

## Case Report

# Clear cell sarcoma of kidney: an uncommon paediatric neoplasm- two case reports and review of literature

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## ABSTRACT

Clear cell sarcoma of kidney is an uncommon neoplasm accounting for approximately 5% of all pediatric renal neoplasms, with a peak incidence between 1-3 years of age. Males are most commonly affected (M:F ratio – 2:1). It is a highly malignant neoplasm with a high propensity than other renal neoplasms to metastasize to bones, hence originally called as bone-metastasizing renal tumour of childhood by Marsden and Lawler. We describe here 2 case reports of clear cell sarcoma of kidney.

**Keywords:** Bone metastases, Clear cell sarcoma, Late relapse, Wilms tumor

## INTRODUCTION

Clear cell sarcoma of kidney is an uncommon neoplasm accounting for approximately 5% of all paediatric renal neoplasms. It is a highly malignant neoplasm with a high propensity than other renal neoplasms to metastasize to bones, hence originally called as bone-metastasizing renal tumour of childhood by Marsden and Lawler.<sup>1</sup> Clear cell sarcoma with its varied histologic pattern can pose a diagnostic challenge.

It is important to distinguish this neoplasm from other pediatric renal neoplasms because of its grave prognosis, which necessitates the patient monitoring for prolonged period. We describe here 2 case reports of clear cell sarcoma of kidney.

## CASE REPORT

### Case report 1:

8 year old male child presented with abdominal pain and abdominal swelling for 6 months. Imaging revealed a

14x11x7 cm in the upper pole of left kidney. Subsequently, left nephrectomy with ureterectomy was done.

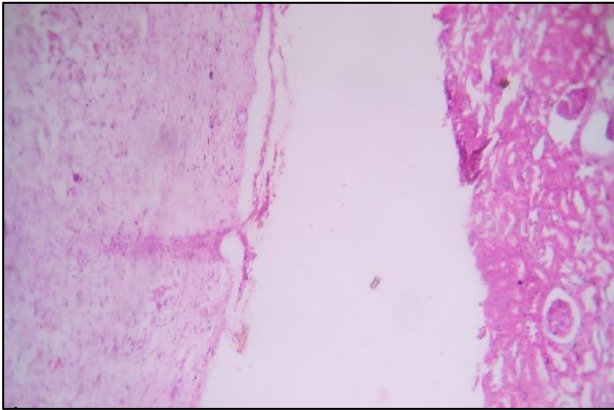
### Gross

Received left nephrectomy specimen measuring 20 x 11 x 10 cm. External surface was smooth and boss elated. Cut surface showed a mass involving the upper pole of kidney predominantly composed of cystic areas measuring 9 x 7 x 5 cm and solid areas measuring 4 x 4 x 3 cm. Solid areas were fleshy, grey white. Cystic areas were multiloculated and filled with clear fluid. Grossly tumor was seen to infiltrate the renal pelvis.

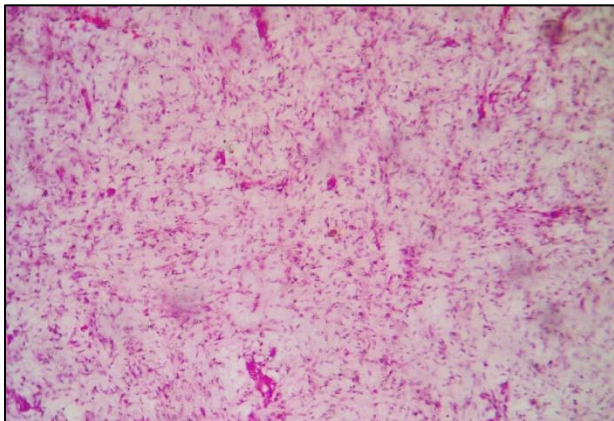
### Microscopy (Figure 1- Figure 6)

Sections showed renal parenchyma with an adjacent neoplasm composed of diffuse sheets of spindle cells admixed with clusters of round to oval cells with scant cytoplasm, dark staining nuclei, some showing nucleolus and intervening clear intercellular matrix. The cells were separated by fibro vascular septa. Stroma showed extensive areas of myxoid change with scattered

