partial nephrectomy [15, 16, 18]. None of them received radiotherapy and chemotherapy. All 9 patients were no evidence of disease (ANED) by follow-up ranging from 8 months to 66 months (median: 24 months; mean: 32 months). It seems feasible that a partial nephrectomy is performed for renal myopericytomas <4 cm in size, but larger (>4 cm) or local infiltrating tumors may be treated by radical surgery. Chemotherapy or radiation therapy is unnecessary, although the timing and frequency of follow-up is essential.

In summary, despite overlapping morphologic features and immunophenotype to myopericytoma of skin and soft tissues, we describe the largest series of renal myopericytomas, characterized by a broad morphologic spectrum of concentrically, perivascularly growth myoid tumor cells which stain with SMA, caldesmon, and MSA but usually are negative for desmin. Most cases of renal myopericytoma behave in a benign fashion, but infiltrating tumor is also reported in this series. Our findings broaden the morphologic spectrum of renal myopericytoma and expand the biological behavior of this entity. There is no standard treatment for renal myopericytoma and complete surgical excision of the lesion seems to be the only potentially curative treatment. As renal myopericytoma is an extremely unusual entity and the currently reported cases may not be sufficient to allow the clinical outcome to be fully evaluated, the timing and frequency of follow-up is essential.

Disclosure of conflict of interest

None.

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