



Case Report

Primary primitive neuroectodermal tumor of the kidney: A rare case report and review of literature

Vidya Rekha R Kamath^{1,*}, Teerthanath S¹, Rajeev T P²

¹Dept. of Pathology, K S Hegde Medical Academy, Mangalore, Karnataka, India

²Dept. of Urology, K S Hegde Medical Academy, Mangalore, Karnataka, India



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ABSTRACT

Background: Primitive neuroectodermal tumors (PNET) is an aggressive, rapidly progressing and metastatic tumor. It rarely arises from the kidney and has an incidence of less than 1%. These are usually mistaken for a wide variety of other small round cell tumors. Young adults and children are commonly affected and have an aggressive course. These tumors are mistaken for a wide variety of other small round cell tumors. Here is a case of a 52-year-old female, who presented with flank pain and gross hematuria. The contrast-enhanced computerized tomogram (CECT) revealed a renal mass with a tumor thrombus extending to the renal vein, inferior vena cava, and the right side of the heart. The patient underwent radical nephrectomy along with IVC thrombectomy and chemotherapy.

Materials and Methods: The sections from formalin-fixed surgical specimens were paraffin-embedded and stained with H & E stain. Immunohistochemistry (IHC) was performed.

Results: Histology revealed small round to oval cells with hyperchromatic nucleus and very scanty cytoplasm. Frequent mitotic figures were noted. Few rosettes were seen at places. Tumor was seen invading the perirenal adipose tissue. The tumor thrombus extended into the right atrium and the right ventricle. IHC evaluation revealed the tumor cells showed a strong positivity for CD99, synaptophysin, neuron-specific enolase, vimentin, and were negative for CD45, pan-cytokeratin, and desmin. Thus, the histological examination and IHC helped in getting a definite diagnosis of PNET involving the kidney. The patient has been undergoing chemotherapy.

Conclusion: PNET has an aggressive clinical course with a poor prognosis. Renal PNET bears many similarities to other small round cell tumors; hence it is important to review the histologic features and immunostaining for definitive diagnosis. Due to the rarity of the disease, there is no standard guideline regarding its management. Achieving accurate diagnosis facilitates the prolongation of survival with definitive treatment.

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1. Introduction

Ewing's sarcoma/primitive neuroectodermal tumors (ES / PNET) are a group of small round cell tumors most commonly involving the bone and soft tissues. Very rarely, they arise from the kidney.¹ Young adults and children are commonly affected and have an aggressive course. As these arise from the primitive neuroectoderm, they have a propensity to different sites. They can occur in

the extremities, brain, spinal cord, trunk and sympathetic nervous system, paraspinous region and less commonly, the urogenital tract.²

2. Case Report

In December 2016, a 52-year-old female was admitted with complaints of left flank pain, gross haematuria and increasing breathlessness on exertion of 3-month duration. The patient was evaluated pre-operatively by history, physical examination, ultrasound and CECT of

* Corresponding author.

E-mail address: kamathvid@gmail.com (V. R. R. Kamath).

the thorax and abdomen. On clinical examination, a round fixed mass was palpable in the left hypochondrium. The ultrasonography showed a large heterogeneous mass measuring 7 x 7.5 cms originating from the left kidney. Further CECT thorax and abdomen indicated a renal mass (Figure 1 A) with tumor thrombus extending into the renal vein and inferior vena cava (Figure 1 B). Ultrasound Doppler was performed to determine the extent of the thrombus. Transoesophageal echocardiogram showed an intra-cardiac thrombus extending up to the right ventricle. The patient was managed with surgery and chemotherapy. Surgical treatment included radical nephrectomy with IVC thrombectomy.

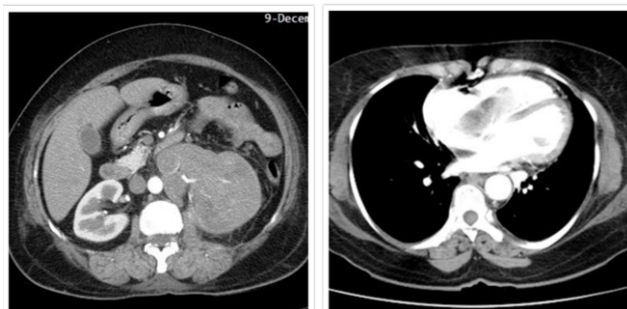


Fig. 1: **a:** Computed tomography scan revealed a huge left renal tumor showing extension into the renal vein; **b:** Contrast-enhanced CT scan of the chest shows a tumor thrombus (TH) in the right atrium

