

## Oncology

# Growing Renal Mass: Lessons Learned on the Road From an Atypical Presentation to Successful Therapy



Eliza Lamin<sup>a,\*</sup>, Dana A. Weiss<sup>b,c</sup>, Kassa Darge<sup>c</sup>, Fumiko Dekio<sup>d</sup>, Douglas A. Canning<sup>b</sup>

<sup>a</sup> Division of Urology, University of Pennsylvania Health System, Philadelphia, USA

<sup>b</sup> Division of Urology, The Children's Hospital of Philadelphia, Philadelphia, USA

<sup>c</sup> Department of Radiology, The Children's Hospital of Philadelphia, Philadelphia, USA

<sup>d</sup> Department of Pathology, The Children's Hospital of Philadelphia, Philadelphia, USA

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## ABSTRACT

A 25 4/7 week boy was born with a prenatal diagnosis of polyhydramnios and enlarged left kidney. Over the next 2 months serial ultrasounds demonstrated abnormal growth of the kidney, with 28.9% split function. At gestational age 39 4/7, he underwent a left radical nephrectomy. Pathology revealed congenital mesoblastic nephroma with mixed classic and cellular features. This case was puzzling due to prenatally diagnosed renal enlargement in a premature infant and inconclusive post-natal ultrasonographic imaging. Although the patient had paraneoplastic signs of polyhydramnios and hypertension, the mass did not have a classic appearance of CMN; possibly due to severe prematurity.

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## Case report

A 32 year-old G2P0 woman with polycystic ovarian syndrome presented for a 20-week gestational ultrasound (US). This demonstrated a male fetus with an enlarged left kidney and moderate polyhydramnios. At 25 4/7 weeks the woman went into premature labor and delivered a 1 kg infant. The boy was intubated emergently for surfactant delivery. Over the next 5 days he developed hypertension and was started on antihypertensive medications. In addition blood cultures grew gram-positive cocci, so he was started on vancomycin and gentamicin. The following day he developed oliguric renal failure, and was transferred to a tertiary care Center Pediatric Hospital. A renal US on day of life 7 demonstrated abnormal enlargement of the left kidney (volume of 36.9 ml vs. 5.7 ml on the right), with apparent perinephric fluid, but no focal parenchymal lesions, no hydronephrosis, no abnormality in

