Metanephric adenofibroma: robotic partial nephrectomy of a large Wilms' tumor variant

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Purpose: *A case of the rare, benign, Wilms' tumor (WT) variant, metanephric adenofibroma (MAF), is presented.*
Materials and methods: *The patient is a 21-year-old female with an incidentally discovered enhancing renal mass. The diagnosis, workup and treatment are outlined.*

Results: *The 19 cm renal mass was ultimately resected via robot-assisted partial nephrectomy. Pathologic diagnosis at our institution was confirmed as a MAF by the National Wilms' Tumor Study Group (NWTSG).*
Conclusion: *Difficult to differentiate from WT, it is imperative that MAF be recognized and appropriately diagnosed because unlike adult WT, the natural history of MAF is indolent and adjuvant chemo/radiation therapy is rarely necessary. This case reinforces the importance of review of potential WT variants by the NWTSG.*

Key Words: metanephric adenofibroma; nephrogenic adenofibroma; Wilms' tumor

Case presentation

A 21-year-old female with no significant past medical history presented to a local emergency room after 2 days of abdominal pain and fever. Initial CT scan of the abdomen revealed an incidental 19 cm left renal mass, Figure 1. MRI demonstrated a bilobed, pedunculated mass arising from and surrounding the left kidney. The R.E.N.A.L Nephrometry Score was 3+1+3+x+3=10x, signifying a highly complex lesion.[1] The differential diagnosis was renal cell carcinoma, fat poor angiomyolipoma, lymphoma and sarcoma. Given the patient's young age and perceived need for definitive diagnosis and treatment, biopsy was not pursued. The patient ultimately opted for definitive surgical removal via a robot-assisted nephron-sparing approach, which was performed according to previous description.[2-3]

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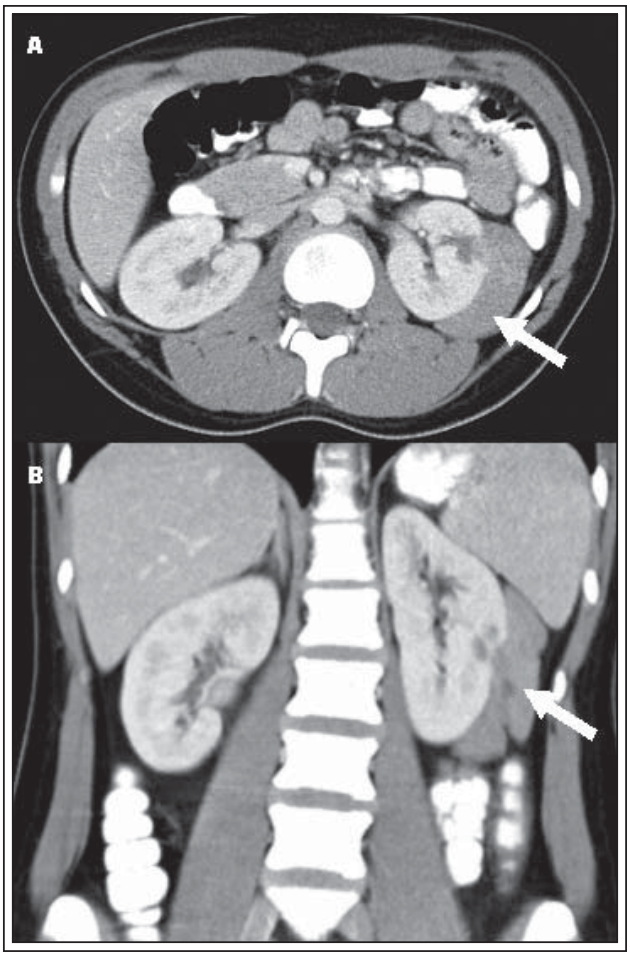

Figure 1. Axial (A) and coronal (B) cuts of a computed tomography scan, demonstrating a large enhancing mass (arrows) arising from the left kidney (R.E.N.A.L. Nephrometry Score = 3+1+3+x+3=10x).

Briefly, once the peritoneal cavity was insufflated with carbon dioxide, robotic ports were inserted, and the robot was docked. The left colon was mobilized medially. The kidney was meticulously defatted, delineating the boundaries of the tumor. Intraoperative ultrasound was utilized to better define the tumor's anatomy. The hilar vessels were individually dissected so that laparoscopic bulldog clamps could be applied. After the blood supply to the kidney was interrupted using these clamps, the mass was excised using round-tipped scissors in a bloodless field. Negative margins were pathologically confirmed on frozen section. The renal defect was closed over oxidized cellulose bolsters in a standard fashion. Hilar bulldog clamps were removed and excellent hemostasis was demonstrated. The patient was discharged after an uneventful 3 day hospital course, returning to normal activity within 3 weeks.

