Pathologic Quiz Case

A Symptomatic Renal Tumor

Adam Kuten, MD; Aria Olumi, MD; Jeffery Goldsmith, MD; Rita A. Monahan-Earley, BA; Ann M. Dvorak, MD; Elizabeth M. Genega, MD

A 27-year-old woman presented to her primary care physician complaining of severe headaches. She was a nonsmoker and denied palpitations, chest pain, or a history of migraines or other severe headache. On physical examination, her blood pressure was found to be 175/125 mm Hg, and her pulse was 74 beats per minute and regular. Follow-up examination revealed persistent poorly controlled blood pressure, and she was started on a calcium channel blocker for better control of her elevated blood pressure. Despite treatment, her blood pressure remained elevated, varying from 140 to 150/80 to 90 mm Hg. Her diagnostic evaluation included a search for secondary causes of the hypertension. Urinary metanephrine levels were within the normal range. A magnetic resonance imaging study, performed to evaluate for renal artery stenosis, revealed a 2.3-cm enhancing mass in the right kidney. Because of enhancement on the radiographic evaluation and inability to rule out carcinoma, radical nephrectomy was performed. Partial nephrectomy was not considered because of the proximity of the mass to the renal hilum.

Gross examination showed a well-circumscribed, 2.3 × 2.0 × 2.0-cm, solid, tan, focally hemorrhagic mass within the renal cortex (Figure 1). Microscopically, the tumor was composed of a relatively monotonous population of round to polygonal cells arranged largely in solid compact sheets with focal areas of papillary and tubular growth (Figure 2). The papillae were lined by flat to cuboidal cells, and the cores of the papillae contained cells similar to those in the areas of sheetlike growth. The round/polygonal tumor cells had largely ill-defined cell borders; amphophilic cytoplasm; and round, centrally placed nuclei without prominent nucleoli (Figure 3). Focal moderate nuclear atypia was present. Little supporting stroma was present; small foci of stromal edema were seen between tumor cells, creating a microcystic appearance. Thin-walled and thick-walled blood vessels with focal wall hyalinization were present within the neoplasm. Mitotic figures and necrosis were absent. Immunohistochemical studies showed the tumor cells were positive for CD34 and actin, and negative for cytokeratin.

Electron microscopy demonstrated round and elongated cells with blunt cell protrusions. These extensions contacted each other in contiguous cells by gap junctions. Tumor cells were encased in basal lamina. The extracellular space had focal areas of long-spaced interstitial collagen. Cytoplasmic sub–plasma membrane dense bodies completed the collection of organelles, commonly present in cells of smooth muscle origin, that were identified in this tumor. Tumor cells differed from typical smooth muscle cells by the presence of cytoplasmic granules typical for those normally present in cells of the juxtaglomerular apparatus. These characteristic rhomboid renin protogranules were membrane-bound and contained a 6- to 10-nm periodic crystalline array, some of which had an electron-dense ''zig-zag'' pattern traversing the crystalline array (Figure 4). Tumor cells also displayed electron-dense spheroidal granules. In addition to tumor cells, the electron microscopy sample contained large numbers of mast cells.

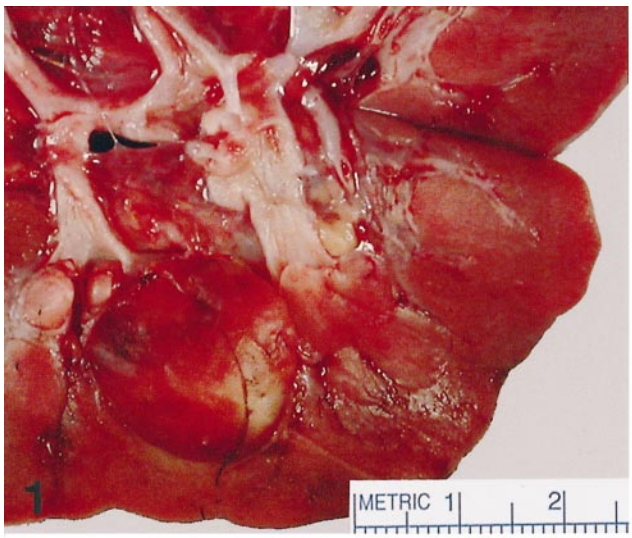
What is your diagnosis?

