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Case Report

Adult onset wilms tumor ☆

Madhangi Parameswaran, MBBS[a,e], Alison M. Friedmann, MD[b,e], Gregory M. Cote, MD, PhD[c,e], Keyan Salari, MD, PhD[d,e], Mukesh G. Harisinghani, MD[a,e], Rory L. Cochran, MD, PhD[a,e,]*

[a] *Department of Radiology, Massachusetts General Hospital, Boston MA*
[b] *Department of Pediatrics, Massachusetts General Hospital for Children, Boston MA*
[c] *Department of Medicine, Mass General Brigham Cancer Center, Boston MA*
[d] *Department of Urology, Massachusetts General Hospital, Boston MA*
[e] *Harvard Medical School, Cambridge MA*

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ABSTRACT

Wilms tumor (WT) is the most common primary renal malignancy in the pediatric population and has very good overall survival with contemporary treatment protocols. In contrast, WT in adults is extremely rare and is associated with a poorer prognosis. The clinical presentation and imaging features of WT in adults are nonspecific and overlap with other more common forms of renal cancer, often leading to a delay in diagnosis. Here we describe the imaging findings of a 27-year-old female with WT initially presenting with hematuria, right lower quadrant pain and fever.

Introduction

Nephroblastoma, or Wilms tumor (WT) as it is more commonly referred to, is the most common renal malignancy in children comprising more than 90 % of malignant renal tumors in pediatric patients and primarily affecting children younger than 5 years of age [1,2]. Females and individuals of African descent are more commonly affected, and there is a lower incidence amongst the East Asian population [2]. While multiple heritable syndromic associations with WT are well established (e.g. WAGR, Denys-Drash, Beckwith-Wiedemann, etc.), the sporadic form is most common [3]. WT is most commonly solitary; however, up to nearly 10 % of cases may be bilateral, which is more commonly associated with the syndromic form [3]. WT is thought to arise from disrupted metanephric mesenchymal development during embryogenesis and persistent nephrogenic rests. In contrast to children, WT in adults is extremely rare with an incidence of less than 0.2 cases per million per year [4]. Despite the very good prognosis of pediatric patients with 5- and 10-year survival rates exceeding 90 %, prognosis in adults is less favorable [5]. Unfortunately, the clinical presentation and imaging features of WT in adults is nonspecific, which may lead to a presumed diagnosis of renal cell carcinoma (RCC), the most common malignant renal tumor in adults. Some experts have posited that delay

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* Corresponding author.
E-mail address: rcochran@mgh.harvard.edu (R.L. Cochran).

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in diagnosis may contribute to the poorer outcomes amongst adults [6]. Here we present a sporadic case of WT in a young female who presented with hematuria.

Case report

A 27-year-old female with no significant past medical history presented with gross hematuria, right lower quadrant pain and a low-grade fever. Prior to presentation the patient was evaluated at an urgent care facility for hematuria, for which she was treated with a 5-day course of empiric nitrofurantoin for presumed urinary tract infection. Following the course of antibiotics her hematuria recurred, and she developed new right lower quadrant pain, prompting presentation to the emergency department for further evaluation. At presentation her examination was notable for a fever to 38.8°C and tenderness to palpation over the right upper quadrant and right suprapubic region. Urinalysis revealed 2+ blood, but no evidence of infection and urine beta-human chorionic gonadotropin (β-hCG) was negative. Laboratory analyses demonstrated a normal leukocyte count and mild anemia with a hemoglobin of 11.2 g/dL (normal: 12.0-16.0 g/dL) and hematocrit of 33.2 % (normal: 36-46 %). Renal and hepatic function testing were normal.

Initial abdominopelvic imaging was performed with a noncontrast CT which revealed a large heterogeneously attenuating right renal mass with foci of intra-lesional hyperattenuation and ipsilateral retroperitoneal edema (Fig. 1). No nephrolithiasis or hydronephrosis was present, and the left kidney appeared normal. A subsequent contrast enhanced CT was performed which revealed a 10.2 cm heterogeneously enhancing expansile mass in the upper pole of the right kidney with invasion of the collecting system, right renal vein and inferior vena cava (IVC) (Fig. 1). A subsequent contrast enhanced