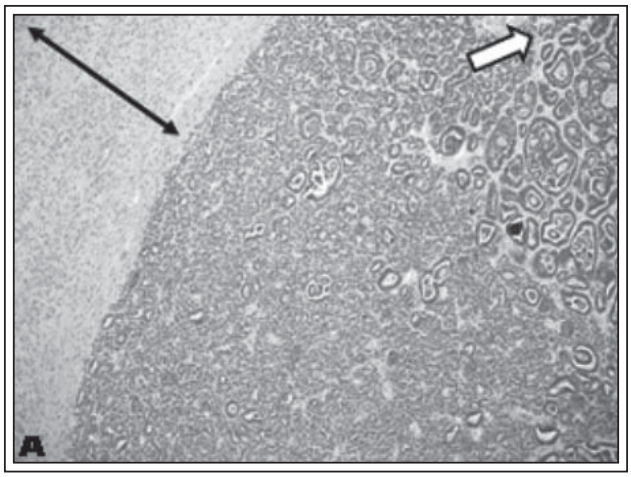

Figure 2a. Hematoxylin and Eosin stains (10x). Metanephric adenofibroma (A) demonstrating both stromal component (black arrow) and epithelial component (white arrow). Epithelial cells in top right corner are visibly less organized and represent primitive blastic elements (white arrow).

The specimen consisted of a 15 cm x 8 cm x 3 cm rubbery to firm mass. The entire tumor was submitted for histological examination. Upon sectioning, two distinct regions were observed: epithelial and stromal, Figure 2a. Uniform epithelial cells in the central region formed elements of tubular, papillary and glomeruloid structures, Figure 2b. A spindle cell component within surrounding stroma was noted at the periphery, Figure 2c.

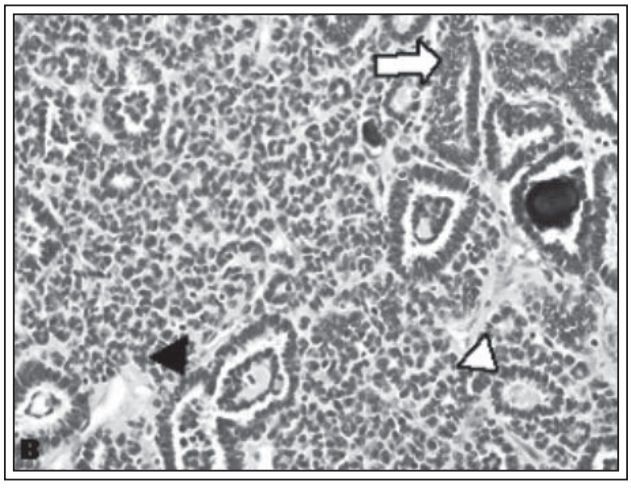

Figure 2b. Hematoxylin and Eosin stains (40x). Shown in high power (40x), the epithelial component of metanephric adenofibroma (B) with blastic (white arrow) and papillary (black arrowhead) manifestations. Aborted tubules (white arrowhead) can be identified. Mitotic figures are absent.

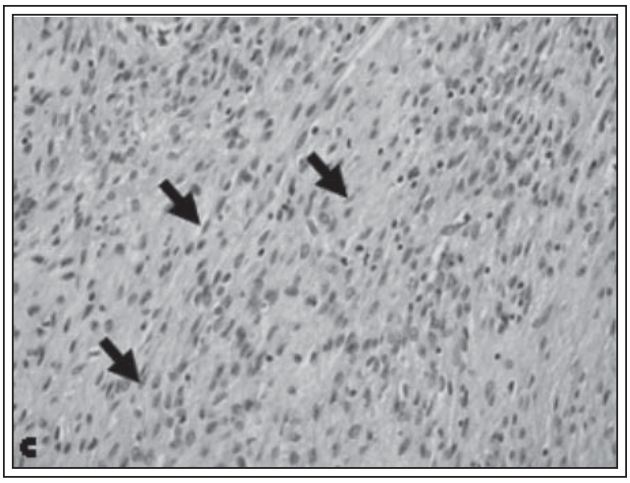

Figure 2c. Hematoxylin and Eosin stains (40x). The stromal component of metanephric adenofibroma (C), again in high power (40x), is exemplified by ubiquitous spindle cells within the stroma (black arrows).