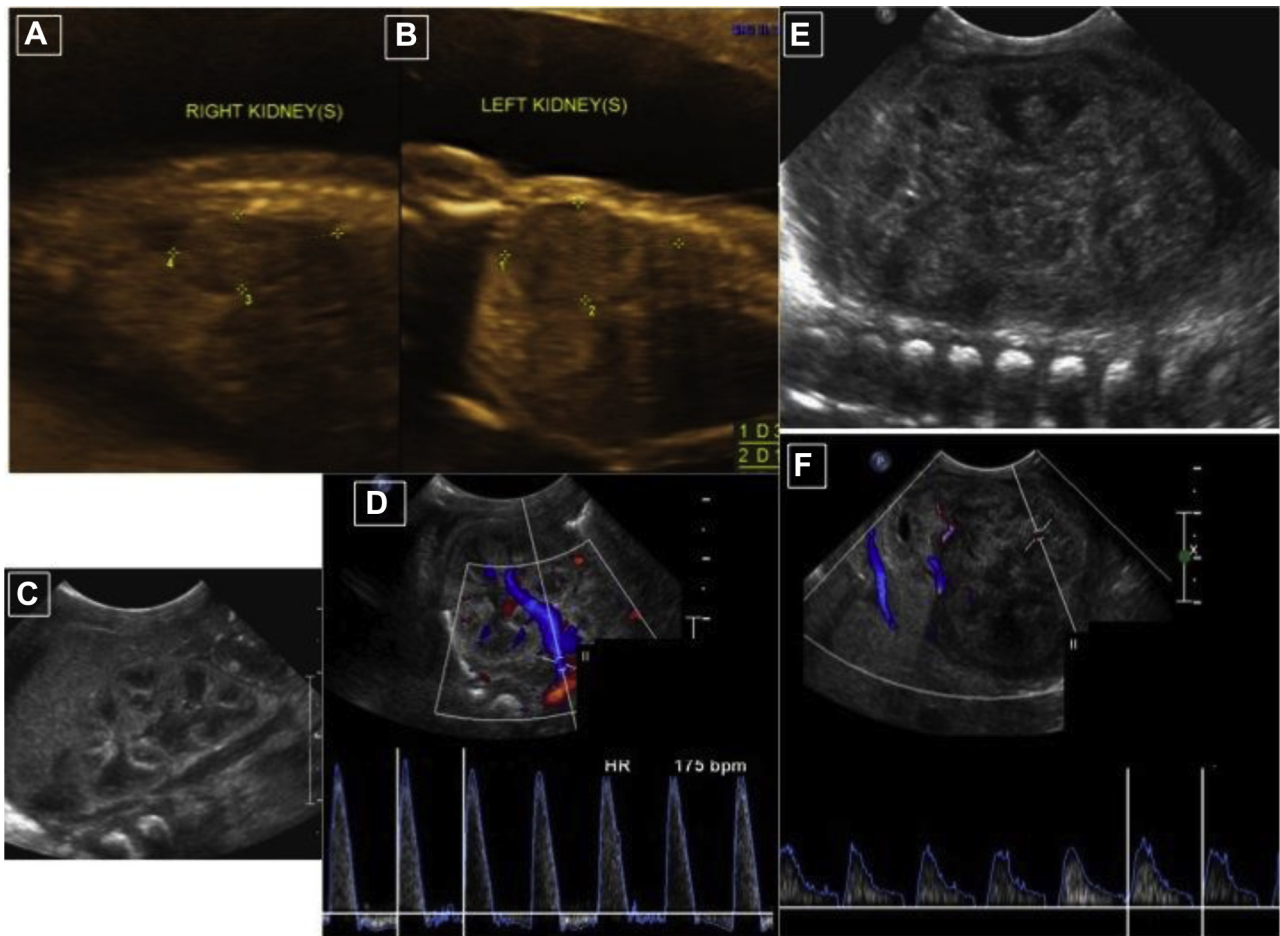
corticomedullary differentiation. Dopplers showed preserved perfusion, with elevation of the peak systolic velocities and loss of diastolic flow. The main renal vein and artery were patent. While the right kidney appeared normal, the Doppler US also showed reversal of diastolic flow with elevation of peak systolic velocities (Fig. 1). These findings, in conjunction with the antenatal finding of an enlarged left kidney and the current oliguric renal failure, were thought to represent an early vascular insult with bilateral renal venous thrombosis and subsequent recanalization of the right, and worse injury to the left. 3 days later a repeat US showed improved spectral Doppler waveforms on the right but persistent elevation of peak systolic velocities on the left, still thought to be due to a chronic vascular insult.

The patient's increasing abdominal girth prompted serial US over the following 2 months. The left kidney lost all corticomedullary differentiation by day 20 of life, and grew from a volume of 37.4 ml to 52.7 ml and finally to 197.7 ml, while the right remained a normal size of 17.7 ml by day of life 87. At this time, due to the increasing size of the left kidney causing pulmonary compromise, urology was consulted for potential nephrectomy. A DMSA study showed 30% function on the left, and a CT scan demonstrated a massive left renal mass displacing the aorta and vena cava to the right, but with no vascular involvement or signs of metastatic disease<sup>1</sup> (Fig. 2). On day of life 93, and gestational age 39

Abbreviations: US, ultrasound; CMN, congenital mesoblastic nephroma; RVT, renal venous thrombosis.

\* Corresponding author. Tel.: +1 2674960162.

E-mail address: [Eliza.lamin@uphs.upenn.edu](mailto:Eliza.lamin@uphs.upenn.edu) (E. Lamin).



