Case Report Renal myopericytoma with nephrotic syndrome: report of a case and review of literature

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Abstract: Objectives: With its other counterparts like myofibroma, angioleiomyoma and glomus tumor, myopericytoma is a benign subtype of pericytic tumors and only 4 cases are involved in kidney in literature. Methods: Standard pathological examination (including macroscopical and histopathological analysis) and immunohistochemistry of sections were performed. Results: We described a 19-year-old woman, who discovered a renal mass in her 24th gestational week with nephrotic syndrome. Radical right nephrectomy was done after careful examination and induced labor. Microscopically, the tumor was composed of numerous slit-like, thin-walled vessels, surrounded by spindle-shape or polygonal neoplastic cells in a strip-like arrangement. Immunohistochemical staining revealed positive expression in actin, CD10 and bcl-2, negative in Vimentin, Melan-A, HMB-45, CD34, pan-cytokeratin, HMWcytokeratin, Desmin, E-cadherin, et al.; Ki-67 index showed a low proliferative rate, thus the diagnosis of myopericytoma (MPC) was established. This is an uncommon finding of MPC in morphology. After a follow-up of 8 months, the patient showed no evidence of tumor recurrence or metastasis. We also review other reports of renal myopericytoma. Conclusions: Our case is the fifth case of renal myopericytoma according to the reported literature. At the same time, our case has uncommon pathological morphology.

Keywords: Myopericytoma, kidney, nephrotic syndrome, histology, immunohistochemistry

Introduction

Myopericytoma, as well as myofibroma, angioleiomyoma and glomus tumor, falls into the categories of pericytic (perivascular) tumors and shares similar histology features of its counterparts. It usually presents with a slowly growing asymptomatic mass involving dermal or subcutaneous tissue in extremity, neck, trunk or oral cavity. Grossly, it is a well-demarcated mass with even texture. Typical pathological findings are narrowed spaced vessels surrounded by uniformed, concentrically arranged oval to spindle-shaped neoplastic cells .Some cases show other pattern like fascicular or whorled arrangement, glomus-celllike features with cuboidal shape that resemble its other counterpart. The cells usually widely express SMA and h-caldesmon, and less often CD34 and desmin in immunohistochemical staining [1].

Renal myopericytoma is extremely rare compared with elsewhere of the body, and manifests similar histological patterns as those in other sites. However, some reports elicited variant morphology in renal involvement [2]. Here, we describe a case with morphological features that differed from its classical pattern.

Materials and methods

The resected samples of the tumor were fixed in 10% buffered formalin and embedded in paraffin. They were sectioned in 4-µm slices and stained with hematoxylin and eosin.

Standard immunohistochemistry of sections from paraffin-embedded tissue blocks were conducted. Briefly, the sections were deparaffinized in xylene and rehydrated. The sections were then treated with 3% hydrogen peroxide to exhaust endogenous peroxidase activity. The antigens were retrieved in 0.01 M sodium citrate buffer (pH 6.0) using a microwave oven. The sections were incubated using a primary antibody. The negative control was used by PBS instead of the primary antibody. Then, the sec-



Figure 1. Macroscopic feature. The oval and solitary mass measuring 7*6*4 cm was in the upper side of kidney. It was well-demarcated, solid, firm and tan-white or grey-red.

tions were incubated with EnVision-HRP secondary antibody (Dako, Carpinteria, CA). Last, the tissue slides were treated with a nonbiotin horseradish peroxidase detection system according to the manufacturer's instructions.

Immunohistochemical study was performed using the following primary antibodies: pancytokeratin (RTU, Dako), HMW-cytokeratin (RTU, Dako), Vimentin (RTU, Dako), CD10 (RTU, Dako), bcl-2 (RTU, Dako), CD31 (RTU, Dako), CD34 (RTU, Dako), Ki-67 (RTU, Dako), Melan-A (RTU, Dako), HMB-45 (RTU, Dako), S-100 (RTU, Dako), actin (RTU, Dako), Desmin (RTU, Dako), CD99 (RTU, Dako), CD117 (RTU, Dako), MyoD1 (RTU, Dako), E-cadherin (RTU, Dako), CK7 (RTU, Dako), CD68 (RTU, Dako), CD56 (RTU, Dako), Inhibin-a (RTU, Dako), Syn (RTU, Dako), D2-40 (RTU, Dako) and CgA (RTU, Dako).