Concentric calcifications were noted, and mitotic figures were absent. Immunohistochemical staining was performed. The epithelial component was cytokeratin positive and the stromal component CD34 positive. Focal WMT-1 staining was also present. Serial sectioning of the whole tumor revealed no classic blastic WMT component and no undifferentiated areas. The final pathological diagnosis was MAF, which has been confirmed after NWTSG review. Cytogenetic analysis revealed a normal female karyotype. DNA copy number analysis of the tumor, using high-resolution oligonucleotide arrays, detected no genomic imbalances.

Discussion

Primitive metanephric precursor cells differentiate into components of the mature kidney. Theoretically, the persistence and uncontrolled proliferation of these embryonic cells gives rise to WT. WT is predominantly diagnosed in children, accounting for 7% of all childhood cancers.[4] Adult WT is exceedingly uncommon, with only 2% occurring after age 15.[5] Since 1969, the NWTSG has kept meticulous records regarding all documented WT cases, thus offering a better understanding of WT biology and management, which contributed to improving the 4 year survival rates in children to > 90%.[4] Unfortunately, survival rates in adults reach only 70% at 5 years, highlighting the need for careful diagnosis and treatment in this population.[5]

Regardless of the patient's age, WT is comprised of blastic, epithelial, and stromal components.[4] Further study has identified a continuum of metanephric lesions similar to WT. The various subtypes are generally associated with less aggressive clinical courses than WT and are classified based on cellular composition.[6-8] These benign variants include the purely mesenchymal metanephric stromal tumor, epithelial metanephric adenoma, and the mixed metanephric adenofibroma.[6,7]

Using samples from the NWTSG tissue bank repository, Hennigar and Beckwith published the first report of a novel renal neoplasm designated nephrogenic adenofibroma.[8] They reclassified five previously diagnosed WT as this new entity, since renamed MAF, which, as previously mentioned, fits into the spectrum of benign metanephric tumors and the wider spectrum of WT.

Several attributes support a link between MAF and WT. Both neoplasms are biphasic, containing spindle-cells of mesenchymal origin and discrete nodules of embryonal epithelium.[6-9] Unique islands of primitive blast cells, called nephrogenic rests, are often found in MAF and WT long after organogenesis.[4] The maturation of these elements is thought to contribute to the stromal component of both MAF and WT.[6]

The main difference between these lesions hinges on an increased presence of active mitosis found in WT but not metanephric neoplasms. Some experts believe that transition from active WT into these slow-growing metanephric variants can occur as cells mature and mitosis ceases. Specimens with both metanephric histology and uncharacteristic areas of active mitosis support this maturation. These appear to be a missing link in the differentiation from WT to metanephric tumors.[6] Thorough sectioning of the tumor presented here revealed no mitotic activity.

Typically, MAF is diagnosed later in childhood or adolescence, whereas 90% of WT occur in patients younger than 7 years of age.[4,5] The most common presenting symptom for MAF is hematuria, occurring when central lesions penetrate the renal collecting system.[7] Furthermore, while chromosome abnormalities are present in most WT cases, a recent study revealed a lack of genomic imbalances in MAF specimens,[10] as we report. Surgical resection of MAF serves therapeutic and diagnostic purposes. Classically, resection is accomplished via radical nephrectomy.[6,9]

If misclassified, patients with pure MAF are often unnecessarily subjected to adjuvant chemo/radiation therapy used to combat the more aggressive WT.[5] In pure MAF, complete excision alone may be curative,[6,9] although patients require vigilant long term follow up.[6] Since the initial five cases of MAF, 12 additional

cases have been documented with a mean diameter of 3.85 cm.[6,8,9] Only one tumor was treated by partial nephrectomy.[9] At 19 cm in diameter, our case represents, to our knowledge, the largest MAF reported and is the first documented MAF to be resected using robot assistance.

WT and its variants are rare; nevertheless, the adult urologist can certainly encounter this pathology. Caution must be exercised if suspecting these diagnoses. Treatment and prognosis for adult WT is vastly different from its benign variants, making distinction essential. If either diagnosis is being considered, referral to a tertiary center with appropriate expertise is imperative. □

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