Case Report

Glomangioma of the Kidney: A Rare Case of Glomus Tumor and Review of the Literature

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1. Background

Glomus tumors are rare benign mesenchymal neoplasms arising from the neuroarterial receptors called glomus bodies [1]. These are very specialized receptors that comprise an efferent arteriole, anastomotic Sucquet-Hoyer canal, and afferent venule [1]. Any overgrowth and/or hyperplasia in one of these structural parts may result in the formation of glomus tumors. Glomus bodies are normally located in the stratum reticulare of the skin, with greater concentration in the lateral aspects of the digits and the palms [1]. Interestingly, glomus bodies are also found in the precoccygeal soft tissue [2]. These bodies are believed to play a role in thermoregulation [3]. Glomus tumors are rare entities that account for less than 2% of all soft tissue tumors. They are typically localized at the peripheral soft tissues with more tendency to involve the subungual zones of fingers and toes [1, 3]. Visceral organs are rarely prone to develop glomus tumors due to lack or even absence of glomus bodies [4]. An extensive review of the literature revealed only eighteen cases of primary renal glomus tumors. All but three are reported as benign glomus tumors with no evidence of recurrence or metastasis during follow-up [5–17]. These three cases include two cases of malignant glomus tumors [18, 19] and a case of uncertain diagnosis of malignant potential [2]. Our case is the 19th case of glomus tumor of the kidney reported in the world literature and the 16th case of benign primary glomus tumor of the kidney. The 4th edition of the new WHO classification system of the kidney tumors does not include the pericytic tumors and the exceptionally rare glomus tumors [20].

In this study, we discuss the nature of the tumor, challenges in reaching a diagnosis through clinical history and radiological studies alone, and the differential diagnosis to consider. Furthermore, we present a review of all reported cases in the medical literature.

2. Case Report

A 57-year-old man presented to the hospital with a two-month history of vague “on-and-off” abdominal discomfort.
Figure 1: Computed tomography (CT) scan of the abdomen. (a) Axial section and (b) coronal section showing a well-defined heterogeneous lesion measuring $2 \times 1.5$ cm located at the posterolateral upper pole of the left kidney, most likely arising from kidney cortex.

No associated symptoms such as radiating pain, weight loss, hematuria, or change in bowel habits were reported by the patient. The patient's medical, surgical, and family history were irrelevant. He also had no history of smoking. Physical examination revealed a soft lax abdomen with unremarkable systemic examination. The results of laboratory investigations, including a complete blood count, blood chemistry, serum urea, and urine analysis, were normal. An abdominal computed tomography (CT) scan showed a well-defined heterogeneous enhancing lesion measuring $2 \times 1.5$ cm located at the posterolateral upper pole of the left kidney. The lesion was in close proximity to the spleen. There was no evidence of hydronephrosis or kidney stones. The renal vein was patent. These findings suggested renal cell carcinoma (Figure 1). Two weeks later, the patient underwent left partial nephrectomy. The resected specimen was sent for histopathological analysis. Gross examination revealed a well-circumscribed but uncapsulated white-tan soft mass with homogeneous cut surface measuring $2 \times 1.5 \times 1$ cm located at the upper pole of the left kidney. The mass abutted but did not invade the renal capsule. No areas of necrosis were seen. No gross abnormality was observed in the rest of the renal parenchyma. Microscopic examination reveals a well-demarcated lesion composed of sheets of cells that were admixed with large, gaping, dilated cavernous-like spaces filled with blood (Figures 2(a) and 2(b)). These cells are monotonous, small, and round to oval, each containing a moderate amount of eosinophilic to amphophilic cytoplasm (Figures 2(e) and 2(f)). No pleomorphism was present. There was no evidence of necrosis (Figure 2(c)) or increased mitotic activity of more than 2/50 high-power field (HPF) (Figure 2(d)). No atypical mitosis was seen. High-power examination showed small nuclei with fine chromatin (Figure 2(f)) and smooth nuclear membrane embedded in a myxoid stroma (Figures 2(g) and 2(h)); other adjacent areas revealed hyalinized stromal reaction (Figure 2(d)). Capsular and lymphovascular invasion were not observed. Tumor cells showed diffuse and strong positivity for smooth muscle actin (α-SMA) (Figure 3(a)), vimentin, and pericellular net-like positivity for collagen type IV (Figure 3(b)). The tumor was negative for cytokeratins 7 and 20, RCC antigen, cluster of differentiation (CD10), epithelial membrane antigen (EMA), desmin, CD34, CD117, CD 99, synaptophysin, chromogranin, S100, renin, Melan A, and human melanoma black-45 (HMB-45). Periodic acid-Schiff (PAS) stain failed to reveal any cytoplasmic granules in any of the examined cells. CD31 and CD34 highlighted the vascular spaces and capillary network only. Ki67 index was less than 2%. Altogether, histopathology and immunohistochemical revealed findings consistent with primary glomangiomata (glomus tumor) of the kidney. One year after surgery, a follow-up examination revealed that the patient was doing well and no tumor recurrence and/or metastasis was detected.

