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Primary Ewing's sarcoma of the kidney: a rare masquerader of renal cell carcinoma on imaging

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Abstract

Background: The Ewing sarcoma family of tumors comprises a group of high-grade small round cell tumors, including Ewing sarcoma of bone, extra-skeletal Ewing sarcoma, peripheral primitive neuro-ectodermal tumor (PNET), and Askin tumor (thoraco-pulmonary PNET). They are more prevalent in young children and adolescents. Ewing's Sarcoma is an aggressive tumor majorly described in bones. Primary renal Ewing's sarcoma is an extremely rare entity, characterized by a very aggressive course, with very few reported cases in the literature.

Case presentation: We present an 18-year-old girl who presented with sudden onset left flank pain and hematuria. The patient had histopathology-proven primary renal Ewing's sarcoma, which was initially misdiagnosed as renal cell carcinoma on imaging.

Conclusions: Owing to its non-specific radiological appearance, a high index of suspicion and a systematic approach is essential for detection of renal Ewing's Sarcoma.

Keywords: Renal Ewing's sarcoma, Ultrasound, Computed tomography, Magnetic resonance imaging

Background

All Ewing sarcoma family of tumors (ESFT) are characterized by small round blue cells on histology and show similar chromosomal translocations [1]. Fusion of the Ewing sarcoma gene on 22p12 with one of several related transcription factors, the most common (90%) being FLI1 on 11q24 is the common thread in all ESFTs [1]. All these tumors are of neuro-ectodermal origin [2]. Classically, Ewing's sarcoma is described as a tumor of long and flat bones. Extra-osseous Ewing's is a rare clinical entity. Rarer still is its manifestation as a primary renal mass, with a reported incidence of slightly more than 100 cases globally [3]. We report the case of an eighteen-year girl with biopsy-proven extraskeletal Ewing's sarcoma in the kidney, which was indistinguishable from renal cell carcinoma (RCC) on imaging.

Patient presentation

An 18-year girl, presented with sudden onset left-sided flank pain and hematuria, after minor trauma to the left flank. Her vitals were stable on presentation at the hospital. An ultrasound evaluation of the bilateral kidneys was done. There was an ill-defined iso-to slightly hypoechoic lesion seen in the upper pole of the left kidney with mass effect in form of compression and displacement of the renal sinus fat (Fig. 1). On Colour Doppler interrogation, there was no obvious vascularity seen in the mass (Fig. 1). The right kidney was normal (Fig. 1). Contrast-enhanced computed tomography (CECT) abdomen in renal protocol was done to characterize the mass. It showed a large hypo-dense, heterogeneously enhancing mass in the upper pole of the left kidney with few variable-sized calcified foci within and along the antero-superior aspect of the mass. No areas of internal hemorrhage or fat were appreciated. On the cortico-medullary phase, the mass appeared hypo-enhancing, compared to the remaining renal parenchyma, with internal non-enhancing necrotic