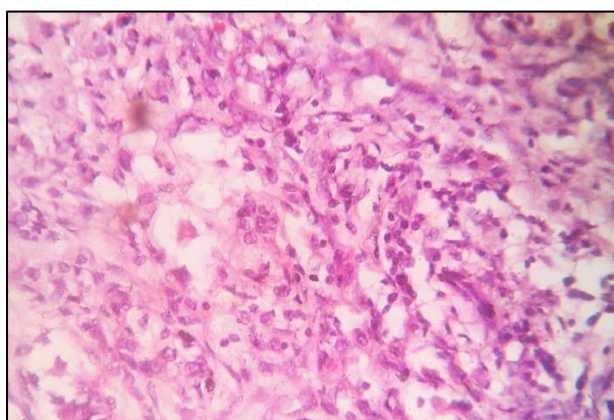
multinucleated giant cells. Focal mitotic figures were also seen. Immunohistochemistry revealed diffuse positivity in tumor cells for vimentin and was diagnosed as clear cell sarcoma of kidney.



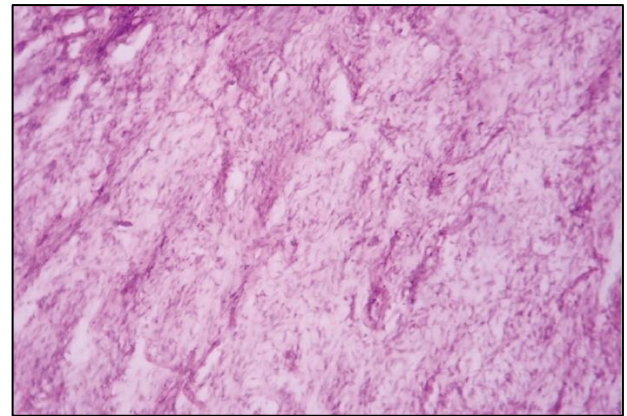
**Figure 1: Renal parenchyma with adjacent neoplasm (H and E - 40x).**



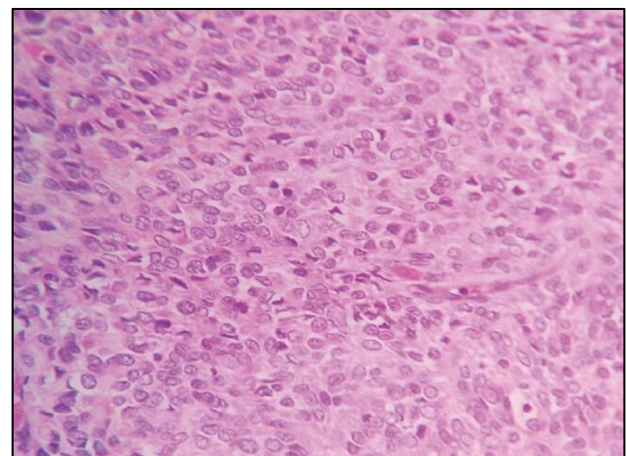
**Figure 2: Clusters of spindle cells with clear intercellular matrix separated by fibrovascular septa (H and E - 100x).**



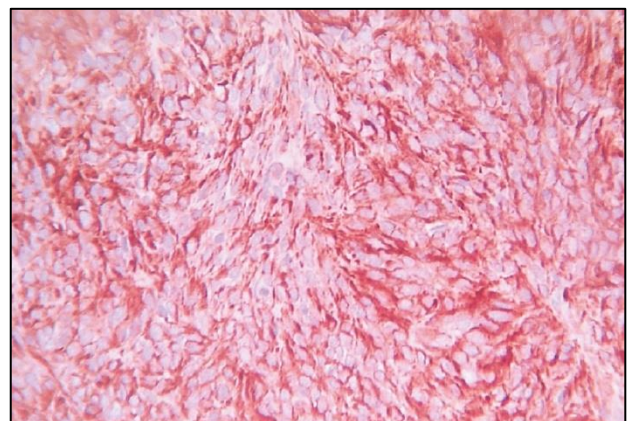
**Figure 3: Myxoid pattern (H and E - 400x).**