3. Discussion

Glomus bodies are a specialized arteriovenous physiological structure containing a rich nerve supply [17]. Glomus tumors were first described in 1924 by Masson [21]. These tumors are perivascular mesenchymal neoplasms composed of cells closely resembling modified smooth muscle cells of normal glomus bodies [3]. Glomus tumors are found equally in both genders, with a slight female predilection in subungual tumors, and are most common in young adults (20–40 years old) [3]. They are typically located at the distal extremities (particularly nail bed) as small, red-blue nodules, often solitary and painful [3]. Complete surgical excision is the treatment of choice, with excellent prognosis in conventional glomus tumor [3, 9, 10]. One-quarter of glomus tumors are found in the visceral organs, which typically lack glomus bodies [17]. Consequently, an accurate diagnosis can be missed. The exact pathogenesis of glomus tumor in the parenchymal organs is not well understood, since most glomus tumors arise in the soft tissue in association with the normally present glomus bodies. Few reported cases in the literature document primary glomus tumor in the female genital tract [22], gastrointestinal tract [3], bone [23], lung [24], mediastinum [25], larynx [26], trachea [27], oral cavity [28], pancreases [29],...
Figure 2: (a) Low-power view of multilobular growth pattern with lobules containing markedly expanded vascular spaces; the lobules are separated by fibrous bands (H&E; ×40). (b) Well-demarcated but unencapsulated tumor demonstrating large gaping vascular spaces surrounded by clusters of glomus cells (H&E; ×100). (c) Tumor cells exhibiting nodular growth pattern, no necrosis seen (H&E; ×100). (d) Sheets and nests of bland cells with oval nuclei with stromal hyalinization (H&E; ×200). (e) Focal areas adjacent to the vascular spaces show solid glomus tumor, consisting of nodules of bland small round to oval monotonous cells with low mitosis (H&E; ×100). (f) Round to ovoid glomus cells with hypercellularity and distinct cell borders, each containing a single centralized, uniform, round, small “punched out” nucleus (H&E; ×400). (g) Glomus tumor forming trabeculae in abundant myxoid areas (H&E; ×200). (h) Small, round, uniform, and with pale eosinophilic to amphiphilic cytoplasm (H&E; ×400).

Figure 3: (a) Immunohistochemistry of the tumors cells shows strong and diffuse positivity for alpha smooth muscle actin (α-SMA) (H&E; ×200). (b) Nicely uniform pericellular positivity for type IV collagen (H&E; ×200).
suggested the following criteria for malignancy: (1) size

Furthermore, Folpe and colleagues noted the prominent diffuse staining seen in the tumor cells as glomus tumor cells, nerve, and vessels [35]. One study shows p53 positivity in the malignant areas stronger and prominent compared with the benign areas [36]. Estrogen and progesterone weak positivity were noted in the case of ovarian glomus tumor [37].

