Ewing's sarcoma of the kidney: A rare tumor in children

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ABSTRACT

Ewing's sarcoma of the kidney is a rare malignancy, especially in the pediatric population. It belongs to what is called the Ewing sarcoma family tumors. It is not common as a differential diagnosis in renal tumors during childhood, with a nonspecific presentation as abdominal pain and hematuria. It is usually seen in late childhood and adolescent patients. The radiological features are neither specific nor pathognomonic. So, we rely on histopathology, immunohistochemistry and molecular/ cytogenetic studies for diagnosis.

Once the diagnosis is established, multimodal chemotherapy is started according to the treatment protocols found in the literature and centers' experiences in these cases.

Reporting and publishing these rare tumors will help in understanding the course of the disease and its response to the treatment protocol.

Key Words: Ewing's sarcoma of the kidney.

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Introduction

Ewing sarcoma of the kidney is a rare renal tumor in children with 10 cases reported in the literature since its first description in 1975[(1)]. It is mainly a genetic disease, with some sporadic cases. Most tumors contain a translocation mutation with a fusion between the EWS gene on Chromosome 22 and FLI1 on Chromosome 11 t (11,22). The original cell of this tumor is unknown; but, the thought till now is that it is derived from neural cells and neural crest cells [(2)].

We report a case of a 10 year old male patient diagnosed with Ewing sarcoma of the kidney. After radical nephrectomy, a significant response to multi-agent chemotherapy and radiotherapy was observed, with an excellent outcome.

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Case presentation

A 10 year old male, otherwise healthy, presented to the emergency room with a history of sudden onset of gross hematuria associated with right flank pain. There was no history of weight loss, decreased appetite, night sweats, vomiting, or dysuria. No dysmorphism or neurological manifestations were seen.

Blood tests were normal, urine analysis revealed bloody sample, urine culture was normal.

A CT scan of the abdomen showed a well- defined mixed density soft tissue mass lesion measuring 78x62 mm arising from the upper pole of the right kidney, possible lymph nodes in the right aortocaval region of the upper abdomen (Figure 1a and 1b). Chest CT (Figure 3) revealed no evidence of lung nodules. So, the patient underwent right-sided radical nephrectomy on 17/7/2018 as shown in the postoperative CT scan (Figure 2).

Histopathology revealed a malignant small round blue cell tumor. Immunohistochemical (IHC) stains revealed positive staining of the tumor cells for CD99, vimentin and neuron specific enolase (NSE) (Figure 4). The differential diagnosis was blastema predominant Wilms tumor versus Ewing sarcoma /PNET. The paraffin blocks containing tumor tissue were referred to another center for FLI-1 IHC stain and Fluorescence in situ hybridization (FISH) studies. The results were positive for FLI-1 IHC stain and EWSR1 gene rearrangement by FISH confirming the diagnosis of Ewing sarcoma ,This technique was performed using vysis LS1 EWSR1 dual color, break -apart rearrangement probe ,this probe hybridizes to chromosome 22 at band(q12,2)(spectrum green on the centrometric side and spectrum orange on the telomeric side of the EWSR1 gene breakpoint),total of 200 interphases were analyzed in this study, split signals were observed in 73% of the interphases indicating EWSRI gene rearrangement positive cells.

The patient was then started on chemotherapy according to Ewing sarcoma protocol (children's oncology group) by using alternating vincristine 2mg/m^2 D1 -doxorubicin 37.5mg/m^2 D1,2-cyclophosphamide 1200mg/m^2 D1 and ifosfamide 1800mg/m^2 D1-D5-etoposide 100 mg/m^2 D1-D5 cycles, two weeks between cycles for 14 cycles ,with filgrastim(5mg/kg/day)between cycles .

primary tumor treatment with surgery and radiation begin at week 13 after cycle 6 radiation doses was 45 Gy.

