

## Case Reports

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**PRIMARY RENAL EWING'S SARCOMA**

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**Summary.-** OBJECTIVE: To report two new cases of Ewing's sarcoma / primitive neuroectodermal tumor of the kidney, one of them with tumor thrombus in cava.

METHOD: Characterization of two new cases and literature review by PubMed search.

RESULTS: We report the cases of two men diagnosed with primary renal Ewing's sarcoma, who have been treated with nephrectomy and adjuvant chemotherapy, being in complete remission to date.

**CONCLUSION:** Ewing's sarcoma / primitive neuroectodermal tumor of the kidney is a rare condition that mainly affects young adults. The natural history of these tumors is the evolution towards metastatic disease and death. Treatment is multimodal, combining surgery and chemotherapy. The role of radiotherapy is not well established.

**Keywords:** Primary Ewing's sarcoma of the Kidney. Renal cancer.

**Resumen.-** OBJETIVO: Presentación de dos nuevos casos de sarcoma de Ewing / tumor neuroectodérmico primitivo renal primario, uno de ellos con trombo en cava.

MÉTODO: Caracterización de los dos casos clínicos y revisión bibliográfica mediante búsqueda en pubmed.

RESULTADO: Presentamos los casos de dos varones diagnosticados de sarcoma de Ewing renal primario, que han sido tratados con nefrectomía y quimioterapia adyuvante; encontrándose en remisión completa hasta la fecha.

CONCLUSIÓN: El sarcoma de Ewing / tumor neuroectodérmico primitivo renal primario es una entidad rara que afecta mayoritariamente a adultos jóvenes. La historia natural de estos tumores es la evolución hacia una enfermedad metastásica y la muerte. El tratamiento es multimodal, y combina cirugía y quimioterapia. El papel de la radioterapia no está bien establecido.

**Palabras clave:** Sarcoma de Ewing renal. Cancer renal.

**INTRODUCTION**

Primitive neuroectodermal tumors / Ewing sarcoma (EWS / PNET) are a family of malignant tumors that show neuroepithelial differentiation. They are distinguished from the point of view of its pathogenesis by presenting a balanced translocation t (11; 22) (q24, q12), which influences the expression of a fusion gene (FLI-1).

Its most common presentation is as a mass in the axial skeleton and soft tissue mass in the trunk. It is most prevalent in adolescents and young adults (1). Rare cases have been described in other locations, one of them is the kidney (2).

The renal PNET is a separate entity which must be properly diagnosed for correct treatment. The diagnosis is made by the pathologist, through studies with immunohistochemistry and cytogenetic techniques. Its clinical course is aggressive, progressing in its natural history to metastatic disease leading to the death of the patient (3).

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We present two cases diagnosed in our department over the past two years, one with thrombus in the cava vein. So far they have been reported in the literature about forty cases, of whom only three had thrombus in the cava vein.

## CASE REPORTS

### Case Report 1

20 year-old-man presented in emergency with gross hematuria. In CT (computerized tomography) performed, is objectified an heterogeneous, dependent on the upper pole of left kidney, seven cm. diameter renal mass.

We performed open radical nephrectomy.

Histopathologic features: solid growth of tumor cells weakly positive for CD99 small diffusely. The study by FISH (fluorescence in situ hybridization) confirmed the diagnosis of Ewing's sarcoma.

In the CT scan three months after surgery were observed multiple lung metastases and retroperitoneal carcinomatosis.

He was treated with a chemotherapy regimen IE-VAC (vincristine, adriamycin, cyclophosphamide, ifosfamide and etoposide) associated with colony stimulating factors prophylactically, noting the disappearance of pulmonary nodules. Also, we proceeded to the pathology confirmed complete response of

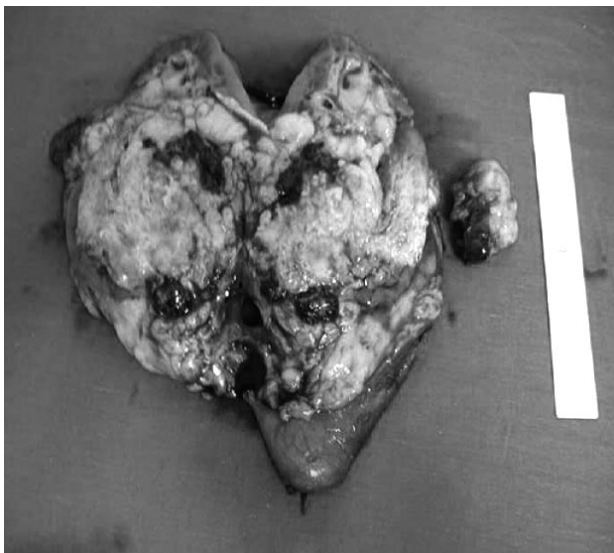


FIGURE 1. Macroscopic view of the kidney and tumoral thrombus alter nephrectomy.

retroperitoneal implants through an exploratory laparotomy with biopsy. Today, after 24 months from diagnosis, is in complete remission.

### Case Report 2

43 year-old man who enters another facility for acute pneumonic process.

During his admission CT is performed in which diagnosed a renal mass. In nuclear magnetic resonance study, we objectified an infiltrating mass occupying the renal vein up to the inferior cava vein in its extrahepatic portion.

In the extension study were visualized preoperatively multiple pulmonary nodules consistent with metastases. Was conducted through open right nephrectomy with removal of thrombus in cava (Figure 1).