**Figure 1.** (A/B) Antenatal US at 20 4/7 weeks. R:  $2.7 \times 1.2$  cm; L:  $3.5 \times 1.9$  cm. (C/D) DOL 6 (26 3/7 weeks actual age). Color Doppler Ultrasonography – R:  $3.0$  cm  $\times$   $1.8$  cm  $\times$   $1.1$  cm; Elevated peak systolic velocity of 313 cm/s. (E/F) DOL 6 (26 3/7 weeks actual age). Color Doppler Ultrasonography – L  $5.4$  cm  $\times$   $3.8$  cm  $\times$   $1.8$  cm; Elevated peak systolic velocity of 35.9 cm/s.

4/7, the infant was taken to the operating room for a left radical nephrectomy and local lymphadenectomy. Pathologic analysis identified a congenital mesoblastic nephroma (CMN), with mixed classic and cellular features (Fig. 3).

## Discussion

CMN's are the most common tumor in the first 3 months of life, and make up 5% of all pediatric renal tumors,<sup>2–4</sup> with a male predominance of 1.5–2:1.<sup>1</sup> CMN's often present with a palpable abdominal mass, polyhydramnios, and premature delivery, and babies may have hypertension and hypercalcemia. These findings are due to increased renin levels in the kidney leading to hypertension, as well as secretion of prostaglandin and parathyroid-hormone-like substance leading to the hypercalcemia.<sup>5</sup> Our patient had several of these findings, but also several others, which caused ambiguity in his presentation.

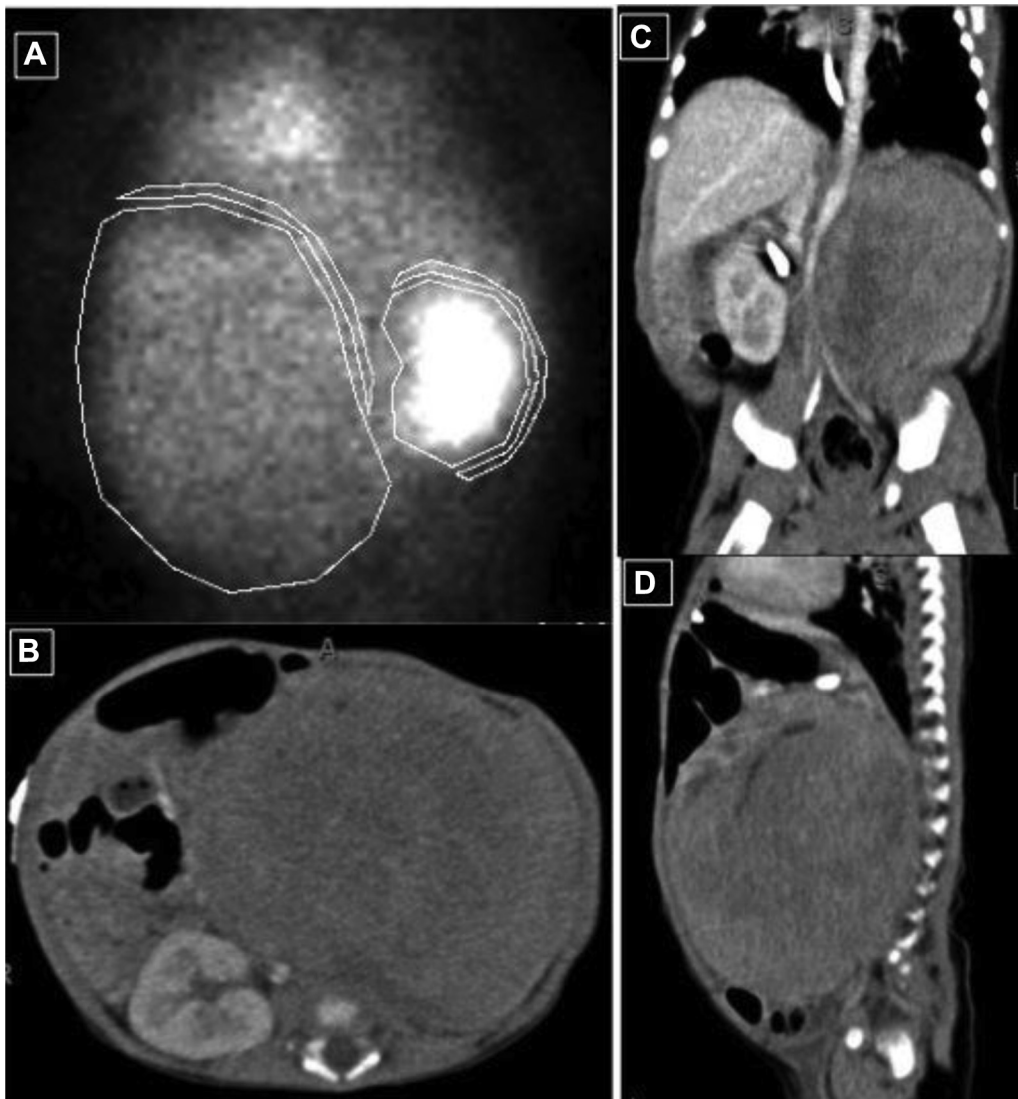
The antenatal US presented an enlarged left kidney and moderate polyhydramnios. The initial postnatal renal US showed bilateral renal vascular changes with bilateral reversal of diastolic flow, which, in the absence of systemic cardiac abnormalities, seemed consistent with a vascular insult, such as renal venous thrombosis (RVT). In the acute phase, RVT presents with renal enlargement, hematuria, and hypertension.