**Figure 4: Spindle cell pattern (H and E - 100x).**



**Figure 5: Epithelioid pattern (H and E - 400x).**



**Figure 6: IHC-Vimentin positivity (400x).**

#### **Case report 2:**

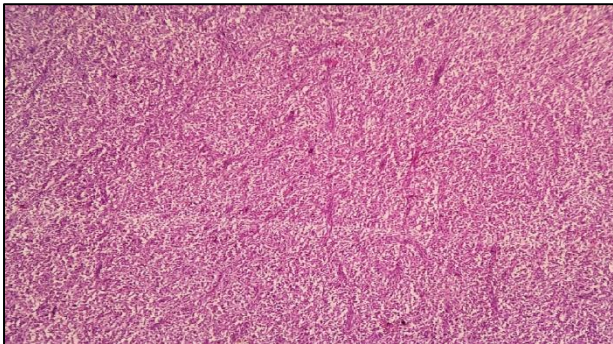
2½ year old male child presented with a history of abdominal distension one year ago. Imaging revealed a 9.5 cm x 7.6 cm mass in right mid and lower pole of kidney. Nephrectomy was done and on histopathological examination, was diagnosed as Wilms Tumour. Chemo radiation was given. One year later, the child presented



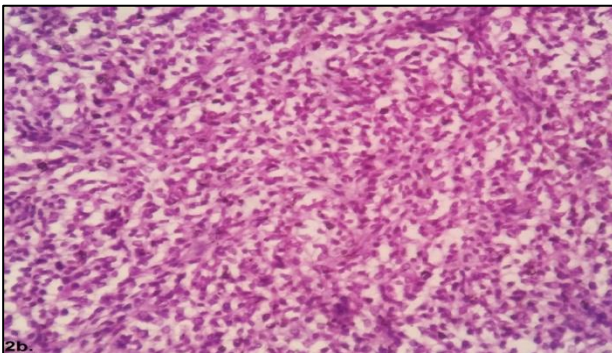
with multiple osteolytic lesions and pulmonary nodules. Previous histopathological slides were reviewed.

#### Microscopy (Figure 7- Figure 12)

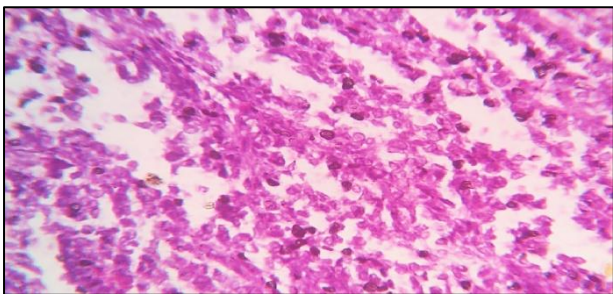
Sections showed a neoplasm arranged in sheets and trabecular. The cells were round to oval with scant cytoplasm, hyperchromatic nuclei with intervening fibrovascular septate displaying a chicken-wire vasculature pattern. The neoplastic cells were also separated by a clear myxoid matrix in some areas. Immunohistochemistry revealed diffuse and strong positivity for vimentin and WT-1 negativity in tumour cells and was diagnosed as clear cell sarcoma of kidney.



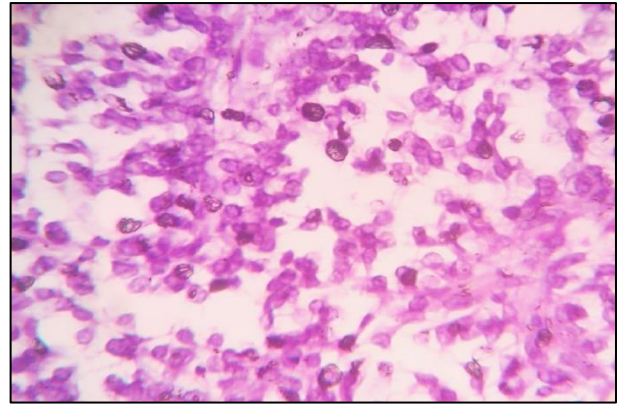
**Figure 7: Neoplasm in sheets separated by fibrovascular septa (H and E, 40x).**