Results

Clinical features of patients

A 19-year-old woman was presented to our hospital, with renal mass of the right kidney. In her 20+ gestational weeks, she felt flank pain of the right side, without hematuria or weight loss. Abdominal computed tomography in the local hospital revealed a well-demarcated mass in the upper side of right kidney. The mass was rich in blood flow and combined with multiple calcifications, without invasion in renal vein or inferior vena cava. Thus the suspicion of renal cell carcinoma or angiomyolipoma was made. After induced labor in her 24th gestational week (no more detailed medicine information can be collected) in local hospital, the patient was transferred to our hospital for further management of the renal mass.

Systemic laboratory examination was completed on admission. Urine test revealed protein+++, serum albumin was 27.5 g/L (normal limit 35 g~50 g/L), suggestive of nephrotic syndrome. After symptomatic supportive treatment, radical right nephrectomy was performed.

Macroscopical and histopathological analysis

The gross specimen showed a 14*6*6 cm radical nephrectomy kidney with a oval and solitary mass in the upper side which was well-demarcated and measuring 7*6*4 cm. On cut section, the mass was solid and firm, tan-white or grey-red (Figure 1). Foci of hemorrhage were identified, but necrosis was not found. Light microscopy showed a clear margin between tumor and the peripheral normal tissue (Figure 2A). The tumor was composed of large numbers of narrow spaced or slit-like thin-walled vessels, surrounded by sheets or cords of oval or polygonal neoplastic cells. Unlike a typical myopericytoma, the tumor cells did not grow in characteristically concentric pattern around the vessels, but rather, in a reticular pattern, with inter anastomosing configuration (Figure 2B). The cells showed mild atypia, with oval to round contour and rich in eosinophilic or bland cytoplasm. The nuclear was ovoid or round, some with prominent nucleoli. Mitosis was occasionally found (Figure 2C). In the peripheral area, thick-walled vessels could also be found. In addition, the stroma of the tumor was composed of large amount of intervening coarse and short collagen (Figure 2B). No fat component could be identified after widely sampling of the tumor. Other part of the kidney did not manifest with significant pathological changes.

Immunophenotypic analysis

In immunohistochemistry (IHC), the neoplastic cells showed positive expression in actin, CD10







and bcl-2; with a very low Ki-67 proliferative index (**Figure 3A-D**). CD34 and CD31 outlined the slit-like vessels. Other IHC stain as Melan-A, HMB-45, CD34, Vimentin, CD31, S-100, pancytokeratin, HMW-cytokeratin, Desmin, CD99, MyoD1, CD117, E-cadherin, CK7, CD68, CD56, Inhibin-a, Syn, D2-40 and CgA were all negative (**Figure 3E-G**). Thus the diagnosis of myopericytoma was established. In the 8 months followup after surgery, the patient was alive without tumor recurrence. She did not take a urine test after discharge, but claimed to have no puffiness in her eyelids and extremities

Discussion

Myopericytoma was first described in 1996 by Requena L. as an alternative form of adult solitary myofibroma and showed pericytic features in IHC [3]. The nomenclature of "myopericytoma" was elicited by Granter et al. in 1998 [4]. With a histologic pattern as narrow-spaced or stag-horn thin-walled vessels surrounded by oval to spindle cells, myopericytoma was once coined into hemangiopericytoma (HPC) [5]. However, the term "hemangiopericytoma" actually comprises of heterogeneous entities and could be divided into three categories that either displays the hemangiopericytomatous features or a small subset representative of true hemangiopericytoma. And these three categories include: 1. Tumors with hemangiopericytomatous growing pattern, e.g. synovial sarcoma, mesenchymal chondrosarcoma etc.; 2. Tumors with pericytic or myoid differentiation from modified smooth muscle cells, .e.g. myopericytoma, myofibroma, angioleiomyoma, and glomus tumor and 3. Solitary fibrous tumor group(SFT), which contains SFT, lipomatous HPC, giant cell angiofibroma, sinonasal hemangiopericytoma, myofibromatosis/infantile hemangiopericytoma [6]. Granter further grouped the second type into: infantile-type myofibromatosis; tumors featuring between glomus tumor and hemangiopericytoma; and tumors composed of cells with myoid differentiation in concentric perivascular pattern, which included myopericytoma. And the morphology among these groups overlapped to each other. MPC might represent the "real/true" HPCs based on its origin [5, 6].