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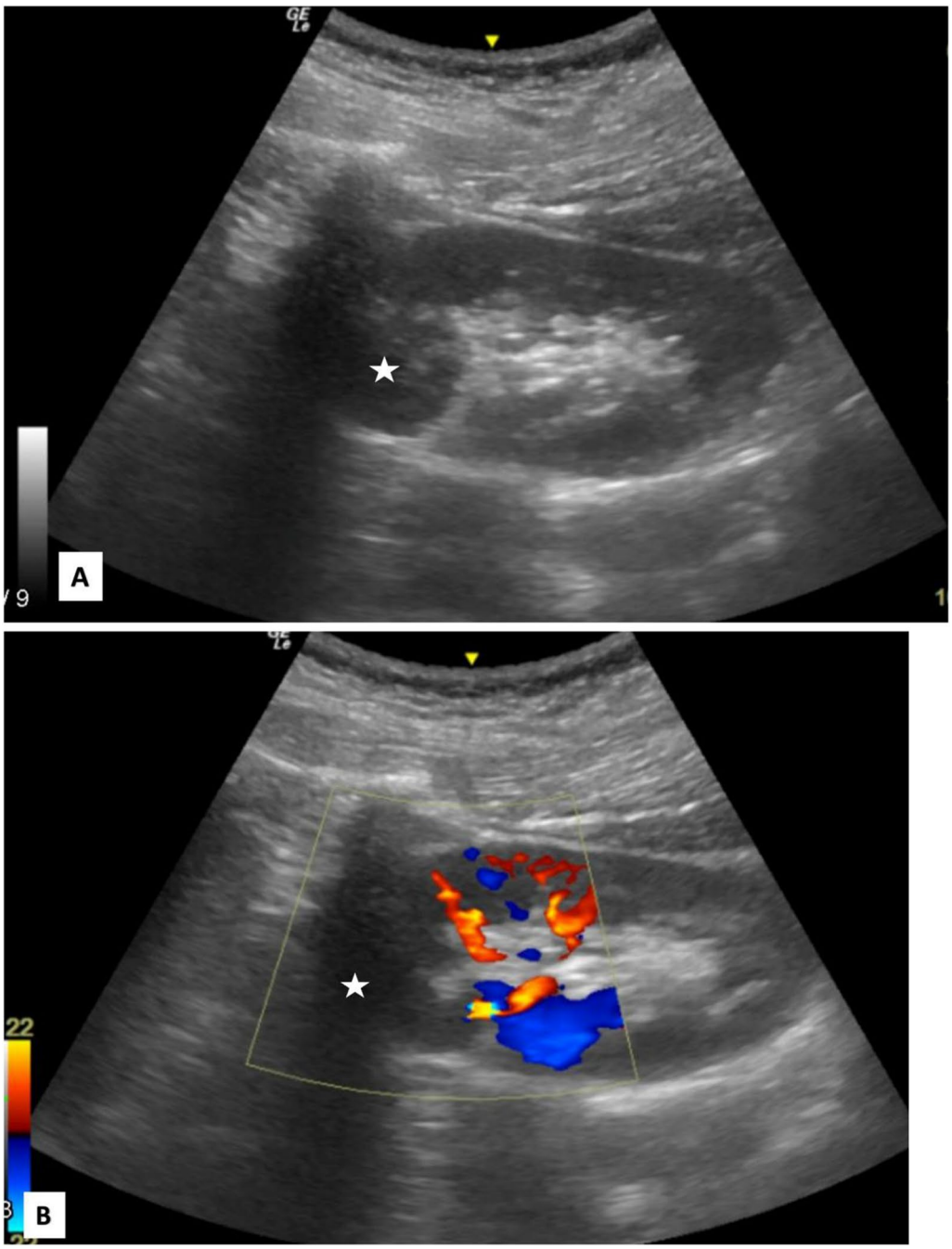

Fig. 1 **A** Sagittal Gray Scale Sonography image of the left kidney shows an ill-defined hypoechoic mass (asterisk) in the upper pole causing compression and displacement of the renal sinus fat. **B** Colour Doppler image, using low frequency curvilinear transducer does not show any obvious vascularity of the mass lesion (asterisk) in the upper pole of the kidney

areas (*tumor to aorta ratio: 0.33*) (Fig. 2). There was a progressive increase in enhancement in the nephrographic phase and in the delayed phase, the enhancing areas became isodense to the normal renal parenchyma (Fig. 2). The mass had invaded into the upper segmental renal veins, however, no thrombus or filling defect was seen in the left main renal vein and the inferior vena cava. There was extension of the mass into the anterior and posterior pararenal space, 11th left posterior intercostal muscles, left crus of the diaphragm, and the left

