Case Report

Characterization of Glomus Tumors of the Kidney

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Clinical Practice Points

- Renal glomus tumors are traditionally thought to be benign mesenchymal tumors of the kidney.
- We report the first case of recurrent renal glomus tumor after surgical resection, and demonstrate the importance of long-term clinical follow-up.
- Potential clincopathologic features increasing the risk of metastasis include large size, mild and diffuse nuclear atypia, presence of necrosis, scattered mitoses, and lymphovascular invasion. These risk factors need to be validated in future cases.

Clinical Genitourinary Cancer, Vol. ■, No. ■, ■-■
Keywords: Glomangioma, Glomus tumor, Kidney neoplasm, Malignant glomus tumor, Vascular tumors

Introduction

Glomus tumors are rare mesenchymal neoplasms arising from the neuromyoarterial glomus, a cutaneous structure that functions in temperature regulation via arteriovenous shunting of blood.[1] They typically occur as painful nodules in the areas rich in glomus bodies, such as the subungual regions of digits and deep dermis of the palm, wrist, forearm, and foot. Congenital familial multiple glomus tumor leads to multifocal tumors and demonstrates an autosomal dominant inheritance pattern with variable expressivity and incomplete penetrance.[2] Mutations in the *glomulin* gene, located in 1p22.1, have been implicated.[3] In addition, somatic mutations involving fragile sites on chromosome 1p were found to complete the Knudson 2-hit model, leading to formation of the glomus tumors.[4]

Visceral organs are devoid of glomus bodies, and thus rarely give rise to glomus tumors.[5] A recent comprehensive review of the literature yielded 19 cases of primary renal glomus tumor, all but 1 of which were localized to the kidney without evidence of malignant progression.[5] We report a series of 3 cases of renal glomus tumors accessioned at the Armed Forces Institute of Pathology over a 15-year period. Of these, 1 exhibited pathologic features concerning for local invasion, whereas another suffered distant metastases 7 years after primary resection.

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Submitted: Aug 25, 2017; Accepted: Sep 1, 2017