The 2013 WHO classification of soft tissue and bone had categorized pericytic neoplasm into

glomus tumor (glomus tumor, glomangiomatosis and malignant glomus tumor), myopericyto-

Author	Gender	Age	Clinical manefestation	Treatment	Follow-up
Lau SK [14]/2010	f	59	painless and palpable mass	partial nephrectomy	8 month alive
Dhingra S [2]/2012	m	40	hypertension for 10 year	partial nephrectomy	24 month alive
Zhang Z [15]/2014	m	39	upper respiratory tract symptoms and hemoptysis.	radical nephrectomy	20 month alive
Zhao M [16]/2014	f	59	flank pain on the right side	left radical nephrectomy	14 month alive
Present	f	19	pain on the left side of the abdomen and frequent urination	radical nephrectomy	8 month alive

 Table 1A. Clinical information of 5 cases

ma (including myofibroma) and angiomyoleioma. Microscopically, myopericytomas are characteristically composed of oval to spindle cells around vessels in a multilayered, concentric growing pattern, with varied cellular density. The numbers and sizes of the vessels are also variable from thick-walled to narrow thin-walled formation. Foci of myofibroma-like or angioleiomyoma-like changes could also be observed, in which cells arranged in fascular/whorled pattern or resembled glomus cells with cuboidal outlines and clear borders. The stroma is either myxoid or hyalined. In addition, some MPCs might present with unusual morphology pattern. Recently, Li J et al. reported a hepatic myopericytoma with rhabdoid-like cellular changes with bi-nucleation, multinucleation, eosinophillic cytoplasm in a sheet-like arrangement, in addition with typical areas of MPC morphology. Immunohistochemistry studies showed similar expression of these two different cell groups, indicating that MPCs might showed variant growth pattern [7]. Sadhna D. Also discovered glomus tumor-like pattern in a case of renal MPC [2]. These findings expanded the histological continuum of MPC. Similar with other perivascular tumors, myopericytoma express muscle-specific actin (HHF-35), smooth muscle actin (SMA), muscle-specific actin, h-caldesmon, and tropomyosin and less often desmin in IHC, while CD34 is often negative [1, 8]. Cytogenetic and molecular analyses had revealed abnormal karyotype, gene translocations and corresponding fusion genes in MPCs, such as [t(7;12)(p22:q13)]: ACTB-GLI1 fusion transcript, t(4;21)(q31;q22): HHIP, and t(4;5) (p14;q33): PDGFRB , associated with Heghog signaling regulation [9, 10]. In our present case, the morphology differed from typical MPCs with a inter anastamosing and strip-like growth pattern, and the diagnosis of MPC was confirmed through IHC application. This indicated that MPCs might show different histological changes with typical IHC profiles.

Myopericytoma are noduar or lobular lesions, most commonly found in subcutaneous area of

extremities, neck, trunk and oral cavity, with a single lesion no more than 2 cm [11]. Unusual sites or multicentric lesion were occasionally reported, including liver, lung, heart, gastrointestine, intravascular location, urinary tract and kidney [7, 12, 13]. Tumors in uncommon sites were sometimes larger, containing clear margins with peripheral tissue. To date, only 4 cases of renal myopericytoma were reported in literature. We summarized the features of these cases and compared with our present case (Table 1A and 1B) [2, 14-16]. The age arranged from 19 to 59 years old, and most of the clinical manifestation was related with tumor compression. Grossly, all tumors were well demarcated, between 3 cm to 20 cm, without necrosis or hemorrhage. The morphological changes and IHC expressions were characteristic as those in elsewhere, with concentric growing pattern as a main growth pattern, or a hybrid of other histological presentation. All cases showed positive findings in SMA/MSA, or actin, only one case showed CD34 expression. Surgery were performed in all cases as the only treatment, no adjuvant therapy was applied after surgery. Our present case shared some similar features with the other four cases in kidney. However, the histological pattern was different from the onion skin-like pattern, and it displayed sheets or cords-like pattern. So IHC staining was applied to investigate the expression pattern and make out differentiated diagnosis. A diffuse positivity of actin revealed a smooth muscle cell differentiation, thus the diagnosis of MPC was confirmed.

Most of myopericytoma present with benign behavior, with a slowly growth, and favorable clinical outcome after resection. Malignant cases were uncommon, with morphological atypia, prominent mitotic figure, necrosis and invasion. As well, clinical aggression were featured by recurrence, distal metastasis and death [11, 12]. Surgery excision was adopted as optimal treatment of MPCs. For the malignant forms, adjuvant therapy as radiation and chemotherapy were applied after operation,

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Table 1B. Pathological features of 5 cases