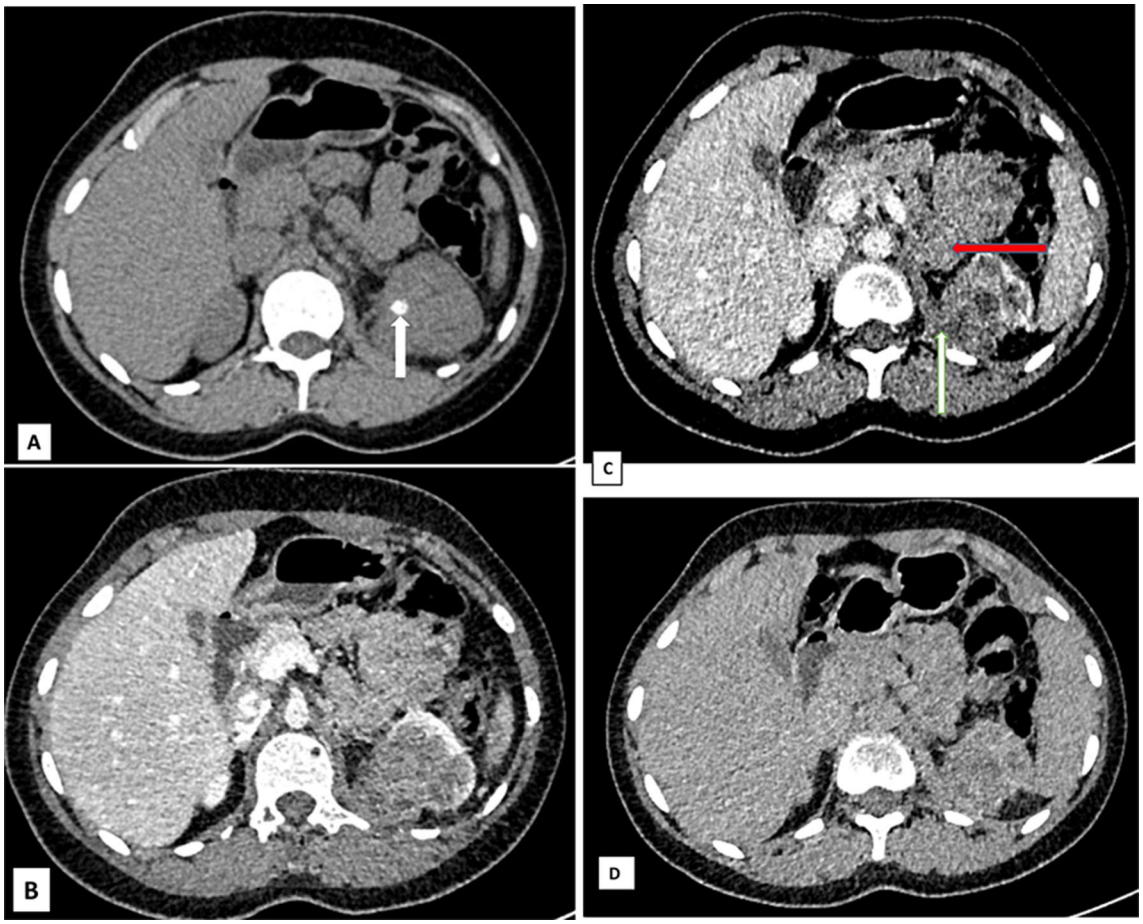

Fig. 2 **A** Axial non contrast CT shows an isodense mass lesion in the upper pole of the left kidney with an eccentric focus of calcification (arrow). **B** Axial CECT in cortico-medullary phase shows a hypoenhancing mass lesion in the upper pole of the left kidney, with internal non-enhancing necrotic areas. **C** Axial CECT in nephrographic phase shows progressive enhancement of the mass lesion in the superior pole of the left kidney. There is extension of the lesion into the left crus of the diaphragm (white arrow) and a metastatic para-aortic node (red arrow). **D** Axial CECT in delayed phase shows further progressive enhancement of the mass, appearing almost isodense with the adjacent renal parenchyma

psoas major muscle (Fig. 2). Few enlarged retroperitoneal nodes were seen, with a calcific focus noted in a necrotic renal hilar node. The scan on the bone window revealed few lytic and sclerotic lesions in the spine, pelvic bones, clavicle, and sternum (Fig. 3). Multiple rounded metastatic deposits were seen in the bilateral lung fields (Fig. 3). Based on the imaging findings, a provisional diagnosis of renal cell carcinoma was made.

The patient then underwent ultrasound-guided biopsy of the renal mass. Light microscopy showed multiple small round blue cells with a high nucleo:cytoplasmic ratio arranged in sheets (Fig. 4). On Immunohistochemistry (IHC), the tumor cells were positive for CD99 and negative for leukocyte common antigen (LCA), WT-1, CD-33, CD-20, Chromogramin, and Synaptophysin (Fig. 4). The pathology report suggested extra-skeletal Ewing's Sarcoma of the kidney. Being metastatic on presentation, the patient was started on combination chemotherapy comprising of Cyclophosphamide, Etoposide, and Mesna.

Discussion

More than 90% of masses in the kidney are renal cell carcinomas [4]. Renal sarcomas are rare neoplasm, accounting for < 1% of masses [5]. Ewing's sarcoma of the kidney is an extremely rare but highly aggressive neoplasm with a rapid increase in lesion size and metastasis, as seen in our case [6].

