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CASE REPORT

Glomus tumors in the urinary tract: a rare case and literature review

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ABSTRACT

Introduction: The Glomus tumor is a rare mesenchymal tumor that predominantly affects the subcutaneous skin of the distal extremities. Solid organs are rarely affected, and the urinary tract has been the reason for isolated reports. This paper reviews the occurrence of glomus tumors in the entire urinary tract.

Case Report: We report a case of a 56-year-old female, asymptomatic, with a 5.5 cm renal glomus tumor, and review the literature about the urinary tract involvement by this rare neoplasia.

Conclusion: Glomus tumor mostly behaves as a benign lesion that rarely affects solid organs, being the kidney, the most affected organ in the urinary tract. It should be considered in the differential diagnosis of another renal cell tumor, especially those that are eosinophilic.

Key words: Glomus tumor, Urinary tract, Kidney, Bladder, Immunohistochemistry

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Introduction

A glomus tumor is a perivascular mesenchymal neoplasm composed of cells from the glomus body which is a contractile neuromyoarterial structure that affects blood pressure and thermoregulation by altering cutaneous blood flow. It is part of a spectrum that includes myopericytoma, myofibroma, and angioleiomyoma. It constitutes 2% of mesenchymal tumors and affects young adults, mostly females. Although affects most frequently the skin and subcutaneous of distal extremities, particularly the nail bed, wide distribution has been described, including visceral organs as gastrointestinal tract, bone and intrathoracic region (1). The urinary tract is rarely affected, being the kidney the most frequent location, followed by bladder, testis and prostate. We report a case of a kidney glomus tumor and review the literature of the involvement of the entire urinary tract.

Case Presentation

A 56 year-old female, asymptomatic, discovered incidentally, by an abdominal ultrasound, a left renal mass measuring 5.5 cm. A computerized tomography (CT) was performed and the expansive solid, vascularized and heterogeneous lesion was observed in the upper third of the left kidney (Figure 1). The radiologic diagnosis indicated a solid renal tumor, and no biopsy was performed before surgery.

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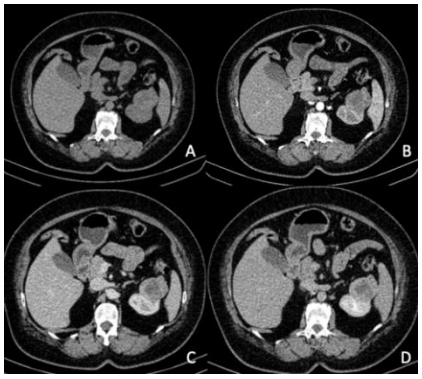

Figure 1: Computed tomography images before (A) and after intravenous injection of iodized contrast. The images show a 5.0 cm expansive lobulated, solid, vascularized, and heterogeneous lesion in the upper third of the left kidney. (B) Represents the arterial phase. The lesion exhibits greater peripheral uptake of contrast in the later stages, portal (C) and excretory (D), with hypovascularized central areas (liquefaction). Additionally, it is more than 50% exophytic and has a discreet impression in the upper calyceal group, completely above the upper polar line.

She underwent a partial left robotic assisted nephrectomy, with the use of intra operatory ultrasound, and a 5,2 cm tumor mass was resected. The surgical time was 120 minutes, the estimated blood loss was 200 ml, no drain was left in the abdomen, and the procedure was considered uneventful. Patient evolved well, and was discharged home on the first day of post-operative. She is well and an abdominal CT six months after surgery showed no sign of recurrence. This report was conducted in accordance with the Declaration of Helsinki of 1975.

Pathological Findings

The pathological analysis showed that the cut surface was uniform, brownish with no necrosis or hemorrhage. Histologically the tumor was characterized by small, epithelioid, regular, round cells, with a pale, eosinophilic cytoplasm with a round, regular, centralized nucleus. There was focal and mild atypia. The mitotic index was <1/50HPF and there were no atypical mitoses. The tumor had pushing borders and there was no necrosis, neither vascular invasion. The surgical margins were free of tumor. Immunohistochemistry study showed expression of Smooth Muscle Actin (SMA), Caldesmon (CALD), Calponin (CALP) and Vimentin (VIM). Proliferative activity (Ki67 – MIB1) was 2% (Figure 2). PAX8, Desmin, CD34, CD117, Cytokeratin 7, Cytokeratin 20, GATA3, Chromogranin, Synaptophisin were negative. The expression of Succinil-Desidrogenase B (SDHB) and Fumarate Hydratase (FH) was preserved.

