# Metanephric adenoma of the kidney: an unusual diagnostic challenge

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## Abstract

Although metanephric adenoma (MA) is a rare, benign neoplasm of epithelial cells, it is often difficult to distinguish this entity from other malignant neoplasms preoperatively. We report a case of a large renal mass for which preoperative diagnosis was indeterminate, with the differential diagnosis including Wilm's tumor, MA, and papillary renal cell carcinoma (PRCC). Accurate postoperative differentiation of MA from PRCC is critical because adjuvant therapy is considered after surgical resection of PRCC tumors.

## Introduction

Metanephric neoplasms comprise a spectrum of kidney tumors containing renal epithelial or stromal cells or both.[1] Metanephric adenoma (MA) is a rare neoplasm, accounting for 0.2% of adult renal epithelial neoplasms.[2] The majority of cases occurs in patients 50-60 years of age[3-5] and is seen predominantly in females by a 2:1 ratio.[4] Although MA is usually benign, a few cases of metastatic disease have been reported.[1,6] Several diseases can resemble MA including Wilm's tumor, metastatic lung carcinoma, and metastatic papillary thyroid carcinoma; however, it is most difficult to distinguish MA from papillary renal cell carcinoma (PRCC). We describe here a case of a large renal mass and the challenge of establishing a preoperative diagnosis.

## Case Report

A 28-year-old woman presented with a history of three urinary tract infections in the course of six months, and associated right flank pain with no hematuria or weight loss. She reported frequent urination of 6-8 times a day and urethral tingling at the end of urination. During one of these infections, she was treated with ciprofloxacin because the urine culture was positive for enterococcus. However, when she experienced similar symptoms a month later, both urinalysis and urine cultures were negative at that time. Because nephrolithiasis was suspected as a possible cause of recurrent urinary tract infections, a non-contrast computer tomography (CT) scan of the abdomen was performed. A large heterogeneous soft tissue mass (7.6×10.6×7.3 cm) was found arising from the superior pole of the right kidney and displacing the liver anteriorly. Hyperdense areas within the mass were consistent with recent hemorrhages. A small amount of fluid was found adjacent to the mass and in the dependent pelvis. A left-sided paraaortic lymph node measuring 1.1 cm was seen, as well as several small lymph nodes in the mesentery. The liver, spleen, and pancreas were unremarkable, and the left kidney showed no evidence of mass or hydronephrosis. Magnetic resonance angiography (MRA) revealed intra-renal arteries draped around the mass, although no definite tumor vascularity was seen and the tumor did not extend into the renal veins or inferior vena cava. MRA also revealed a normal renal artery, two renal veins, and a ureter on the right side. Magnetic resonance imaging (MRI) detected no fat within the mass (Figure 1). Sagittal T1-weighted and axial T2-weighted MRI showed no evidence of metastatic disease in the brain.

The possibility of hydatid cyst or parasitic infection was considered in the differential diagnosis owing to the unusual multicystic appearance of the mass with peripheral vascular supply and recent exposure to parasites endemic to Paraguay. No detectable levels of echinococcus antibody or *Entamoeba histolytica* antibody were observed in ELISA analysis. In addition, the sedimentation rate and C-reactive protein level were within the normal range, indicating that the mass was not an abscess or parasitic infection. The peripheral blood count and hemoglobin level were normal.

Preoperative diagnosis was indeterminate, with the differential diagnosis still including Wilm's tumor, MA, and metastatic PRCC. Given the size of the mass and possibility of malignant disease, a radical nephrectomy was performed. Although the resected tumor was well circumscribed with a pseudocapsule, it was not well encapsulated. The mass was tan in color, measuring 10×6.5×7.5 cm and involving the upper pole and the middle portion of the kidney. On the cut surface, the tumor was well circumscribed, tan and lobulated, with multiple foci of hemorrhage and one focus of cystic degeneration. The tumor extended to, but not through, the renal capsule and occluded the upper pole collecting system at the renal pelvis.