Ewing's sarcoma of the kidney is seen in the young age group (mean age of 28–34 years) [7]. They are initially asymptomatic and when large enough, usually present with symptoms like flank pain and hematuria [8].

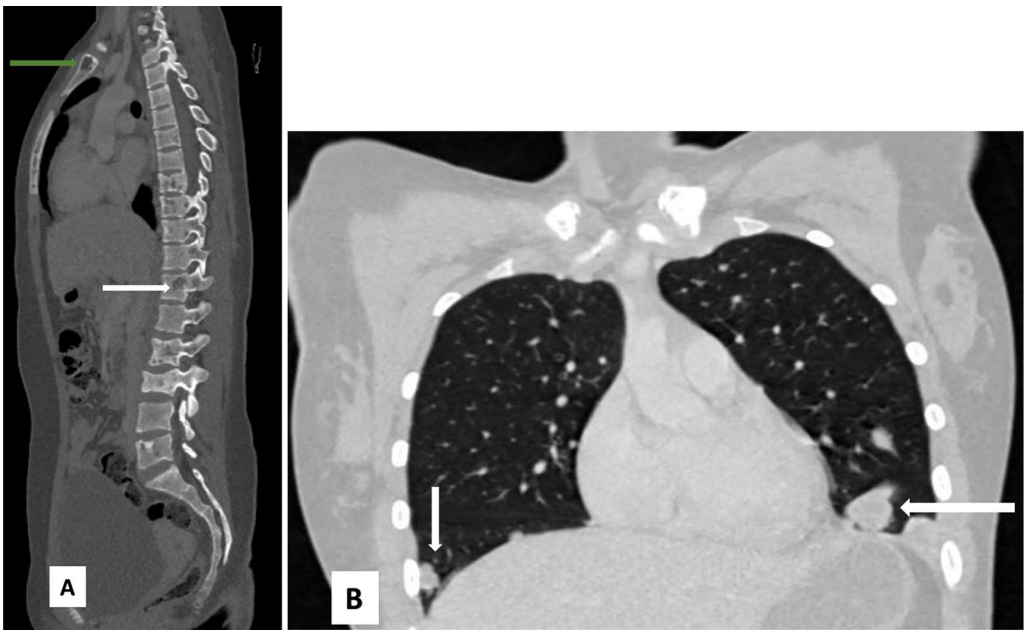

Fig. 3 **A** Right parasagittal CT image in bone window show multiple lytic lesions in the thoraco-lumbar spine (white arrow). A well-defined lytic lesion is also seen in the manubrium sterni (green arrow). **B** Coronal CT Reformat Image in lung window shows multiple round metastatic deposits (white arrows) in the bilateral basal lung segments

No specific imaging features are seen in imaging and it is impossible to differentiate renal Ewing's from much more prevalent RCC by imaging alone. Ultrasound shows an ill-defined hypo to isoechoic mass lesion, with minimal or no internal vascularity. CECT shows a hypodense, hypo-enhancing (as compared to the normal renal parenchyma) mass [7]. Calcification is found only in approximately 10% of tumors and usually appears faint and amorphous. On magnetic resonance imaging (MRI), these tumors are classically iso to hyperintense to skeletal muscle on T1-weighted images and hyperintense on T2-weighted images. Although smaller tumors appear homogeneous, larger tumors typically show heterogeneity owing to internal hemorrhage and necrosis. They usually do not cross the midline [1], but have a strong tendency to extend into perinephric and renal sinus fat, cause lymphovascular invasion, and distant metastases to lungs and bones, similar to RCC [8].

On imaging, differential diagnosis of solid, aggressive, primary renal tumor includes RCC, transitional cell carcinoma, lymphoma, and other mesenchymal malignancies like osteosarcoma, rhabdomyosarcoma, leiomyosarcoma, etc. RCC and sarcomas can have a similar heterogeneous appearance with areas of necrosis, hemorrhage, and calcification. Although bulk fat is common in angiomyolipoma, fat-containing RCCs are also common. Renal osteosarcomas have areas of calcification or ossification within [9]. Transitional cell carcinoma maintains the renal shape and involves the pelvicalyceal system. Lymphoma typically shows homogeneous enhancement and calcification in untreated lymphoma is extremely rare [10].