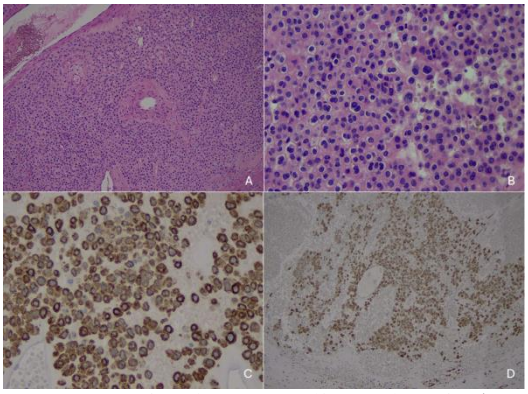

Figure 2: Routine hematoxylin and eosin (H&E) staining demonstrates a proliferation of homogenous round cells with round to ovoid nuclei arranged in multicellular layers around blood vessels. There are mild nuclear atypia and no mitoses (A) 100 × magnification; (B) 400 × magnification. Immunohistochemistry shows expression of Smooth Muscle Actin (C) and Vimentin (D). 400 x and 100 x magnification respectively.

Discussion

Glomus tumor affecting internal organs is rare, and few cases have been described in the urological tract. Kidney is the most frequently affected with 25 cases published in the literature (Table 1). It affects man twice as women, from 8 to 81 years old (mean 48.4 years old). Measures from 10 to 160 mm (mean 46.6 cm). The surgical procedure was partial or radical nephrectomy,

10 cases each. Two cases were described as inoperable, and the method of treatment was not described in 3 reports The great majority had a benign behavior and patients are described as alive and well from two to 62 months (mean 14.8 months). Three cases (12.0%) were described as malignant. Two of them inoperable and one measuring 16 cm that have recurred after a radical nephrectomy. The two patients with inoperable tumors died of the disease, six and seven months after diagnosis.

Bladder is the second urinary tract organ affected by glomus tumor (Table 2) (2-6). There are six cases published in the literature, affecting twice as men than women, with a mean age of 69.7-year-old. Gross hematuria was the main symptom. Tumor size was variable from 6.0 to 65.0 mm (mean 24.8 mm). The larger tumor showed nuclear atypia, necrosis, and high mitotic rate, and patient died from the disease 2 months after treatment. A second malignant glomus tumor was managed with radiotherapy, showing resistance to treatment, and patient died from COVID with disease 12 months after diagnosis.

There are isolated cases of glomus tumor in testicle (7, 8) both benign and one malignant glomus tumor affecting the ureter and the prostate (9, 10).

Immunohistochemistry shows consistently expression of SMA, Vimentin and type IV Collagen. CD34 positivity is variable, mostly negative. Desmin, CD31, S100, Cytokeratins, Chromogranin and Synaptophysin are negative. Genetic studies have been shown rearrangements of NOTCH genes, and BRAF (V600E) and KRAS (G12A) mutations (11).

The main differential diagnoses are myopericytoma, paraganglioma and carcinoid tumor.

Considering the kidney, the main differential diagnoses are the juxtaglomerular tumor, angiomyolipoma and eosinophilic tumors especially SDHB deficient carcinoma. Immunohistochemistry can easily exclude angiomyolipomas (HMB45 positive) and SDHB deficient as well as other eosinophilic tumors (PAX8 and cytokeratin positives). Recently, it has been demonstrated that juxtaglomerular tumors express GATA3, serving as a useful marker to differentiate them from glomus tumors (12). GATA3 was absent in the current case.

Malignant glomus tumor are rare and the main criteria for malignancy are marked nuclear atypia, mitotic activity, the presence of atypical mitosis, deep sited tumors and size over 20 mm.

Table 1: Summary of the clinical, histological and immunoexpression aspects of the glomus tumor affecting the kidney