Author		Marahalatti	IHC and molecular detection		
	Size (cms)	worphology	Positive	Negative	
Lau SK [14]/2010	3.0	Small- to medium-sized thin-walled vessels or dilated vessels surrounded by oval to spindle- shaped cells in a concentric or glomangiopericytoma-like manner, with bland cytoplasm, mild nuclear and prominent nucleoli, some focus resembling paraganglioma. Cellular atypia and mitotic figures were rare. No evidence of necrosis or invasion. The stroma wasedematous and hyalinized.	MSA, SMA, CD34, bcl-2	Keratin, HMB-45, Melan-A, S-100, EMA, des- min, CD31, chromogranin, Syn	
Dhingra S [2]/2012	3.8*3.0*3.0	Small- to medium-sized blood vessels surrounded by ovoid to bipolar spindle cells showing smooth muscle differentiation, or clusters of epithelioid glomoid cells in a concentrica pattern; The stroma was edematous/myxomatous and hyalinized. Cellular atypia and mitotic figures were rare. Intervening stroma was loose and/edematous.	Vimentin, SMA, SMA(H), MSA	HMB-45, S100, desmin, Mart 1, Epstein-Barr virus (EBV); Chromogenic in situ hybridization for Epstein-Barr virus–encoded RNA (EBER)	
Zhang Z [15]/2014	20*13*10	Numerous variably-sized blood vessels cuffed by nests or fascicles of spindle-shaped myoid cells in a concentric pattern. Nuclear atypia and mitotic figures were rare.	SMA, CD10	Cytokeratin, CD34, HMB-45, S-100, desmin, bcl-2, CD99	
Zhao M [16]/2014	3.6*2.8*2.7	Peripheral area: numerous small, anastomosing thin-walled vascular surrounded by denselly arranged cells that were glomus-like, plump rich in cytoplasm, with prominent intracytoplas- mic vacuoles and clear cell borders, some resembling lipoblasts or signet ring cells. Nuclear atypia were present, while mitotic figure rare. Central area: staghorn and dilated vessels concentrically surrounded by elongated large cells within edematous and hyalinized stroma, resembling smooth muscle cells.	SMA, desmin, caldesmon, vimentin, calponin	Cytokeratin, cathespin K, CD34, HMB-45, Melan-A, S-100, CD31, EMA, C-kit, NSE, CgA, Cyn, CD10, ER, PR, EBER (in situ hybridization)	
Present	7*6*4	Narrow spaced or slit-like thin-walled vessels, surrounded by sheets or cords of oval or polygonal neoplastic cells in a reticular pattern, with inter anastomosing configuration. The cells showed mild atypia, plump contour, rich in eosinophillic or bland cytoplasm. The nuclear was ovoid or round, some with prominent nucleoli. Mitosis were occasionally found. In some areas, thick-walled vessels could also be found. In addition, the stroma of the tumor was composed of large amount of intervening coarse and short collagen.	Actin, CD10, bcl-2	Pan-cytokeratin, CD34, Melan-A, HMB-45, S-100, CK-HMW, Vimentin, CD31, Desmin, CD99, MyoD1, CD117, E-cadherin, CK7, CD68, CD56, Inhibin-a, Syn, D2-40, CgA	

however, due to the limited incidence, its effect needed further discussion [17]. According to the reports of renal myopericytoma cases, all patients were alive with no recurrence or metastasis just as our patient's follow-up.

In particular, our case also presented with nephrotic syndrome (proteinuria and hypoproteinemia). Nephrotic syndrome was an infrequent paraneoplastic syndrome in malignant systemic solid tumor from respiratory system, digestive system, reproductive system or in rare circumstances, hematopoietic system [18, 19]. In kidney, renal cell carcinoma was the most common malignancies with concurrent nephrotic syndrome. Pathological changes include minimal change disease, focal segmental sclerosis, and membranous nephropathy [20, 21]. Spontaneous remission of nephrotic syndrome may appear after the resection of tumor [22-24]. The pathogenesis of neoplasm related nephrotic syndrome was unknown. Hypothesis were concerned with type III hypersensitivity caused by immune complex deposition in glomeruli, which were composed of tumor-specific antigen and its antibodies [23]. Other possible mechanism included impaired T-cell function, abnormal production of cytokines and NF-kB overexpression [19]. To our knowledge, this is the first case of renal myopericytoma accompanied with nephrotic syndrome. However, since the patient was at her 20+ gestational week when the tumor was discovered, nephrotic syndrome might be due to pregnancy associated disease rather than a paraneoplastic syndrome, which need further exploration.

Conclusion

MPC is a benign perivascular tumor with a concentric growing pattern and smooth muscular differentiation. Kidney involvement was rare and the prognosis is excellent after surgical treatment. IHC expression profiles and histological features might help differentiate other benign entities in kidney. In our present case, the tumor was identified when the patient was at her 20+ gestational week, accompanied with nephrotic syndrome. Microscopically, the tumor showed varied histological pattern of strip-like cells around thin-walled vessels. With the help of IHC, the diagnosis of MPC was made. This case might indicate a new histological pattern of MPCs with nephrotic syndrome.

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Disclosure of conflict of interest

None.

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