The differential diagnoses include solitary fibrous tumor, myopericytoma, paraganglioma, angiomylipoma, renal hemangioma, juxtaglomerular cell tumor (JGCT), carcinoid tumor, and lymphoma. Less likely differential diagnoses include Ewing sarcoma/peripheral primitive neuroectodermal tumors, leiomyoma, and renal cell carcinoma. A solitary fibrous tumor will usually have a hemangiopericytoma-like pattern that shows a characteristic spindle or oval cell proliferation arranged in a storiform and fascicular pattern embedded within a hyalinized stroma, which strongly reacts against signal transducer and activator of transcription 6 (STAT6) and CD34 [38]. A myopericytoma is a type of the pericytic neoplasms that grows with a pericytomatosus appearance with neoplastic cells arranged in a concentric multilayered fashion surrounding the blood vessels and the dilated branching vascular lumina. One recent study reported a strong expression of CD34 [39] in such a tumor. Paraganglioma is composed histologically of a well-circumscribed mass composed of nested growth pattern of tumor cells known as Zellballen pattern, with a highly vascularized fibrous stroma. Paraganglioma is typically positive for synaptophysin and chromogranin, with S100 positivity in the sustentacular cells in between. Angiomyolipoma (AML), one of the perivascular epithelioid cell tumors (PEComa), was excluded in our case by the lack of melanocytic markers. Renal hemangiomas are considered rare kidney neoplasms [40]. Two types of hemangiomas are documented: the capillary and, more commonly, the cavernous type. Both are composed of variable-sized blood vessels and vascular spaces lined by a single layer of endothelial cells. The underlying stroma may show features of hyalinization with red blood cells extravasation and hemosiderin deposition. SMA might show little positivity in the vessel walls, which should not be confused with the prominent diffuse staining seen in the tumor cells
| Case number | Author [reference] | Age/sex | Presentation | Site | Size | Treatment | Follow-up (months) |
|-------------|--------------------|---------|--------------|------|------|-----------|-------------------|
| (1)         | Our case           | 57/male | Vague abdominal discomfort | Upper pole of left kidney | 2 × 1.5 × 1 cm | Partial nephrectomy | NED (12) |
| (2)         | Lazor et al. (2016) [17] | 68/female | Incidental (case of bladder cancer, after BCG therapy) | Left renal cortex | 1 cm | Partial nephrectomy | NED (7) |
| (3)         | Nowis et al. (2016) [16] | 66/male | Incidental (elevated PSA) | Right kidney | 5.8 × 5.5 × 4.7 cm | Radical nephrectomy | NA |
| (4)         | Venyo et al. (2012) [15] | 32/male | Vague upper abdominal discomfort | Left kidney | 4 × 2.3 × 4 cm | Partial nephrectomy | NED (20) |
| (5)         | Sasaki et al. (2011) [14] | 62/male | Unexplained weight loss, nausea, and anorexia | Left kidney | 1.8 cm | Partial nephrectomy | NED (2) |
| (6)         | Onishi et al. (2010) [13] | 36/female | Regular follow-up (elevated proteinuria) | Right congenital hypoplastic kidney | 1.7 cm | Retroperitoneoscopic nephrectomy | NED (8) |
| (7)         | Nuwayhid et al. (2010) [12] | 17/male | Incidental (during workup for ulcerative colitis) | Upper pole of right kidney | 2.1 × 1.4 × 1.9 cm | Wedge resection | NA |
| (8)         | Sugimoto et al. (2010) [11] | 41/male | Incidental (regular checkup for leukodermia) | Right kidney | 1 cm | Partial nephrectomy | NA |
| (9)         | Al-Ahmadie et al. (2007) [10] | 36/male | Abdominal tenderness | Anterior interpolar region of the right kidney | 2.3 × 3.2 × 3.3 cm | Partial nephrectomy | NED (62) |
| (10)        | Al-Ahmadie et al. (2007) [10] | 81/male | Incidental (history of prostatic adenocarcinoma) | Lower pole of right kidney | 4 cm | Total nephrectomy | NED (24) |
| (11)        | Al-Ahmadie et al. (2007) [10] | 48/male | Incidental | Midpole of the right kidney | 7.3 cm | Total nephrectomy | NED (33) |
| (12)        | Herawi et al. (2005) [9] | 53/female | Discomfort in right flank, microscopic hematuria, hydronephrosis | Distal renal pelvis, right kidney | 2.5 cm | Radical nephrectomy | NED (6) |
| (13)        | Siddiqui et al. (2005) [8] | 55/female | Incidental | Lower pole of her left kidney | 2 cm | Partial nephrectomy | NA |
| (14)        | Gravet et al. (2015) article in French | 60/male | Incidental | Left upper pole | 2.5 cm | Partial nephrectomy | NED (8) |
| (15)        | Billard et al. (1990) article in French | 71/male | Incidental | Right renal capsule | NA | NA | NA |
| (16)        | Schwarz et al. (1957) article in German | 34/female (pregnant) | Flank pain radiating to the back | Renal parenchyma | NA | NA | NA |