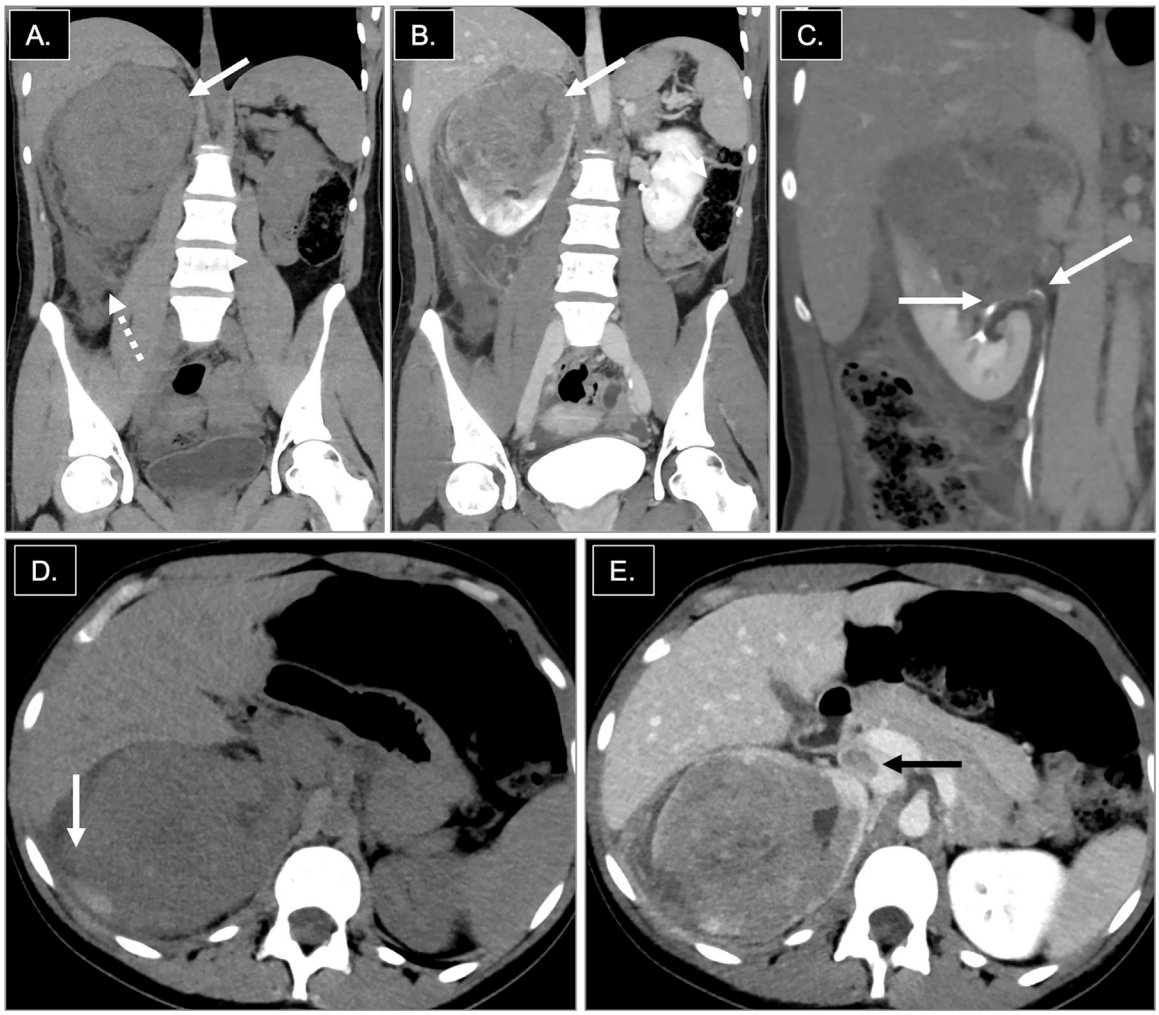

Fig. 1 – Computed tomography. (A) Noncontrast coronal CT image demonstrating an expansile right upper pole renal mass (solid white arrow) and surrounding perinephric edema (dashed white arrow). (B) Nephrographic phase postcontrast coronal CT image demonstrating heterogenous hypo-enhancement of the renal mass (solid white arrow). (C) Postcontrast coronal CT image demonstrating collecting system invasion (solid white arrows). (D) Noncontrast axial CT image demonstrating hyperattenuating intra-lesional components associated with the mass (solid white arrow), most consistent with intralesional hemorrhage. (E) Postcontrast axial CT image demonstrating IVC invasion (solid black arrow).