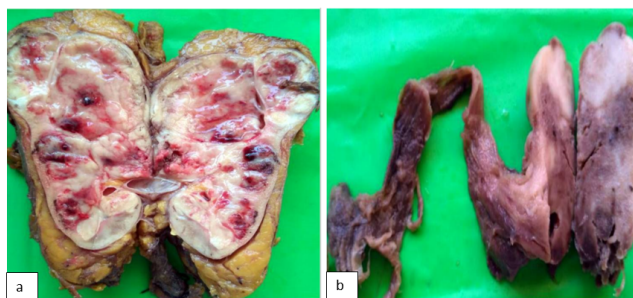


Fig. 2: **a:** Cut surface shows an encapsulated, friable, greyish white, lobulated mass with extensive areas of necrosis and hemorrhage; **b:** Right atrial-IVC thrombectomy specimen

Gross examination revealed an encapsulated, friable, greyish white tumor mass measuring 14x10x5cms, replacing almost the entire kidney, with a small uninvolved portion at the lower pole (Figure 2 A). The cut surface showed extensive areas of hemorrhage and necrosis. The tumor thrombus (Figure 2 B) is seen extending into the left renal vein, IVC and right atrium. Microscopically, cohesive sheets of monomorphic, small, round cells separated by fibrous bands were seen (Figure 3 A). The tumor cells have hyperchromatic nuclei, inconspicuous nucleoli, scant cytoplasm, and brisk mitotic activity. Rosettes are

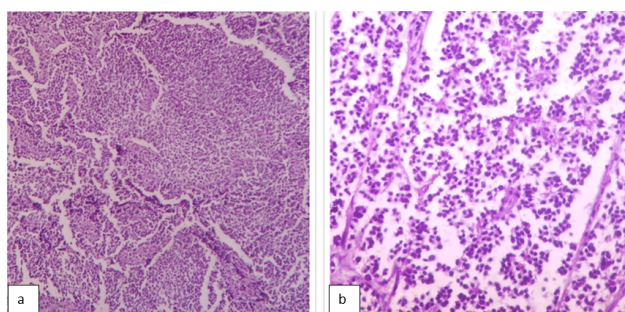


Fig. 3: **a:** Microscopy revealed a monotonous population of small, round blue cells with uniform nuclei and scanty cytoplasm separated by fibrous bands. (H & E magnification X 10); **b:** Rosettes are seen in the microscopic picture. (H & E magnification X 40)

seen in places (Figure 3B). The tumor cells showed strong membranous positivity for CD99, chromogranin-A, neuron-specific enolase and negative for desmin, CD45 and cytokeratin (Figure 4 A-F).

The patient was then treated with 2 cycles of chemotherapy with VAC-IE protocol using vincristine, adriamycin, cyclophosphamide, alternating with ifosfamide and etoposide 2 weeks apart. The patient remained disease-free for 24 months.

3. Discussion

The peripheral Primitive Neuroectodermal Tumor (PNET), was first described by Arthur Purdy Stout in 1918 and was included in the family of "small round-cell tumors".³ There are very few cases reported in the literature. Young adults and children are commonly affected and have an aggressive course. In the kidney, the medullary/pelvic region is more commonly affected. Differential diagnosis includes Non-Hodgkin lymphoma, synovial sarcoma, Wilms tumor, neuroblastoma, embryonal rhabdomyosarcoma and small-cell carcinoma.¹

Renal PNET occurs commonly in adolescents and young adults, with a male predilection (male-to-female ratio of 3:1).⁴ In our case, the patient is an elderly female which is a rare presentation. The symptoms of PNET involving the kidney are nonspecific and include flank pain and hematuria. CT of renal PNET is also without any characteristic signs, mostly revealing a solitary, large, ill-defined, or heterogeneous mass.⁵

The diagnosis of renal PNET remains a challenge owing to several mimickers. Although radiological features may be helpful, histopathological examination with immunohistochemistry is required to confirm the diagnosis. PNET of the kidney is characterized by small uniform round cells with dark nuclei, inconspicuous nucleoli, scanty ill-defined cytoplasmic borders, and poorly formed rosette-like structures. The histopathologic features overlap

