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# Primary renal sarcoma with *BCOR-CCNB3* gene fusion in an 18-year-old male: a rare lesion with a diagnostic quandary

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## Abstract

Primary renal sarcoma with *BCOR-CCNB3* gene fusion is a rare tumor with only 7 cases reported in English literature. The morphologic features of this tumor strikingly overlap with clear cell sarcoma of the kidney and synovial sarcoma. Accurate diagnosis can be challenging. In this article, we report a case of an 18-year-old male who presented with hematuria. Subsequent imaging study showed a left renal mass with level II (infra-hepatic) inferior vena cava (IVC) thrombus, which was resected. Detailed pathologic findings, immunohistochemical and molecular studies revealed an ovoid to spindle cell renal mass with a *BCOR-CCNB3* gene fusion.

### Keywords

Primary renal sarcoma; *BCOR-CCNB3* gene fusion

## Introduction

*BCOR-CCNB3* fusion sarcomas are a subclass of Ewing-like sarcoma of bone and soft tissue that presents in older children with primitive round to spindle tumor cells[1]. Primary renal *BCOR-CCNB3* sarcoma was consecutively reported in cohorts of clear cell sarcoma of the kidney (CCSK)[2–3]. Several small case serieshave subsequently been published[4–5] and a total of 7 cases, including five pediatric and two adult cases, have been described in English literature. Accurate diagnosis can be challenging, because of the overlapping morphologic features and lack of awareness amongst practicing pathologists due to its rarity. We present an 18-year-old male with an ovoid to spindle cell renal mass with a *BCOR-CCNB3* gene fusion identified by RNA sequencing.

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## Case report

An 18-year-old male presented with hematuria and was found to have a left renal mass with level II (infra-hepatic) inferior vena cava (IVC) thrombus (Figure 1). MR imaging showed a well-encapsulated, solid mass with homogenous appearance except focal area of hemorrhage. Cystic spaces were noted within the tumor thrombus only. Chemical shift images demonstrated no intratumoral fat. He underwent radical nephrectomy and thrombectomy. Close observation with MRI imaging every 3 months was indicated and he has no evidence of disease 6 months after surgery.

### GROSS FEATURES

Grossly, an 8.4 cm tumor exhibited a smooth lobulated pale pink-tan cut surface with areas of hemorrhage (Figure 2A).

### HISTOLOGY

The tumor was comprised of predominantly high cellularity (Figure 2B–2C) focally alternating with hypocellular areas in which discohesive tumor cells were embedded in myxoid stroma (Figure 2D). Hypercellular areas showed sheets of uniform cells with oval to spindle nuclei, open chromatin, indistinct cell borders, and moderate amounts of cytoplasm (Figure 2B–2C). Angulated thin-walled vessels and entrapped renal tubules were present (Figure 2E–2F). Mitotic figures were readily observed. No tumor necrosis was seen. The tumor thrombus showed similar morphology within cystic areas (Figure 2G).

### IMMUNOHISTOCHEMISTRY (IHC)

Tumor cells showed diffuse strong immunoreactivity for TLE1 (transducing like enhancer of split), cyclin D1 (Figure 2H), and BCL2 (B-cell lymphoma 2), and were negative for PAX-8 (paired box-8), pan-cytokeratin (AE1/AE3), CD34, CD31, STAT6 (signal transducer and activator of transcription-6), smooth muscle actin, desmin, S100, cytokeratin7, WT-1, and cathepsin-K.

### MOLECULAR FINDINGS

Fluorescence in-situ hybridization (FISH) for *SS18* gene rearrangement was negative. Subsequently, RNA sequencing revealed a *BCOR-CCNB3* fusion transcript (Figure 2I).

## Discussion

Primary renal *BCOR-CCNB3* fusion sarcoma is a rare entity that has recently been reported in four small case series (2–5). All seven cases have occurred in males (age range: 8–46 years: median age: 12 years). The majority of the patients presented with large renal masses (>12 cm), two of whom had IVC involvement[4]. Follow up was available in five patients and one case had abdominal recurrence 15 months after nephrectomy. The morphology varies but predominantly consists of uniform spindle to oval cells with swirling growth patterns. Two tumors with extensive cystic change have been reported[3]. The clinicopathologic spectrum of primary renal *BCOR-CCNB3* fusion sarcoma is not well established and awareness of it in the differential diagnosis of renal sarcoma need to be emphasized.