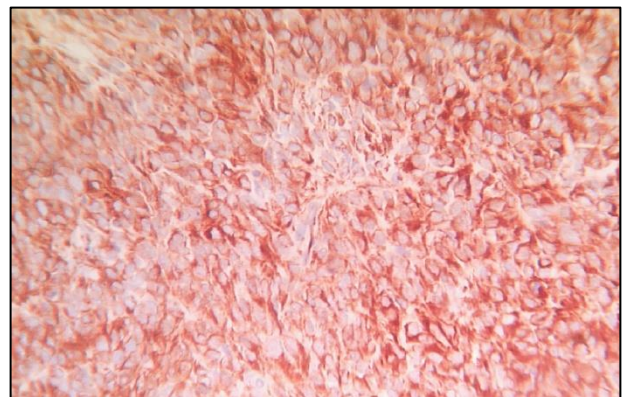
**Figure 8: Sheets of neoplastic cells with intervening chicken-wire vasculature (H and E, 100x).**



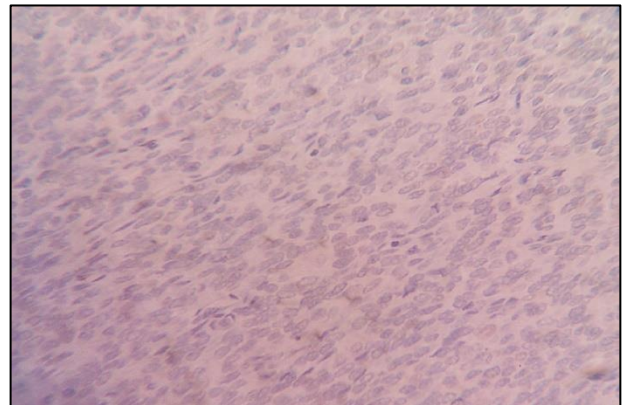
**Figure 9: Neoplasm arranged in trabecular with intervening clear intercellular matrix (H and E, 400x).**



**Figure 10: Round to polygonal cells with scant cytoplasm and indistinct cell borders (H and E, 400x).**



**Figure 11: IHC-Vimentin positivity (400x).**



**Figure 12: IHC-WT-1 negativity (400x).**

#### DISCUSSION

Clear cell sarcoma of kidney is a malignant mesenchymal neoplasm of the kidney and unlike Wilms tumor, it is not associated with nephrogenic rests. They come under tumors with "unfavorable histology" listed by the National Wilms Tumor Study Group (NWTSG).<sup>2</sup> It is a very rare neoplasm (<1% of all paediatric solid tumours) and very uncommon in the first 6 months of life and has rarely been reported in adolescents and adults, with a

peak incidence between 1-3 years of age (mean age: 1½ years) and having a male predominance (2/3 cases).<sup>2</sup>

### ***Clinical features***

Abdominal mass or swelling and hematuria are the usual presenting signs. Other features include fever, vomiting, decreased appetite, abdominal pain and hypertension. Patients may also present with pathologic fractures due to metastatic tumour. Approximately 5% of patients have metastatic disease at presentation. The most common site of metastasis at the time of presentation is ipsilateral renal hilar lymph nodes. One characteristic feature is the incidence of bone metastases (40%-70%) as compared to the incidence in Wilms tumor (2%).<sup>3</sup>

### ***Imaging features***

On imaging, clear cell sarcoma cannot be distinguished from Wilms tumour. On CT imaging the tumours typically present as a large, solid, heterogeneous renal masses with low attenuation as compared to the adjacent renal parenchyma with cystic and/or necrotic areas. Foci of calcification may also be present.<sup>3,4</sup>

### ***Pathological features***

#### ***Gross***

Grossly, the tumours are large, unicentric, unilateral and irregularly shaped masses. Tumours measure between 4 cm - 21 cm with a mean size of 12 cm. Tumours are usually solid but can be focally cystic with areas of necrosis and haemorrhage. Cut surface is grey-tan to white with focal cysts. The tumours often involve renal medulla with renal vein invasion occurring in approximately 5% of cases.<sup>2,3</sup>

#### ***Microscopy***

The most challenging aspect in diagnosing clear cell sarcoma of kidney is in identifying the histological variability. Nine variants have been described including the classic pattern which occurs in 91% of tumours either as a predominant or as a secondary feature, followed by myxoid pattern (50%), sclerosing pattern (35%), cellular pattern (26%), epithelioid pattern (trabecular or acinar type) (13%), palisading (verocay-body) pattern (11%), spindle cell pattern (7%), storiform pattern (4%) and anaplastic pattern (2.6%). All tumours have multiple patterns in varying proportions.<sup>2</sup>

The three components which occur in varying patterns are the cord cells, septal cells and intercellular matrix.