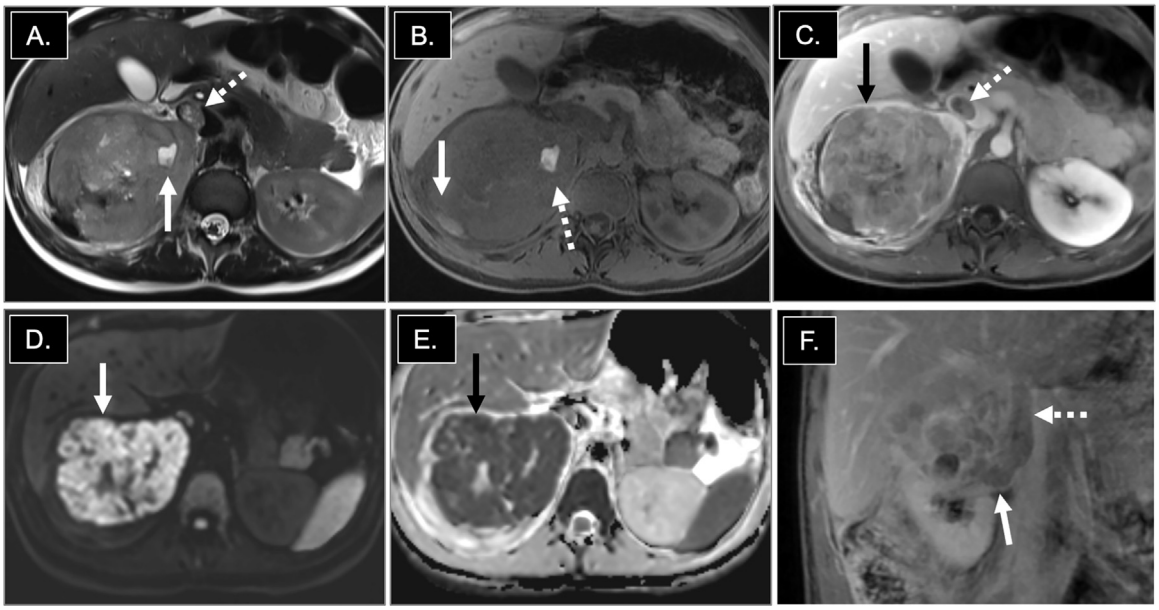

Fig. 2 – Preoperative abdominal MRI. (A) T2-weighted axial images through the level of the kidneys demonstrating a large heterogeneous mass with areas of intralesional cystic change (solid white arrow) and intravascular invasion into the IVC (dashed white arrow). (B) Fat-saturated T1-weighted axial image at the same level demonstrating intralesional hemorrhage (solid white arrow) and hemorrhagic/proteinaceous material associated with the cystic focus in panel A (dashed white arrow). (C) Postcontrast fat-saturated T1-weighted axial image illustrating mass hypoenhancement (solid black arrow), relative to surrounding normal parenchyma, and enhancing IVC tumor thrombus (dashed white arrow). (D) axial diffusion weighted (b = 1500 s/mm2) and (E) apparent diffusion coefficient (ADC) images demonstrating marked diffusion restriction associated with the mass. (F) Postcontrast fat-saturated coronal image demonstrating renal vein (solid white arrow) and IVC tumor thrombus (dashed white arrow).

abdominal MRI was performed, which again revealed a large, enhancing and markedly diffusion restricting right upper pole renal mass, evidence of intra-lesional hemorrhage, tumoral extension into the collecting system and invasion of the renal vein and IVC below the level of the hepatic veins (Fig. 2). Staging chest CT demonstrated nonspecific bilateral solid pulmonary nodules (not shown). Constellation of findings were deemed suspicious for RCC with level 2 IVC tumor thrombus, and she promptly underwent a robotic-assisted laparoscopic right radical nephrectomy with IVC tumor thrombectomy and right renal hilar lymphadenectomy. The postoperative course was uncomplicated, and she was discharged home on postoperative day 3.

Surgical pathology demonstrated WT1-N, WT1-C and CD56 positive tumor staining, a triphasic tumor with predominantly blastemal elements and diffuse anaplasia. Renal vein and IVC tumor thrombus were confirmed and there was no tumor in the one lymph node that was removed. Cytogenetics revealed multiple genomic abnormalities, including monoallelic loss of WT1. Genomic sequencing revealed the following tumor mutations: ASXL1 p.Q623Cfs*81 22.9 % (CCDS13201.1), EPHA7 p.L535P 39.5 % (CCDS5031.1), FANCC p.K231del 43.1 % (CCDS35071.1), and TP53 c.782+1G>A Splice Site Donor 75.9 % (CCDS11118.1). Postoperative re-staging abdominopelvic imaging performed 2 months later revealed expected postoperative changes within the nephrectomy bed without local recurrence. However, thoracic imaging revealed interval enlargement of the previously present pulmonary nodules, rendering them highly suspicious for lung metastases. A multidisciplinary team was convened for her care which included urology, radiation oncology, medical and pediatric oncology specialists, and she subsequently began chemotherapy and radiation. At the time of this writing, she has had no abdominal recurrence and complete response at the sites of disease in the thorax. She was also referred for genetic counseling, which is pending.