We report the eighth primary renal sarcoma with *BCOR-CCNB3* fusion. The tumor demonstrated overlapping clinicopathologic and immunophenotypical features with other entities. The tumor radiographically appeared hypercellular and vascular but imaging findings were not typical for common histologic types of renal cell carcinoma or angiomyolipoma. Histologically, our case exhibited overlap with CCSK and renal synovial sarcoma (RSS). CCSK is the second most common primary renal malignancy of childhood, characterized by *BCOR* exon 15 internal tandem duplications in most cases and *YWHAE-NUTM2* fusion in few others. CCSK has a broad morphologic spectrum with nine major histologic patterns, including classic, myxoid, sclerosing, cellular, epithelioid, palisading, spindle, storiform and anaplstic[6].The classic morphology is usually present, at least focally, which includes plump ovoid cells arranged in broad trabecula or nests, separated by regularly spaced and arborizing fibrovascular septa. The distinctive vasculature of CCSK features “chicken-wire” capillary, either thin-walled or encased within amply thickened fibrocollagenous bands; this was observed in our case. Several studies have demonstrated closer relationship between CCSK and primary *BCOR-CCNB3* fusion sarcoma by gene expression profiling[2–3] and the consistent diffuse immunoreactivity for BCOR protein[7–8]. Most RSSs are composed of sheets or nests of infiltrative spindle cells with scant cytoplasm and indistinct cell borders. Overlapping immunoprofile among these three entities includes immunoreactivity for BCOR, TLE1, and cyclin D1, for example, strong and diffuse BCOR immunoreactivity in primary *BCOR-CCNB3* fusion sarcoma, CCSK and 50% RSSs and 80% CCSKs reportedly positive for TLE1[3]. Accurate diagnosis is important because the clinical course and treatment regimens are different among them. CCSK tends to metastasize to bone, brain, and unusual sites and is associated with late recurrence. Treatment regimens for CCSK incorporate the use of doxorubicin, with its attendant risk of cardiotoxicity, nephrotoxicity and fertility problems.

Immunohistochemistry is of limited value in primary renal sarcoma. BCOR, TLE1, and cyclin D1 can be positive in RSS, CCSK and *BCOR-CCNB3* fusion sarcoma. Ultimately, molecular analysis by FISH or RNA sequencing is needed to resolve this differential as well as identify potential targetable molecular alterations. Early recognition by pathologists of tumor morphologies is paramount in facilitating the diagnosis and guiding treatment regimen of patients.

In summary, we present a primary renal *BCOR-CCNB3* fusion sarcoma with detailed morphologic description to emphasize the importance of including it in the differential diagnosis of primary renal sarcoma. Proper immunohistochemical and molecular work up play an important role in establishing the correct diagnosis.