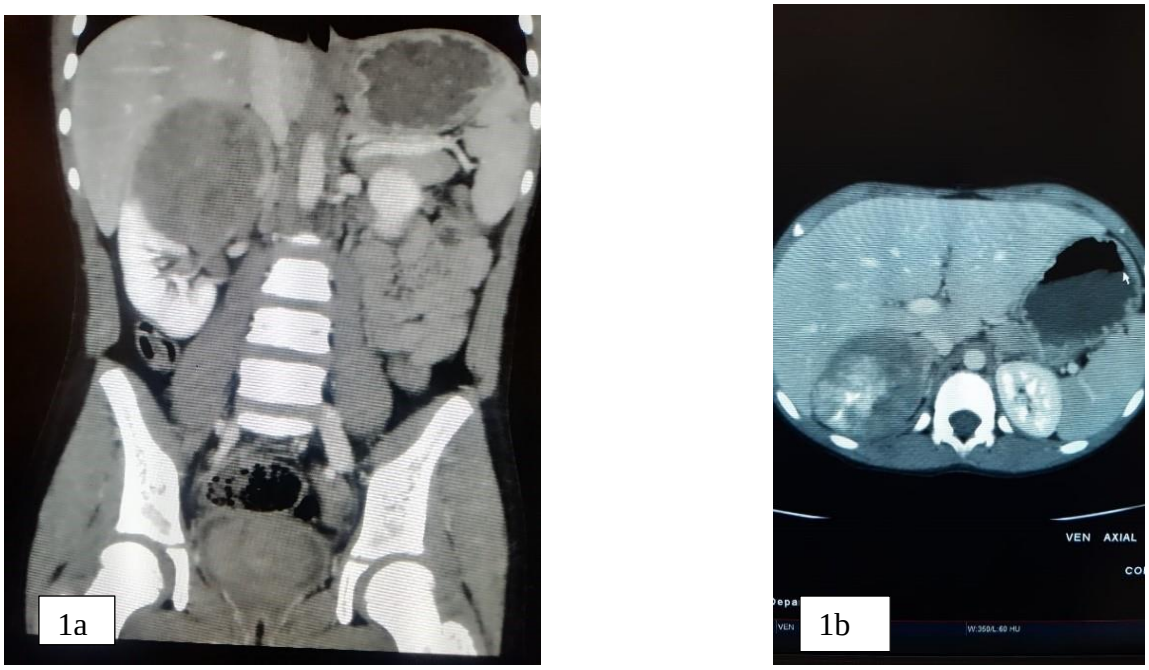

Figure (1a and 1b): Abdominal CT with contrast showing well-defined mixed density soft tissue mass lesion measuring 78*62 mm arising from the upper pole of the right kidney with no venous invasion.

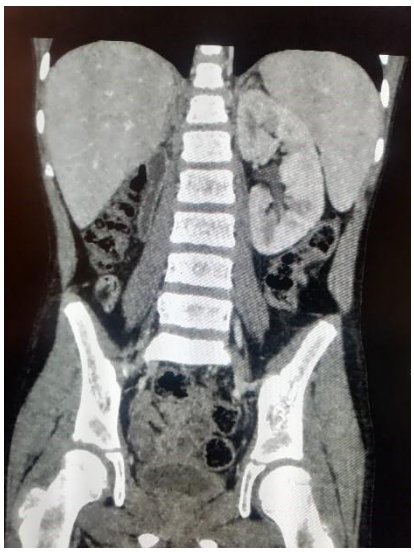

Figure 2: Abdominal CT Postoperatively with radical right-sided nephrectomy.