Ref.	Age	Sex	Presentation	Size (mm)	Nephrectomy	Atypia/ necrosis	IHC (Expression)	Mitotic activity (/50HPF)	Ki67 (%)	Follow-up mo
Our case	56	Fem	Incidental	52	Partial	Focal atypia	SMA/VIM/CALP/CALD	<1	2	NED(3)
(14)	60	Fem	Pain	110	Inoperable	Present	SMA/CIM/CALD/CALP	NA	40	DOD(7)
(15)	67	Male	Microscopic hematuria	27	NA	Absent	SMA/VIM/CD57	None	1	NED (15)
(13)	8	Male	Incidental /TSC	50	Partial	Absent	SMA/P53/RENIN	10	10	NED(16)
(16)	31	Fem	pain/ abdominal	160	Radical	Present	VIM/COLIV	NA	10	DOD (13 y) Local

			mass							recurrence
(16)	33	Fem	Abdominal mass	95	Radical	Absent	SMA/COLIV	NA	NA	NA
(16)	55	Male	Hematuria	15	Partial	Absent	SMA/CALDESMON/ COLIV	NA	NA	NED
(17)	57	Male	Abdominal disconfort	20	Partial	Absent	SMA/VIM/COLIV	2	2	NED(12)
(18)	46	Male	Incidental	NA	Radical	NA	NA	NA	NA	NA
(17)	46	Male	Incidental	50	Radical	Pleomorfism	NA	7	NA	NED(6)
(17)	66	Male	Incidental	58	Radical	Absent	SMA/GATA3	None	NA	NA
(17)	62	Male	Weight loss	18	Partial	Minimal atypia	VIM/SMA/CD57/COLIV	None	<1	NED(2)
(17)	44	Male	Back pain	Inoperable	Inoperable	pleomorfism	SMA/VIM/COLIV/ CD34	Low		DOD(6)
(17)	36	Fem	Incidental	17	Radical	Absent	SMA/VIM	None	NA	NED(8)
(17)	17	Male	Incidental	21	Partial	Absent	SMA/CALD	None	NA	NA
(17)	41	Male	Incidental	10	Partial	Absent	VIM/SMA/CD34	None	<2	NA
(17)	46	Male	Microscopic hematuria	70	Radical	Necrosis and hemorrage	SMA/VIM/CD34	3	10	NED(15)
(19)	36	Male	Abdominal tenderness	23	Partial	Focal atypia	SMA/COLIV	None	1	NED(62)
(19)	81	Male	Incidental	40	Radical	Absent	SMA/COLIV	None	NA	NED(24)
(19)	48	Male	Incidental	73	Radical	Focal atypia	SMA/COLIV	None	1	NED(33)
(17)	53	Fem	Abdominal disconfort	25	Radical	Absent	SMA/CALP/COLIV	3	10	NED(6)
(17)	55	Fem	Incidental	20	Partial	Absent	SMA/VIM	NA	NA	NA
(17)	60	Male	Incidental	25	Partial	Absent	SMA/CD34	NA	NA	NED(8)
(17)	71	Male	incidental	NA	NA	NA	NA	NA	NA	NA
(17)	34	Fem	Flank pain (pregnant)	NA	NA	NA	NA	MA	NA	NA

*DOD – Dead of the disease, NED – No evidence of disease, NA - Not available

A small subset is inherited, being described as part of Multiple Familial Glomus Tumor related to the inactivation of GLMN gene, Neurofibromatosis type 1, related to the biallelic inactivation of NF1 gene and Tuberous Sclerosis (p.Pro1315Leu) (13).

In conclusion, Glomus tumor is a rare mesenchymal tumor, affecting rarely the urinary tract, mostly the kidney, with a benign behavior in the majority of the cases. Smooth muscle antibodies, especially SMA is always positive together with Vimentin and type IV collagen. Large tumors, intense nuclear atypia, mitoses and necrosis are the main characteristics of aggressiveness.

Table 2: Summary of the clinical, histological and immunoexpression aspects of the glomus tumor affecting the bladder.

Ref.	Age	Sex	Presentation	Size (mm)	Atypia/necrosis	IHC (Expression)	Mitotic activity (/50HPF)	Ki67 (%)	Follow-up (months)
(20)	85	Male	Hematuria	NA	Atypia/necrosis	SMA/CALP	NA	60	DWD(12)
(2)	44	Male	Hematuria	16	Absent	SMA	25	5	NED (48)
(3)	57	Fem	Hematuria	6	Absent	SMA/VIM	NA	NA	NED(24)
(4)	58	Male	Incidental	25	Absent	SMA/VIM/BCL2	2		NED (12)
(5)	63	Male	Hematuria	12	Absent	SMA/CD34/IVCOL	NA	5	NED(12)
(6)	57	Fem	Hematuria	65	Atypia/necrosis/ spindle shaped cells	SMA	250	NA	DOD(2)

*DOD – Dead of the disease, DWD – Dead with the disease, NED – No evidence of disease, NA - Not available

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B. Active Participation in Active Methodology
C. Interpretation/ Analysis and Discussion