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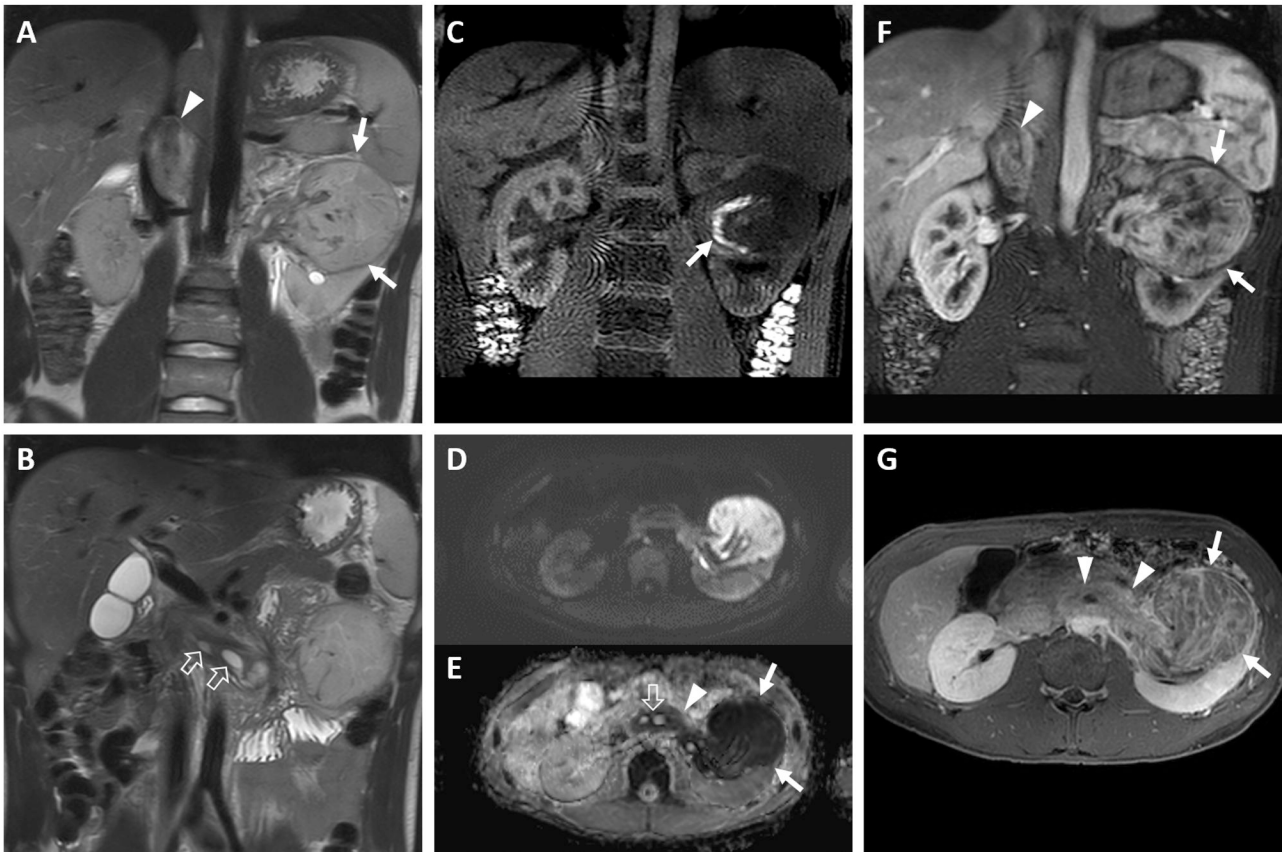


**Figure 1. Magnetic resonance imaging (MRI) findings.**

Coronal T2-weighted single-shot fast spin echo images (A, B) demonstrate a well-encapsulated left renal mass (arrows) with homogeneous signal intensity similar to that of renal parenchyma and tumor thrombus extending to the infra-hepatic inferior vena cava (IVC) (arrowhead). Cystic spaces within the tumor thrombus in the left renal vein (open arrows, B) were present. A focal area of hyperintensity on coronal T1-weighted pre-contrast spoiled gradient echo (SPGR) with fat saturation image (curved arrow, C) is consistent with focal hemorrhage. Note marked hyperintensity on axial diffusion weighted imaging (b= 800; D) and hypointensity on the apparent diffusion coefficient (ADC) map, indicative of high cellularity in the mass. Coronal T1-weighted images (same acquisition than C) during the corticomedullary phase (F) after administration of a bolus of gadobutrol (0.1mmol/kg body weight) shows intense heterogeneous enhancement in the mass (arrows) and tumors thrombus (arrowhead). Delayed axial T1-weighted SPGR acquisition with fat saturation (G) shows heterogenous washout in the mass (arrows) and tumor thrombus (arrowheads) compared to the renal parenchyma.