In retrospect, the antenatal enlargement of the kidney in this baby was due to a mass rather than congestion from a renal venous thrombosis, and the perinephric fluid was actually a hypoechoic rim which can be seen in classic CMN's – a cluster of findings that were misleading to the radiologists.<sup>3</sup>

The appearance of CMN's may correlate with the pathology of the tumor. While the hypoechoic ring and solid mass are suggestive of a classic pathology, a cystic mass with foci of hemorrhage more often correlates with a cellular variant.<sup>3</sup> CMN's can also grow rapidly and relentlessly, causing significant mass effect on surrounding organs. Because most of these tumors are resected soon after diagnosis, the rate of growth is not often so apparent as in this case.

The Doppler US findings were very misleading: not only were they bilateral, but the diastolic reversal in the absence of cardiac findings is often correlated with a renal vascular injury, and when the vascular changes improved with no morphologic change of the kidneys, this seemed to confirm this assessment. Moreover, in later stages of RVT, swelling occurs and the kidney becomes heterogeneous with loss of corticomedullary differentiation and may be surrounded by an echo-poor halo. However, the renal enlargement generally regresses after 2–3 weeks.

The pathology, which showed mixed classic and cellular CMN, serves as a reminder that while generally considered a benign tumor, CMN's are classified into 3 histological variants: classic,



**Figure 2.** (A) Age: DOL 88. DMSA renal scan showing R with 70.2% and L with 29.8% function (per total volume). (B–D) Age: DOL 90. Non-contrast CT scan in axial (B), coronal (C), and sagittal (D) planes: 8.5 cm × 7.5 cm × 8.9 cm. No vascular involvement.

cellular, and mixed. Classic CMN comprises 24% of all the CMN. It is morphologically identical to infantile fibromatosis and histologically it is characterized by interlacing fascicles of fibroblastic cells with thin tapered nuclei, pink cytoplasm low mitotic activity, with an abundant collagen deposition.<sup>3</sup> Infantile fibromatosis are lesions which consist of fibroblasts that are recurring and rapidly growing, but non-metastatic and can occur anywhere.<sup>6</sup>

Cellular CMN, which comprise around 66% of cases, is morphologically identical to infantile fibrosarcoma. Infantile fibrosarcoma is a malignant tumor of fibroblasts found in children of the same age.<sup>7</sup> Rather than being composed of bland spindle cells as the classic variant, has much larger nuclei, is hypercellular, and has increased mitotic activity with frequent necrosis. This variant can be more unpredictable and may be more aggressive with increased risk of local recurrence or even rare metastases.<sup>1,3</sup>

The cellular variant may more often present with hypertension, increased size even leading to respiratory compromise. Both tumors are treated with resection, which confirms the pathology of the mass and is also the sole treatment modality for most tumors.