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Microscopically, the tumor was demarcated from the surrounding renal parenchyma by a pseudocapsule of variable thickness. Architecturally, the tumor was retiform, micropapil-

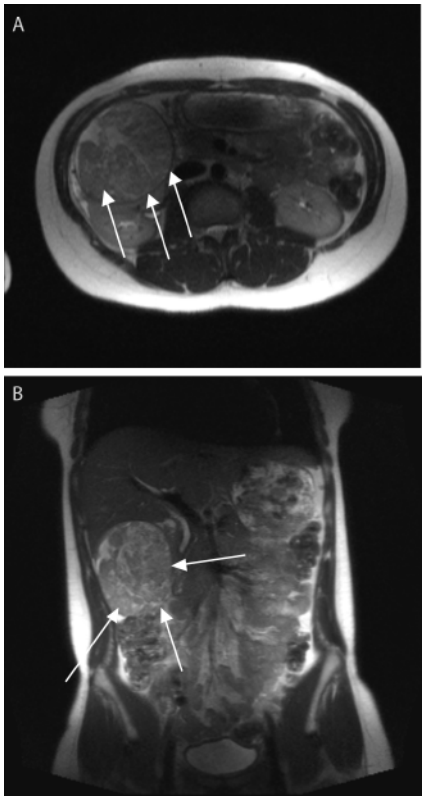


**Figure 1. Magnetic resonance angiography image of the pelvis and abdomen in the axial (A) and coronal (B) planes. Arrows indicate the location of a large mass (7.6×10.6×7.3 cm).**

lary, and cystic (Figure 2A and B), with focal necrosis and hyaline change. It had numerous slit-like spaces and micropapillae lined by small epithelial cells with very scant cytoplasm and oval nuclei showing delicate chromatin, grooves, and focal small nucleoli (Figure 2C). Mitotic figures were very rare. The septa and fibrovascular cores of the tumor varied in thickness and showed hyalinization, edema, and numerous psammoma bodies (Figure 2D). No calcifications were evident.

Immunohistochemically, the tumor showed diffuse positive staining for CD57 (Figure 2E) and WT-1 (Figure 2F), and was only very focally, weakly positive for cytokeratin 7 and epithelial membrane antigen (EMA). Immunostain for racemase (P504s) was negative in the tumor. Interphase cytogenetic studies by fluorescent *in situ* hybridization showed no evidence of trisomy for chromosomes 7 or 17.

PRCC is associated with a gain of chromosomes 7 and 17 and loss of sex chromosome Y, whereas the number of these chromosomes in MA is normal.[7] PRCC is also characterized by the presence of enlarged cytoplasm, large nucleoli, and strongly positive CK7 and EMA immunoreactions,[8] although two cases have been reported with only focal and weak EMA immunoreactions.[3] In our case, the only considerations that supported a diagnosis of PRCC were CK7 positivity and very focal and weak EMA positivity. The predominance of epithelial cells also excluded a diagnosis of Wilm's tumor, which is characterized by epithelial, stromal, and blastemal components. A diagnosis of oncocytoma was excluded by the lack of oncocytic cells (granular eosiniphilic cells), absence of CK8 and CK18 expression, and absence of chromosomal abnormalities (such as loss of chromosomes Y, 1, and 14; absence of translocation of chromosome 11; and gain of chromosome 12). Based on these histolologic and cytogenetic features, a diagnosis of MA was suggested. The patient remains disease free 28 months following right nephrectomy.