Discussion

WT is the most common renal malignancy of childhood with established germline genetic predisposition and syndromic associations [1,2]. However, WT is exceedingly rare in adults, presumably related to its origins as an embryonal malignancy. Indeed, WT is a prototypical example of the complex interplay between the cellular pathways involved in genitourinary development and tumorigenesis, as the majority of genomic and epigenomic alterations characterized in WT tumorigenesis are involved in growth factor signaling and gene expression [3]. WT demonstrates a triphasic pattern on histology with blastema, epithelial and stromal tissues [7]. The blastemal component, which contains small round blue cells, is the most undifferentiated component and is considered to be higher

risk [7]. Additionally, the presence and degree of anaplasia is considered to be a very important prognostic factor for predicting unfavorable outcomes [8]. Unfortunately, our patient presented here had a higher blastemal component and diffuse anaplasia.

The presentation of WT differs between adults and children; while children are typically asymptomatic, adults often present with one or more symptoms most commonly including abdominal or flank pain, constitutional symptoms, hematuria and hypertension [6]. Imaging plays an important role in the diagnostic workup of patients with WT, yet definitive diagnosis of WT is made at histopathology, as the imaging features of WT are nonspecific. By ultrasound, WT often appears as a large heterogeneous renal mass of variable echogenicity which corresponds to the areas of soft tissue, hemorrhage and necrosis. When ultrasound is performed, careful inspection with gray scale and color Doppler should be performed of the renal vein and IVC to assess for tumoral invasion [9]. Tumor in vein will typically appear as an echogenic filling defect within the vessel with varying degrees of flow on Doppler.

While ultrasound is helpful, CT may be the first imaging modality in adults to identify the tumor, as in the case presented here where CT was performed for suspected nephrolithiasis. Tumors in adults are most commonly expansile and large at presentation, with one series reporting a mean size of 13.1 cm at presentation [10]. For very large tumors abutting adjacent structures, the *claw sign* can be used as a reliable tool for establishing intrarenal origin [11]. WT will commonly harbor cystic and hemorrhagic components [10]. Other tumor types in young adults demonstrating hemorrhage include primary Ewing sarcoma of the kidney and renal medullary carcinoma[12]. WT is typically hypoenhancing relative to surrounding normal renal parenchyma and uncommonly harbors calcification [10,12]. CT or MRI with intravenous contrast should be performed to evaluate for venous invasion as well as other intraabdominal disease. In children approximately 11 % of cases harbor intravascular tumor [13]. In the case series by Wu et al., approximately 19 % of adult patients had venous invasion [10]. By MRI, WT most commonly appears iso- or hypointense on T2 weighted images and may harbor foci of T2 hyperintensity corresponding to areas of cystic change. On T1 weighted images tumors will often appear isointense and may harbor foci of intrinsic T1 hyperintensity corresponding to sites of hemorrhage [10,12]. Additionally, WT typically demonstrates restricted diffusion on diffusion weighted images [13,14]. Completion of staging is typically completed with addition of a CT of the thorax, as pulmonary metastases are common.

Standardized staging and treatment of WT in adults is based on the consensus guidelines extrapolated from pediatric patients using the Children's Oncology Group (COG) and the International Society of Pediatric Oncology (SIOP) management strategies [6]. Tumor resection with nephrectomy is the mainstay for patients with operable disease followed by adjuvant chemotherapy ± radiation therapy depending on stage and histology. In patients with inoperable disease, chemotherapy and radiation are the primary modes of treatment, with delayed surgical resection [6].

The incidence of renal tumors in young adults (<40 years) has increased in recent years, which may be in part due to earlier discovery with increased utilization of cross sectional imaging [15]. Interestingly, the distribution of tumor types differs amongst young adults with RCC comprising a smaller proportion compared to older adults [16]. This difference has important implications for diagnosis, influencing when it may be appropriate to perform preoperative tissue sampling and when genetic counseling and germline mutation testing should be considered [16]. At imaging, interpreting radiologists may want to consider broadening their differential diagnosis when large (>10 cm) renal tumors are encountered in young adults (<40 years).

Conclusion

WT is a very rare form of renal cancer in adults and is often not considered in the differential diagnosis of a renal mass. When confronted with a young adult (<40 years old) with a large (>10 cm) renal mass, vascular invasion, intralesional cystic change and hemorrhage, a diagnosis of WT is possible.

Patient consent

Informed consent for publication of the described clinical history was obtained from the patient.

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