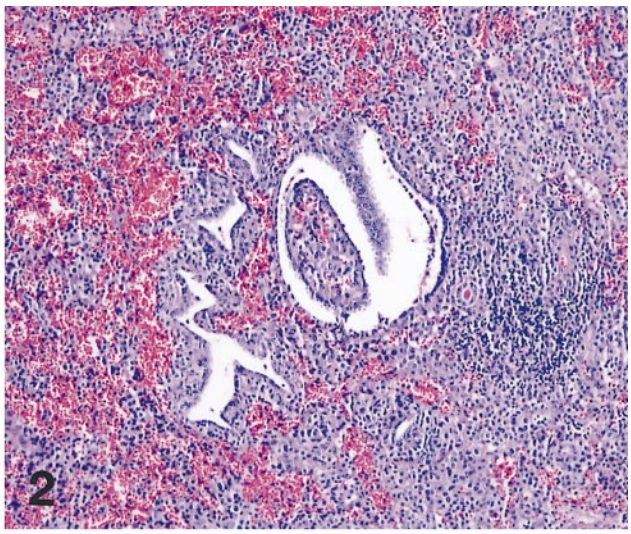
Accepted for publication April 16, 2004.

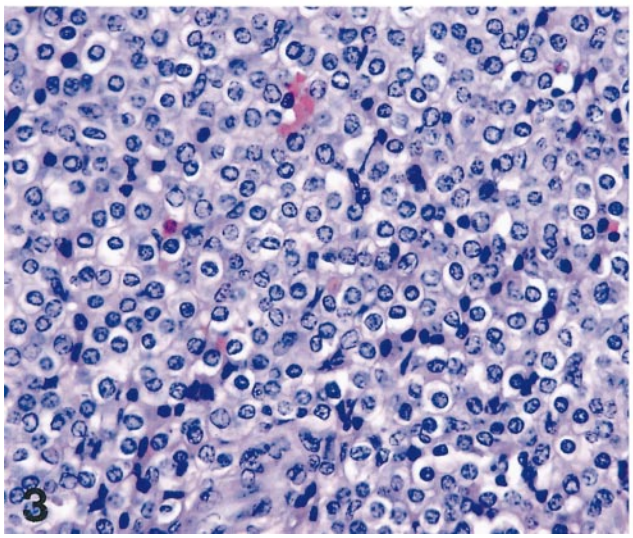
From the Departments of Pathology (Drs Kuten, Goldsmith, Dvorak, and Genega, and Ms Monahan-Earley) and Urology (Dr Olumi), Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Mass.

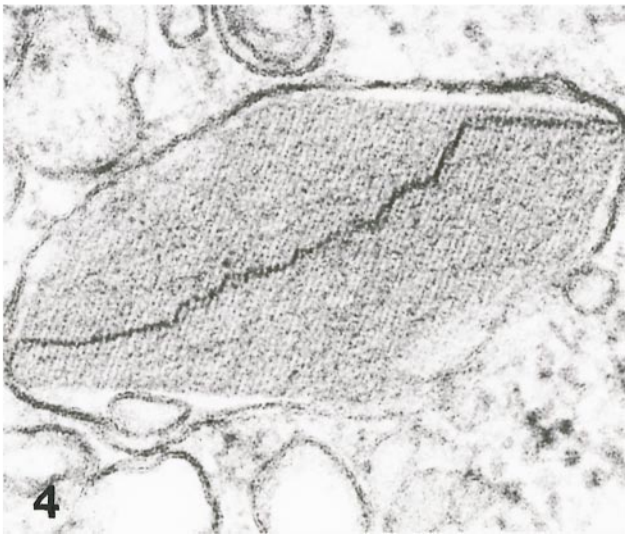
The authors have no relevant financial interest in the products or companies described in this article.

Corresponding author: Elizabeth M. Genega, MD, Department of Pathology, East Campus, Beth Israel Deaconess Medical Center, 330 Brookline Ave, Boston, MA 02215 (e-mail: egenega@bidmc.harvard.edu).