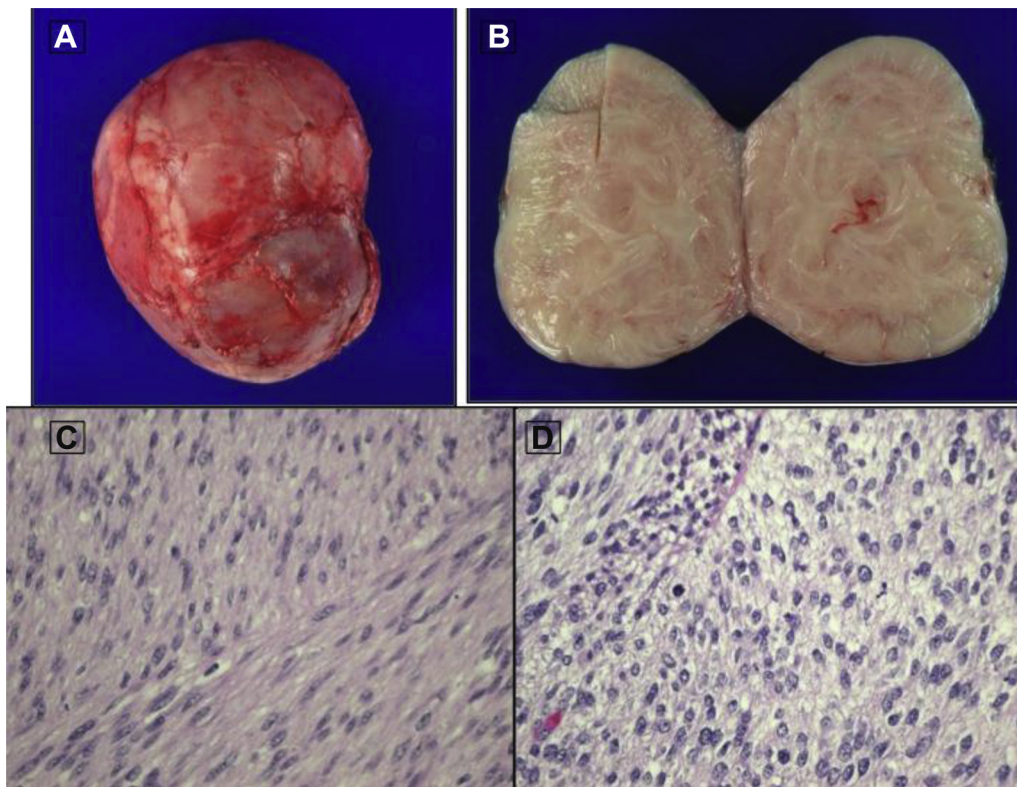
Because cellular variants are known to have more risk of recurrence, these should undergo surveillance studies more often than classic variants.

The finding of unilateral renal enlargement in the antenatal period presents a differential diagnosis that includes a renal venous thrombosis, cystic changes, ureteropelvic junction obstruction or a renal mass. At the time of the first postnatal ultrasound, when the infant was only 26 3/7 weeks old, the finding of bilateral abnormal diastolic waveforms in the absence of significant cardiac disease skewed the differential to a vascular etiology.

### Conclusion

CMN's can have atypical presentations, especially in premature infants, which may give the appearance of a vascular injury, including bilateral vascular changes in the absence of cardiac findings, a lobulated reniform kidney and a hollow ring giving the appearance of perinephric fluid. In any infant with an enlarging kidney, a high index of suspicion for tumor must be retained, with a broad differential diagnosis including CMN, Wilms, or less common





**Figure 3.** (A) Size:  $10 \times 8 \times 8$  cm; 308.22 g. (B) Tumor extended through renal capsule into perirenal fat with renal sinus soft tissue involvement; 0/10 LN involved. (C) Classic type: Majority was classic mesoblastic nephroma with a bland spindle cell proliferation and few mitoses. (D) Cellular type: Several foci of more cellular areas, with higher nucleocytoplasmic ratio and increased mitotic activity.

tumors including rhabdoid tumor, clear cell sarcoma, renal cell carcinoma, angiomyolipoma, and ossifying renal tumor of infancy.

#### Conflict of Interest

None of the authors have any conflict of interest to disclose.

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