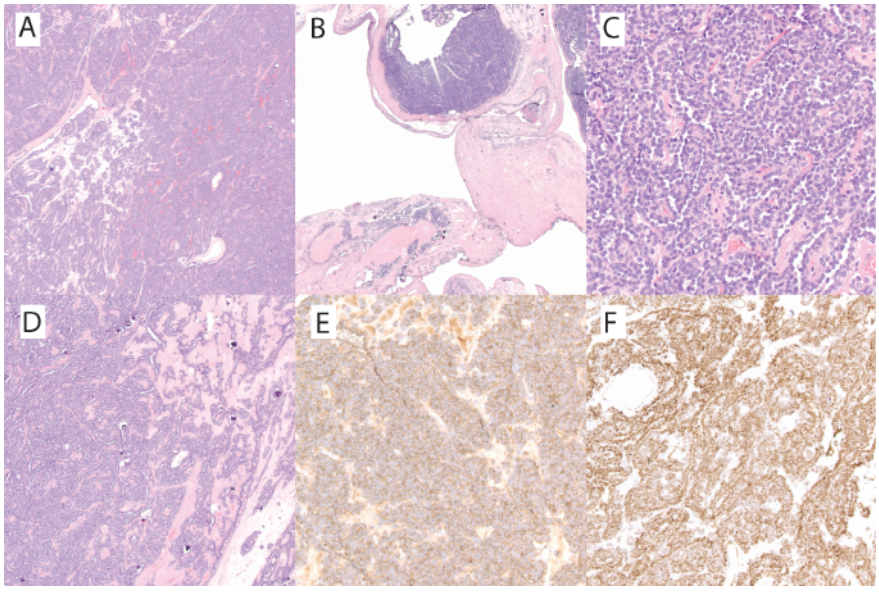


**Figure 2. Microphotographs of the renal tumor. The histopathological and immunohistochemical findings are consistent with metanephric adenoma (MA). (A) Retiform and micropapillary architecture of the tumor [hematoxylin-and-eosin stain (H&E); magnification, 40X]. (B) Focal cystic and hyaline change in the tumor (H&E; 40X). (C) Epithelial cells of the tumor showing scant cytoplasm; oval, often grooved nuclei, and a lack of mitotic activity (H&E; 400X). (D) Hyalinized and edematous tumoral stroma with scattered psammoma bodies (concentrically laminated microcalcifications) (H&E; 100X). (E) Diffuse, strong positive cytoplasmic immunostaining of the tumor for CD57 (200X). (F) Diffuse, strong positive nuclear immunostaining of the tumor for WT-1 (200X).**

## Discussion

MA is a rare neoplasm that often presents as asymptomatic, although symptoms can include abdominal pain, abdominal mass, hematuria, dysuria, fever, or hypertension. Among renal lesions, MA has the highest incidence (12%) of polycythemia.[9] MA tumors appear tan in color with multiple foci of hemorrhage.[9] Calcifications are uncommon, and only occur in approximately 20% of cases.[9] MA is composed of tightly packed uniform small epithelial cells with small regular nuclei, a high nuclei-to-cytoplasm ratio, and no mitotic figures. The differential diagnosis of renal MA includes PRCC and epithelial Wilm's tumor.[10-12] In our case, diffuse positive immunostaining of the tumor for CD57 and WT-1, weak or negative staining for cytokeratin 7 and EMA, negative immunostaining for racemase, and the lack of trisomy for chromosomes 7 and 17 argued against a diagnosis of PRCC, while the patient's age, lack of prominent nucleoli and mitotic activity in the tumor, and positive immunostaining for CD57 argued against a diagnosis of Wilm's tumor.[10-12]

Although MA is usually benign,[13] a few cases of metastatic disease have been reported.[1,6,14] Several diseases can resemble MA, but it is most important to distinguish MA from PRCC. Currently, neither ultrasound nor CT scans can reveal distinct features of MA. Ultrasound scans show both hyperechoic and hypoechoic regions, while CT scans show a non-distinct mass[4] with low attenuation on contrast studies.[13] Fine needle aspiration can be used as another less invasive method to diagnose MA, but it is not as accurate as nephrectomy. Cytological diagnosis using fine needle aspiration can be difficult.[15] Despite being a benign lesion, MA should be routinely resected in order to confirm the diagnosis and rule out PRCC. In our case, continued growth of the tumor would also have caused morbidities more severe than frequent urination, urinary tract infections, and flank pain.

Patients with MA profiles similar to that of our patient have remained tumor-free for four to five years after nephrectomy.[3] Based on this previous clinical experience and the well-differentiated nature of MA epithelial cells, we believe that the present case of MA will follow a benign course. A reliable postoperative differentiation of MA and PRCC is relevant to appropriate clinical management, specifically with regard to the benefit of adjuvant therapy. In our case, no additional adjuvant therapy was required.

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