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Case Reports

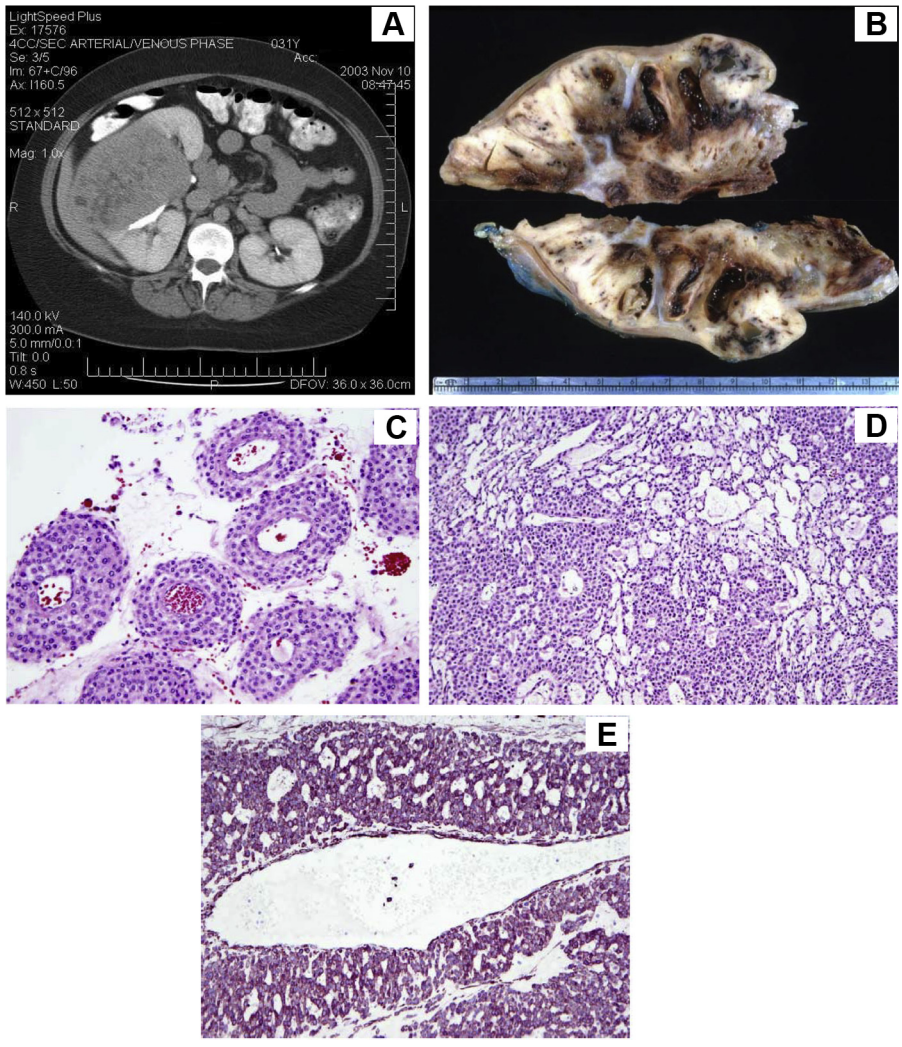
Case 1

A 31-year-old Caucasian woman presented with total gross hematuria of 1 week duration and 2 days of right-flank pain. She denied weight loss, but did report experiencing "hot flashes" for 6 months. A physical examination demonstrated a smooth, non-tender abdominal mass extending approximately 8 cm below the right costal margin. Computed tomography imaging revealed a 16-cm heterogeneous mass with an area of central necrosis (Figure 1A). There was no evidence of extension into the perirenal space or of renal vein thrombosis. Multiple enlarged lymph nodes were present along the inferior vena cava and inter-aortocaval region. Evaluations by bone scan and chest radiograph were unrevealing for metastasis. A right radical nephrectomy with extended lymphadenectomy was performed in an uncomplicated manner through an extended right subcostal incision.

Grossly, the tumor was well-circumscribed and without extrarenal extension. It occupied 80% of the kidney, involving both the cortex and the medulla. The cut surface was variegated (yellow to grayish-white, hemorrhagic, necrotic, and firm) with aberrant small vessels and concentric growth-forming nodules and sheets (Figure 1B). Necrosis was seen in 10% of the tumor specimen. Microscopically, the cells were round and uniform, with centrally placed round nuclei within an amphophilic or eosinophilic cytoplasm. Capillary-size vessels were circumscribed by collars of the small cells (Figure 1C). In other areas, the glomus cells formed a reticular morphology (Figure 1D). Nuclear atypia was rare, and mitotic rate was 10 of 50 high-powered fields (HPFs). Lymphovascular invasion was present. Smooth-muscle actin was expressed by most of the tumor cells (Figure 1E). There was abundant expression of Type IV collagen, and the cells were positive for vimentin and negative for keratin A1/A3. Immunohistochemical stains were also negative for CK7, CK20, CEA, chromogranin, Hale's colloidal iron, EMA, RCC, and CD10.

1558-7673/$ - see frontmatter
http://dx.doi.org/10.1016/j.clgc.2017.09.002

Figure 1 Imaging and Histologic Features of a 33-year-old Caucasian Woman With Renal Glomus Tumor (Case 1). A, Venous Phase Post-contrast Computed Tomography Image Showing Mass Arising Within the Interpolar Region of the Right Kidney; B, Grossly, a 13-cm Variegated, Hemorrhagic Tumor Was Seen Involving the Majority of the Kidney; C, Collars of Glomus Cells Surrounding Capillary-sized Vessels; D, Glomus Cells Circumscribe Small Vessels and Form Expanses With a Reticular Morphology; E, Essentially All Glomus Cells Show Strong Immunoreactivity With Smooth Muscle Actin



After 7 years of uneventful follow-up, the patient was found to have multiple left renal masses. She underwent open partial nephrectomy, yielding 3 distinct tumors, which were 7.4 cm, 5.2 cm, and 7.0 cm in size. Pathologic evaluation of all tumors was consistent with glomus tumors of the kidney. Macroscopic invasion of the peritumoral capsule was present in all 3 tumors, and resection margins were negative of tumor.

After another relapse-free interval of 2 years, recurrent masses were again found in the left kidney remnant, spleen, right gluteal muscle, and brain. She went on to resection of her gluteal muscle and magnetic resonance imaging-guided resection of the brain lesion, both confirmed histologically to be metastatic glomus tumor. Thereafter, progressive metastatic disease was found in the lungs, liver, small bowel, and skin. She received 1 cycle of salvage cyclophosphamide, vincristine, and dacarbazine, with minimal effect. Of note, her cutaneous lesions actively expressed IGF-2, causing non-islet cell tumor hypoglycemia requiring treatment with dexamethasone and intravenous glucagon. After multiple hospitalizations and palliative procedures, the patient succumbed to her disease more than 13 years after original diagnosis.

Case 2

An otherwise healthy 33-year-old Caucasian woman was found to have a left-kidney tumor during evaluation of a heart murmur. Nephrectomy revealed a large lobulated and hemorrhagic tumor measuring 9.5 cm by 6.0 cm. The cut surface had a nodular appearance, and the renal vein was filled with a tumor thrombus. The inferior vena cava also contained tumor, and the tricuspid valve had vegetation positive for tumor cells.