Pathologic Diagnosis: Juxtaglomerular Cell Tumor

Juxtaglomerular cell tumors (JGTs), also known as reninomas, are rare tumors that arise from modified smooth muscle cells of the juxtaglomerular cell apparatus.[1] They typically are found in young adults, most of whom present with hypertension due to autonomous renin secretion by the tumor.[1,2] Women are affected slightly more often than men,[1] and the average age at diagnosis is 27 years.[3] This is a benign tumor, and no cases of bilateral disease, metastases, or recurrence have been reported.[3]

Grossly, these tumors are well-circumscribed and range from 2.2 to 8.0 cm.[1] They are firm, yellow to tan-gray neoplasms that may contain small foci of hemorrhage and occasional small cystic spaces.[1] Frank invasion beyond the kidney has not been reported.[1]

Juxtaglomerular cell tumors have a varied microscopic appearance. The tumor cells may be arranged in solid compact sheets or irregular trabeculae and may demonstrate papillary growth. The stroma may be scanty, myxoid, or edematous, the latter resulting in a cystic appearance.[1] The tumor cells are round to polygonal to spindle-shaped, with scant to moderate eosinophilic cytoplasm and centrally placed nuclei.[1] The papillary structures in these tumors are interesting in that they have a biphasic appearance; the lining cells are flat to cuboidal epithelial cells, shown by electron microscopy to resemble collecting duct epithelium, while the cores of the papillae contain the polygonal cells.[4] Tubules may be present within these neoplasms and whether they are ''entrapped'' tubules or neoplastic is unclear.[1] Thin-walled and thick-walled blood vessels with wall hyalinization and/or branching are scattered throughout the neoplasm. Mitotic activity and tumor necrosis are rare.[1] Immunohistochemically, the tumor cells have been found to be positive for renin, CD34, and actin and negative for cytokeratin.[1] Ultrastructurally, the tumor cells contain renin protogranules[1] and mature renin granules, the former being more abundant.[3]

The differential diagnosis includes several other neoplasms, including renal cell carcinoma, hemangiopericytoma, and metanephric adenoma. Juxtaglomerular cell tumors with nuclear atypia, prominent vasculature, and tubulopapillary growth may be mistaken for a papillary renal cell carcinoma. The branching vessels that may be seen in JGTs are reminiscent of the vasculature seen in hemangiopericytomas; however, this latter tumor is not composed of the polygonal cells seen in JGT.[1] Metanephric adenomas bear a resemblance to JGT because they are highly cellular tumors composed of relatively uniform small cells with round nuclei, inconspicuous nucleoli, and scant cytoplasm. The cells are arranged in acini and tubules, which may be so tightly packed as to appear solid at low magnification.[3,5] Although these neoplasms may have a superficial resemblance to JGT, the histologic features of each neoplasm usually allow for differentiation. When distinction between the neoplasms is difficult, ancillary studies, including immunohistochemical studies and electron microscopy, may be useful. Reactions for cytokeratin and epithelial membrane antigen are positive in renal cell carcinoma and are negative in JGT. Metanephric adenomas may also be positive for cytokeratin and vimentin.[5] Hemangiopericytoma, unlike JGT, is negative for actin and renin.[1] Electron microscopy can be used to demonstrate renin granules within tumor cells of JGT.

Treatment consists of either a partial or complete nephrectomy. This patient underwent a complete nephrectomy because of the proximity of the tumor to the renal hilum. After surgery, the patient's antihypertensive medication was discontinued. At follow-up, the patient's blood pressure had returned to normal, and no other therapy was required.

References

1. Martin S, Mynderse L, Lager D, Cheville J. Juxtaglomerular cell tumor: a clinicopathologic study of four cases and review of the literature. *Am J Clin Pathol.* 2001;116:854–863.
2. Endoh Y, Motoyama T, Hayami S, Kihara I. Case report: juxtaglomerular cell tumor of the kidney: report of a non-functioning variant. *Pathol Int.* 1997;47:393–396.
3. Eble J. Neoplasms of the kidney. In: Bostwick D, Eble J, eds. *Urologic Surgical Pathology.* St Louis, Mo: Mosby–Year Book; 1997:83–147.
4. Tetu B, Vaillancourt L, Camilleri J, Bruneval P, Bernier L, Tourigny R. Juxtaglomerular cell tumor of the kidney: report of two cases with a papillary pattern. *Hum Pathol.* 1993;24:1168–1174.
5. Grignon DJ, Eble JN. Papillary and metanephric adenomas of the kidney. *Semin Diagn Pathol.* 1998;15:41–53.