**Infiltrating glomus tumor of uncertain malignant potential**

| (1)         | Gill and Van Vliet (2010) [2] | 46/male | Microscopic hematuria | Anterior aspect of the lower pole of the right kidney | 7 × 6.5 × 6.5 cm | Radical nephrectomy | NED (15) |

**Malignant glomus tumor**

| (1)         | Chen et al. (2016) [19] | 46/male | Incidental (history of nasopharyngeal carcinoma) | Upper pole of the right kidney | 5 × 4.5 × 4 cm | Radical nephrectomy | NED (6) |
| (2)         | Lamba et al. (2011) [18] | 44/male | Lower back pain (metastasis of tumor is the primary presentation) | Posterior side of right kidney with distal metastasis | Multiple metastasis; the size of the primary tumor was unknown | Palliative therapy | Died after 6 months |

**Total** 19 cases
of glomus tumors. Juxtaglomerular cell tumor (JGCT) is a very important differential diagnosis. Most of these patients present in the second or third decades of life, with a slight female predilection [41]. JGCT cause signs and symptoms of hyperreninism, hyperaldosteronism, hypokalemia, and poorly controlled hypertension. Unlike our case, the radiology studies of JGCT show a solid and hypovascular mass. Renal angiography shows, in the majority of JGCT cases, a hypovascular tumor, which helps to rule out renal artery stenosis. Morphologically, JGCT might show similar features with glomus tumors. In addition, it might reveal papillary pattern and well-developed tubules lined by cuboidal cells. Scattered lymphoplasmacytic infiltrates can be seen. Ultrastructural examination of the tumor shows the typical sharply angulated membrane-bound rhomboid crystals and polygonal granules of renin, which act directly with rennin antibodies and PAS, respectively. Unlike JGCT, our case presented with a distinct history with no increased renin level. Moreover, renin and PAS special stains failed to show any reactivity with the tumor cells. Kodet and colleagues [42] reported diffuse CD34 and CD117 positivity in one serial study. Both were negative in our case. Carcinoid tumors stain positively for keratin 18, synaptophysin, and chromogranin, which are all negative in our case. Lymphomas stain positive for CD45 leukocyte-specific markers, CD20, and CD3, all of which stain negative in glomus tumors. The least likely differential diagnosis was Ewing sarcoma/peripheral primitive neuroectodermal tumors, which consist of a sheet of monotonous cells with scant cytoplasm traversed by thin fibrous bands. Perivascular pseudorosettes may be seen. These tumors show diffuse strong membranous staining for CD99 together with the supportive cytogenetics of Ewing sarcoma translocation. Leiomyomas are rare tumors of the kidney, which shows whorled white-tan bulging cut surface. Morphologically, they consist of interlacing bundles of smooth muscle, with a cigar-shaped nucleus. They are not associated with the blood vessels, contrary to glomus tumors. Renal cell carcinoma is a common epithelial tumor, although it is difficult to distinguish it radiologically. Histopathological and immune studies are different; our case does not express any of the epithelial markers (cytokeratin and EMA) besides the distinct morphological features. Overall, our case fits perfectly with the diagnosis of glomangioma.

4. Conclusions

We have presented the 16th case of primary renal glomus tumor (in the form of glomangioma). Primary renal glomus tumors are rare and may mimic other mesenchymal renal neoplasms radiologically. Furthermore, histological and immunohistochemical findings in glomus tumors overlap with those of other kidney tumors and may contribute to an inaccurate diagnosis. Proper investigation (including histopathological analysis and immunohistochemical staining) of incidentally discovered kidney tumors is essential to make the diagnosis of glomus tumors, which show a benign clinical course following resection.

Conflicts of Interest

The authors declare no conflicts of interest.

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