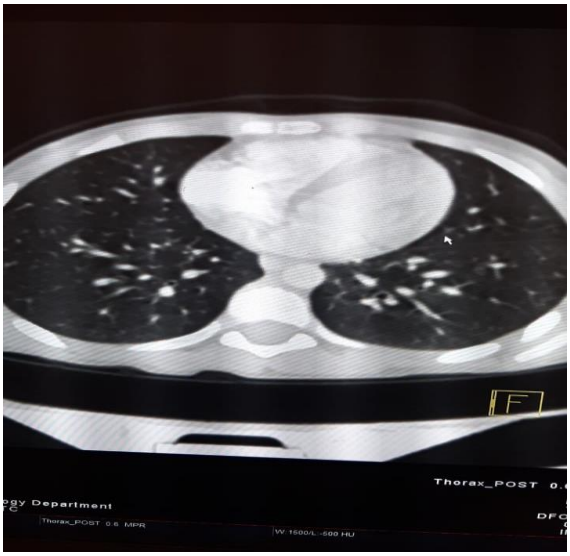

Figure 3: CT CHEST showed no distant metastasis

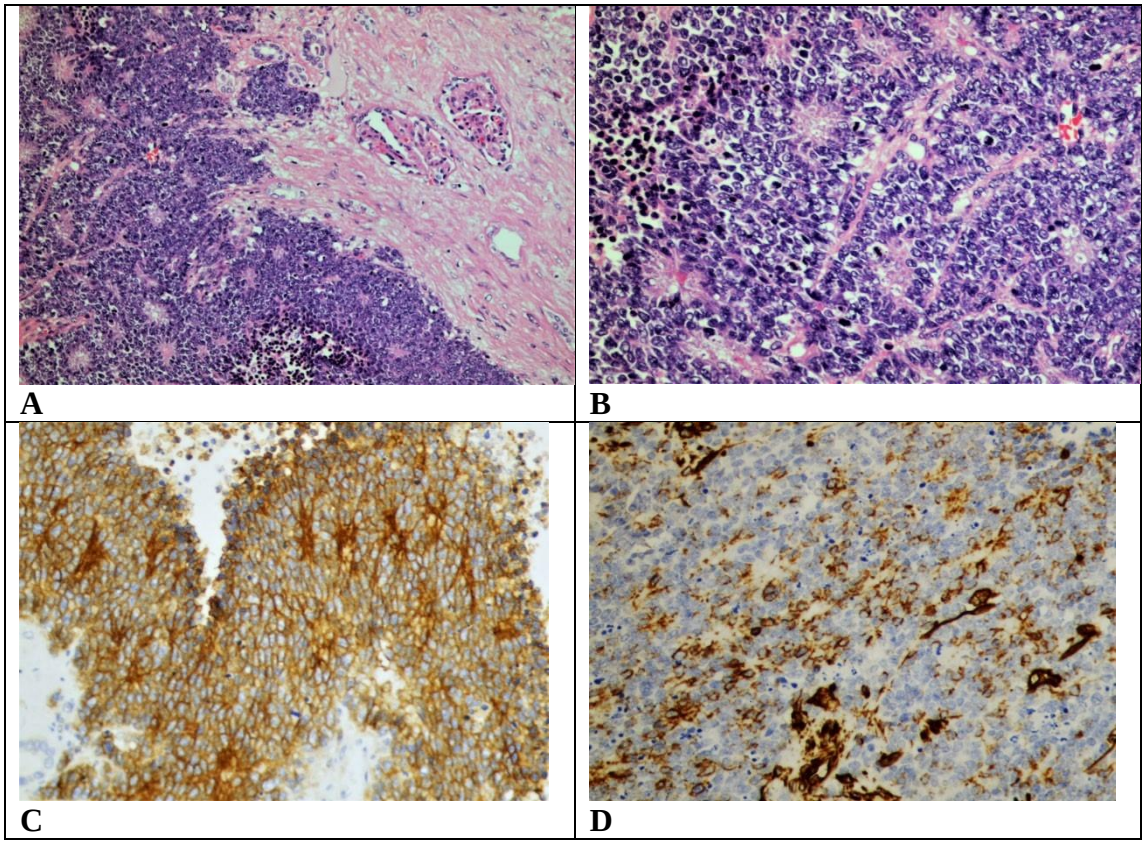

Figure 4:
A: Ewing sarcoma/PNET within the kidney with adjacent glomeruli. Hematoxylin and Eosin stain. 200X
B: Ewing sarcoma/PNET with rosetting. Hematoxylin and Eosin stain. 400X
C: CD99 positive in the tumor cells. Immunohistochemical stain. 400X
D: Vimentin focal positive. Immunohistochemical stain. 400X

Outcome and follow up: no complications appeared during and or post-operation. The patient was started on chemotherapy 10 days after wound healing according to the protocol, and radiotherapy to the tumor bed for local control of the disease and to prevent relapse was done.
2 Years follow up was uneventful for new masses or recurrence.

DISCUSSION

Renal Ewing sarcoma tumor is a rare entity in children. It usually presents in adults and a few cases have been reported in children [3-5]. Majority of the patients affected by of ES of the Kidney are in their second and third decades of life. Approximately 60% of those affected are male. Patients' signs and symptoms mimic that of kidney stones including flank pain (84%), palpable neoplasm (60%), and hematuria (38%) [6].
The cases reported worldwide are 10 cases considering the pediatric age group below 15 years of age [7-10].
Ewing sarcoma of the kidney (ESK) is a rare primary tumor of the kidney and can be mistaken with other round cell tumors, like Wilms tumor blastema predominant. Around 90% of Ewing sarcoma of the kidney have a specific t(11;22), which results in a chimeric EWS-FLI-1 protein. ES of the kidney needs to be differentiated from other small round cell tumors of the kidney because each type of tumor is treated differently. Ewing sarcoma has diagnostic genetical findings. The most common translocation is t(11; 22) (q24; q12) with EWSR1-FLI1 gene fusion (> 90%) [11-12]. We have to differentiate between the two entities as the prognosis is different and each has a distinct treatment modality. For the diagnosis of Ewing sarcoma, the morphological characteristics, immune-histochemical results, and genetic studies are crucial for the diagnosis.

Metastasis was present in 66% of patients at diagnosis with the lungs being the most common site of metastasis in this tumor. Because of its poor prognosis and aggressive course, establishing ESK for diagnosis is important for treatment and follow-up. Diagnosis is usually done after resection of such a tumor. CT scan findings are not specific for the type of renal tumor. Also, the microscopic findings in such tumors are non-specific, so, the cytogenetic analysis and the immunohistochemistry are needed for definitive diagnosis. In around (85 - 90) percent of cases of Ewing sarcoma family tumors, a recurrent chromosomal translocation, t(11;22) (q24;q12), fuses the 5' portion of the *EWSR1* gene on chromosome 22 to the 3' portion of the *FLI1* gene on chromosome 11. This can be detected using fluorescence in situ hybridization (FISH).[13-14]

There is no specific approach to the treatment of Ewing sarcoma of the kidney. Nephrectomy (surgical resection of tumor) with adjuvant or neoadjuvant chemotherapy and radiotherapy is the main management of such tumors.
The reported survival rate of such patients was 26 months in the non-metastatic tumor while 5.6 months in the case of metastasis.

CONCLUSION

Ewing sarcoma of the kidney is an extremely rare tumor in children with the importance of differentiating this type of renal tumor from other types as it has a more aggressive course with inferior prognosis in comparison to other tumors. Although a multimodality approach is helpful, survival rate is mostly limited to 1 year.
The earlier diagnosis with non-metastasis at the time of diagnosis gives more rewarding results.
Reporting such cases will help in the documentation of the treatment used and the outcome of our treatment results to improve survival in such tumors.

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