Primary renal sarcomas are diagnosed on imaging only after exclusion of renal metastatic involvement from a primary sarcoma, secondary renal involvement from a retroperitoneal sarcoma, and ruling out sarcomatoid renal cell carcinoma [9]. However, definitive diagnosis of renal Ewing's is solely by post or pre-operative biopsy. Light microscopy shows the presence of small round blue cells, with high nucleo-cytoplasmic arranged in sheets and can form Homer-Wright Rosettes. The tumor cells are positive for neuro-ectodermal IHC markers like Neuron-specific enolase and Synaptophysin. Demonstration of reciprocal translocation t(11;22)(q24;q12) by cytogenetic studies, is considered to be specific to PNET and Ewing's sarcoma [11]. Unfortunately, karyotyping was not performed in our case as it was not available in our institution.

There is no consensus regarding the treatment of renal Ewing's sarcoma. Most cases have been treated with surgical resection and adjuvant chemotherapy. The effective chemotherapeutic agents are vincristine, doxorubicin, ifosfamide, etoposide, actinomycin D, and cyclophosphamide [12]. Molecular targeted therapy including insulin-like growth factor 1 receptor antibody has shown some promise in ESFT [1]. Postoperative radiotherapy must be

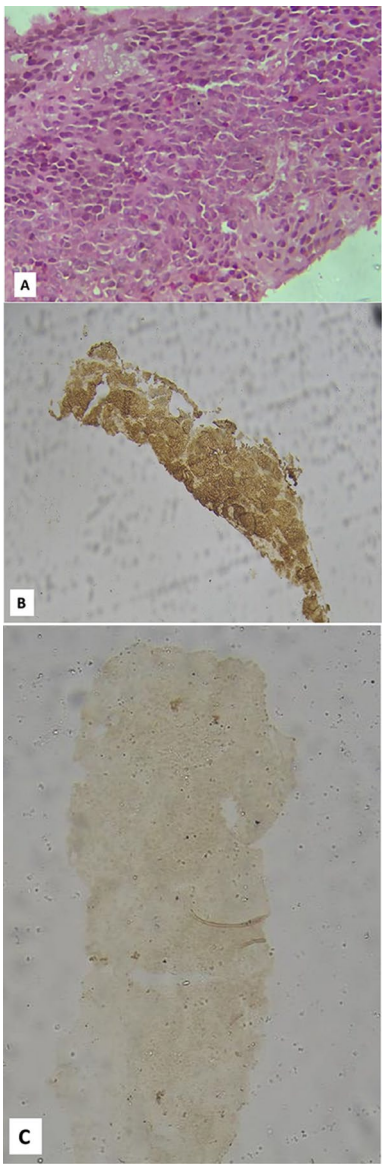

Fig. 4 **A** Hematoxylin and eosin stained section (40×) shows tumor cells arranged in sheets with hyperchromatic nuclei and scant cytoplasm. **B** On Immunohistochemistry, tumor cells are positive for CD99. **C** The tumor cells are negative for leukocyte common antigen (LCA), synaptophysin and chromogramin

added in the case of inadequate surgical margins. Even with aggressive treatment, the prognosis and the survival rate of this tumor are dismal, with the median survival being 15 months [13].

Conclusion

Primary renal Ewing's sarcoma is a very rare but aggressive renal tumor. It has no specific imaging features which can distinguish it from RCC and hence, a possibility of Ewing's sarcoma should always be kept as a differential diagnosis in aggressive renal tumors in young adults. The final diagnosis is by histopathology with IHC and cytogenetic studies. Early detection is crucial for prompt initiation of chemotherapy and Radiology plays an increasingly important role in diagnosis, staging, treatment monitoring, and surveillance.

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Authors' contributions
ARC: conceptualization, methodology, formal analysis, investigation, writing original draft. SGJ: conceptualization, methodology, formal analysis, investigation, validation, supervision, writing-reviewing and editing. AR: conceptualization, methodology, formal analysis, investigation, validation, supervision, writing-reviewing and editing. RGG: conceptualization, methodology, formal analysis, investigation, validation, supervision. NK: methodology, formal analysis, investigation, validation. SK: methodology, formal analysis, investigation, validation. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The consent for this report was obtained from the Institutional Ethics Committee and Informed Consent was taken from the patient.

Consent for publication
Appropriate consent for publication was obtained from the participant.

Competing interests
The authors declare that they have no competing interests.

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