The classic pattern is characterized by nests or cords of polygonal cells separated by fibrovascular septa with a characteristic chicken wire feature. The cells have sparse cytoplasm with indistinct cell margins. The nuclei are round with fine chromatin and without nucleoli and may

have grooves resembling the Orphan Annie eye nuclei of papillary carcinoma of thyroid. The cells are loosely spaced separated by intercellular matrixes which are composed of mucopolysaccharides. The indistinct cytoplasmic border along with the intercellular matrix imparts the clear appearance. The cells along the fibrovascular septa are spindle shaped.

The myxoid pattern is the second most common variant. There is diffuse accumulation of amphophilic extracellular mucoid material which varies from minute deposits to large pools.

The sclerosing variant is characterized by prominent collagen bundles which separate the tumor cells, which can become hyalinized.

The cellular pattern is characterized by diminished extracellular matrix with overlapping of nuclei. There is increased mitotic activity in this variant.

The epithelioid pattern is characterized by the trabecular type of plump cells wherein the cells are away from the surrounding septa resulting in ribbons of one to two cells thick or the acinar type wherein the cells are lined up against the septa.

The palisading pattern features spindle cells in parallel linear arrays alternating with the less cellular areas, a feature similar to schwannoma.

The spindle cell pattern is characterized by proliferation of septal cells with preserved thin fibrovascular septa resulting in obliteration of cell cords and spindle cell transformation of the septal cells. Intersections of these spindle cells resemble the storiform pattern mimicking the fibrohistiocytic neoplasms.

The anaplastic variant is characterized by cells with enlarged, pleomorphic nuclei and bizarre mitotic figures.

### ***Ultra structural features and immunohistochemistry***

Ultra structurally, the cells have high nuclear cytoplasmic ratio with irregular nuclear shapes and elongated cytoplasmic processes. There is abundant extracellular matrix.<sup>6</sup> Almost all clear cell sarcomas of kidney are positive for vimentin. Some show positivity for bcl-2, but are negative for all other markers. The negative markers include cytokeratin, WT-1, CD99, S100, desmin, epithelial membrane antigen, CD56 and NSE.<sup>2,4,5</sup>

### ***Molecular diagnostic features and cytogenetics***

Clear cell sarcoma of kidney has not been associated with any known genetic syndromes or familial inheritance. Overexpression of p53 occurs in anaplastic variant. One study found rearrangement of chromosome 17 (YWHAE) and 10 (FAM22) in some cases. Other common

mutations associated with CCSK include a 1q gain and 19p loss.<sup>7</sup>

### **Differential diagnosis**

#### *Clear cell sarcoma of kidney versus Wilms tumour*

Vascular rich WT may mimic CCSK but can be distinguished by its bilaterality, multicentricity, dense cellularity and presence of heterologous tissues. Immunohistochemistry is also helpful because WT is usually reactive for WT1 and CD56.

#### *Clear cell sarcoma of kidney versus congenital meroblastic nephroma*

Cellular CMN may resemble spindle cell variant of CCSK, but it occurs at a much younger age (<6 months) and is positive for desmin.

#### *Clear cell sarcoma of kidney versus clear cell renal cell carcinoma*

Clear cell RCC is extremely rare in infancy and is positive for cytokeratins.

### **Prognosis and treatment**

Treatment of CCSK includes surgical intervention along with radiation and chemotherapy. The addition of doxorubicin to chemotherapy regimens has dramatically improved the survival rates with a 66% reduction in overall mortality.<sup>8</sup> Six-year survival is 97% for stage I tumors, 75% for stage II tumors, 77% for stage III tumors, and 50% for stage IV tumors. The likelihood of relapse after initial treatment is approximately 20%-40 %, with the most common site of relapse being bone (40%-70%) followed by lung, retro peritoneum, brain, and abdomen. CCSK has a propensity to metastasize longer after nephrectomy than Wilms' tumor (median time 24 months), so that patient monitoring is required for longer periods of time.<sup>8</sup>

### **CONCLUSION**

The importance of early and correct diagnosis is highlighted by the fact that clear cell sarcoma carries an

increased risk of bone metastases, tendency for late relapse, resistance to conventional therapy and a relatively poor outcome compared to Wilms tumor.

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