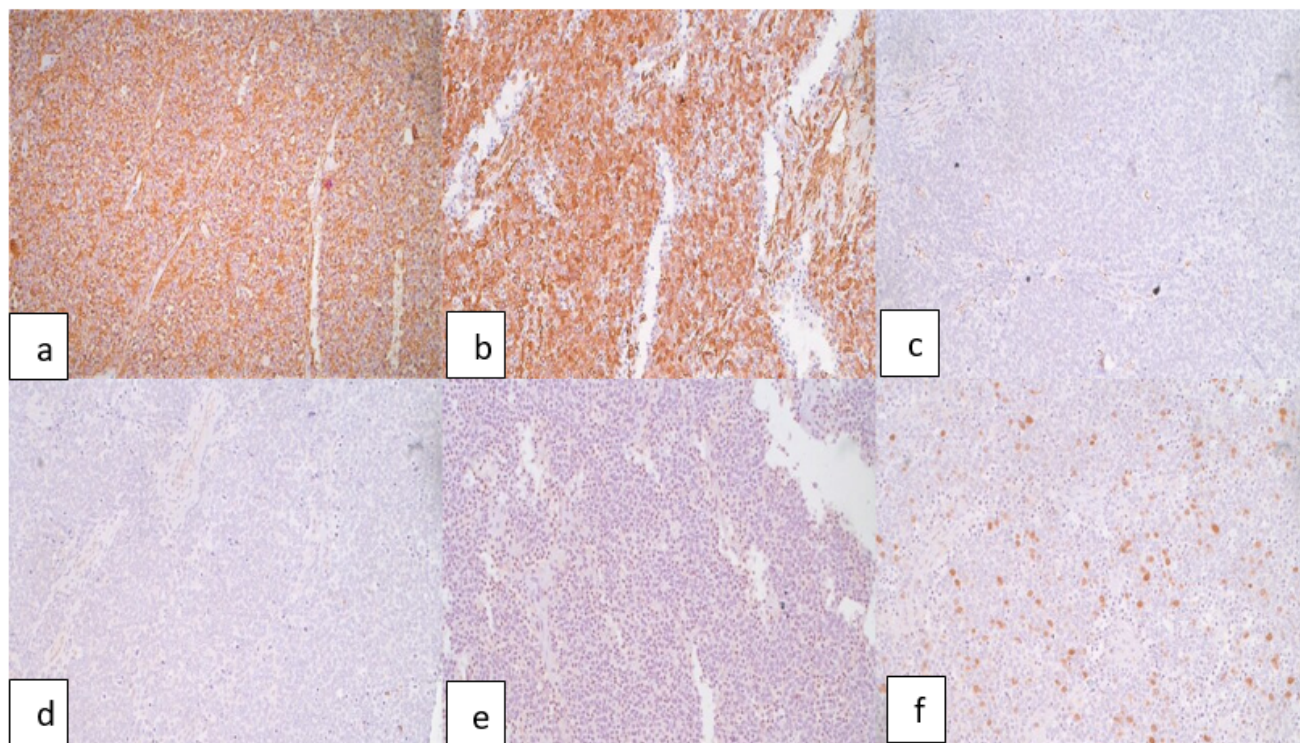


Fig. 4: Immunohistochemistry ($\times 20$) shows the tumor cells exhibited a strong positivity: for CD99 (a) and Vimentin (b) with mild Ki-67 activity of around 5-8% (f) Immunohistochemistry ($\times 20$) shows the tumor cells are negative for CD45 (c), pan-cytokeratin (d) and Wilms tumor 1 (e).

with other mimickers like lymphoma, neuroblastoma, and small cell carcinoma. Immunohistochemistry and molecular studies are crucial in differentiating PNET from other tumors. Tumor cells show strong positivity for MIC-2 gene product and membrane positivity for CD99, which is characteristically seen in more than 90% of PNET cases.¹ Other markers like neuron-specific enolase, vimentin, and S-100 may be positive. Almost two-thirds of the cases show FLI-1 expression.⁶ The chromosomal translocation t(11;22)(q24;q12) is commonly seen in renal PNET, as a result of which EWL/FLI-1 fusion protein is formed.¹

Renal PNET appears to be a rare clinical entity that behaves more aggressively than PNET arising at other sites. Since the tumor is very aggressive, it is more often diagnosed in the later stage when it has already invaded the perinephric fat, renal veins, and the inferior vena cava. The tumor can metastasize to the liver, spleen, peritoneum, and lungs in more advanced stages. The prognosis is generally poor, with a 5-year disease-free survival of 45% to 55% in localized cases. The advanced stage has a median relapse-free survival of 2 years.^{1,7}

The treatment for renal ES / PNET includes surgery, chemotherapy, and radiation. The patients mostly present with a huge mass at the time of diagnosis and the diameter of the tumor is usually more than 10 cms. As it is difficult to get

a definitive preoperative diagnosis, the use of neoadjuvant chemotherapy before surgery is uncertain. Therefore, most of the patients underwent radical nephrectomy as an initial step of treatment. The recommended chemotherapy regimen is vincristine, doxorubicin, and cyclophosphamide alternating with ifosfamide and etoposide for 1 year.⁸ The role of radiotherapy is not very clear, but it is indicated in locally advanced disease and in cases with involvement of Gerota's fascia. Despite aggressive therapy, the overall cure rate of renal PNET is only 20%.⁹

4. Conclusion

The Primitive Neuroectodermal Tumor of the kidney is a rare tumor with an aggressive nature. Differentiating the small round-cell tumors of the kidney can be challenging at times. As the overall prognosis of this tumor is very poor, an early as well as an accurate diagnosis, is important for proper management of these tumors. Despite surgical removal and chemotherapy, disease-free survival is poor in these patients.

5. Source of Funding

None.

6. Conflict of Interest

None.

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Author biography

Vidya Rekha R Kamath, Post Graduate

Teerthanath S, Professor

Rajeev T P, Professor and Head

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