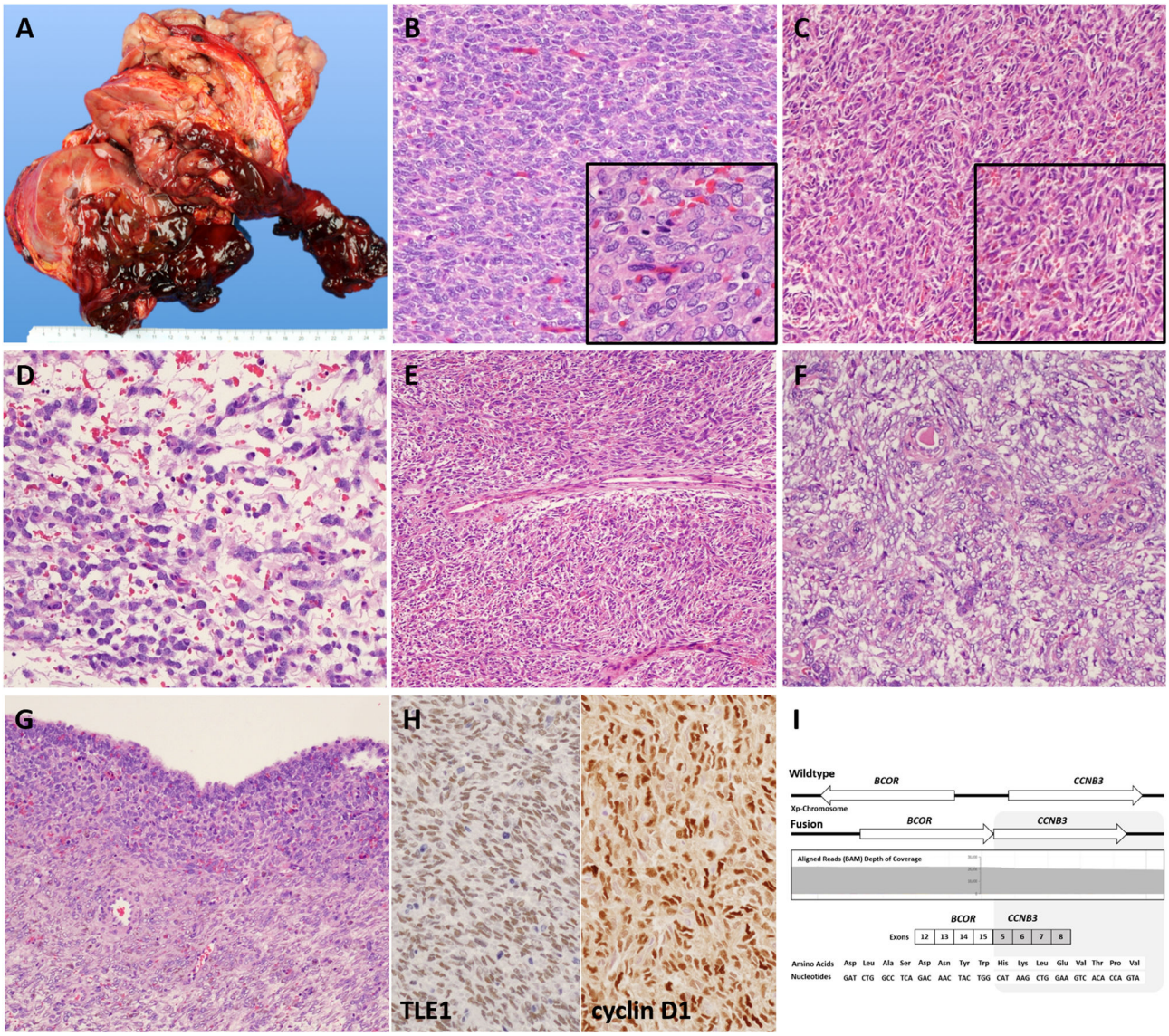


**Figure 2. Pathological and molecular findings of the renal mass.**

The tumor grossly showed smooth lobulated pale pink-tan cut surface with areas of hemorrhage (A). Microscopically, it was predominantly comprised of sheets of uniform cells with oval to spindle nuclei, open chromatin, indistinct cell borders, and moderate amounts of cytoplasm (B, C). Hypocellular areas in which discohesive tumor cells were embedded in myxoid stroma were focally seen (D). Angulated thin-walled vessels (E) and entrapped renal tubules (F) were present. Cystic areas were seen in tumor thrombus (G). Immunohistochemical expression of TLE1 and cyclin D1 were shown (H). RNA-seq detected BCOR-CCNB3 fusion in tumor cells (I).