Histopathologic features (Figures 2 and 3): neoplasm composed of small cells with honeycomb pattern of small nuclei, pleomorphic and hyperchromatic. The sample from the cava vein showed a morphology similar to that described previously. The techniques of immunohistochemistry showed positivity for CD99 and S-100 and negativity for AE1, CK7, enolase, cormogranina, synaptophysin, ALK, LEU7, CD20, D4, TTF and P53. FISH was carried out for Ewing's sarcoma, which was positive.

Nine months after surgery, is currently receiving chemotherapy with VACIE scheme (vincristine, adriamycin, cyclophosphamide, ifosfamide and etoposide) associated with colony stimulating factors for prophylaxis, with good tolerance to date, and remission of metastatic lesions.

## DISCUSSION

Ewing's sarcoma is a primary renal disease entity itself. Histologically, it is characterized to be a neoplasm of monomorphic round cells, that can be arranged in the shape of Homer Wright rosettes. It is part of the group of round cell tumors: Wilms tumor, lymphoma, clear cell sarcoma, synovial sarcoma, small cell tumor and neuroblastoma (4). Of these, lymphoma is the most common tumor that affects the kidney. Because the conventional histology is difficult to make differential diagnosis between the previously listed entities, are fundamental immunohistochemical and molecular studies for correct diagnosis.

From the viewpoint of immunohistochemistry, Ewing's sarcoma is usually positive for CD99 diffusely. Two thirds of cases are positive for the marker Fli-1, which detects the expression of the chimeric protein EWS-FLI1. 20%

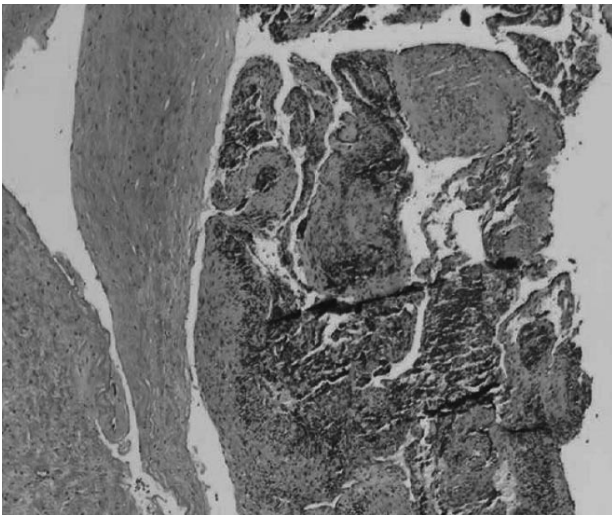


FIGURE 2. Microscopic view of tumoral thrombus with staining with hematoxylin eosin.

are positivity for cytokeratin. The markers of muscle differentiation (MyoD1, myogenin), lymphoid differentiation (CD 20) and WT-1 marker expressed in Wilms' tumor are negative (5).

In molecular studies have been described five possible balanced translocations. 85% of cases express the translocation  $t(11; 22)(q24, q12)$ , which generates the EWS/FLI-1 fusion protein. This protein has oncogenic activity through its extreme N-terminal (transactivation

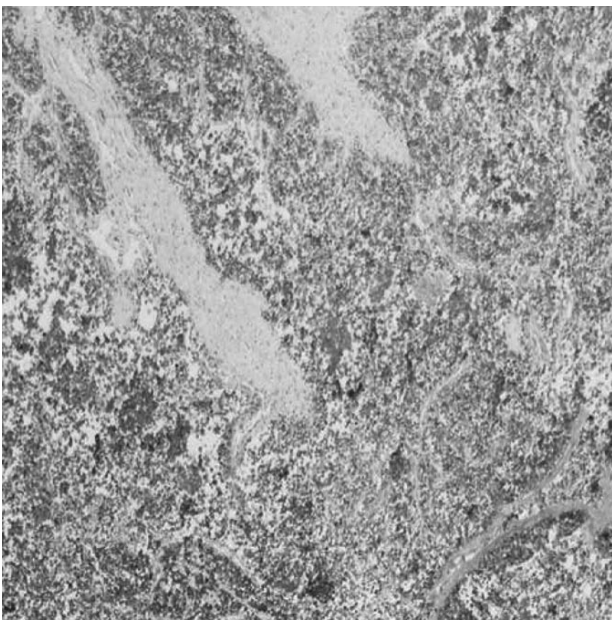


FIGURE 3. Microscopic view of CD99 immunohistochemical staining.

domain of EWS) and carboxy-terminal (DNA binding domain). Other less common translocations are  $t(21; 22)(q22, q12)$  (EWS / ERG),  $t(7; 22)(p22, q12)$  (EWS/ETV-1)  $t(17; 22)(q12; 12)$  (EWS/E1AF) and  $t(2; 22)(q33, q12)$  (EWS / FEV). These translocations can be detected by conventional cytogenetic analysis or by RT-PCR reaction (polymerase chain associated with reverse transcriptase). If not available fresh tissue can conduct a FISH on a sample included in parafina (6).

Since it was first described by Seemayer et al in 1975 (2), has been published about forty cases in the literature. Not all cases described shows long-term clinical follow-up that let us know the cancer-specific survival. With the exception Parham Series (7), which brings together in one range to 146 neuroepithelial tumors of the kidney, with 79 possible cases of PNET / ES pathologically unconfirmed, there are only three published series: the Thyaviahally with 16 patients (8), Jimenez with 11 patients (6) and Rodriguez-Galindo with 41. The rest of the PNET / ES cases reported are unique.

These tumors usually occur in adolescents and young adults (average age 27) (8,9). There is a relationship between man and woman of 1.5:1.

In published series varies the TNM stage at diagnosis. At the time of diagnosis, between 37% (8) and 100% (1) had distant metastases, mainly pulmonary.

To date, have been published only three cases of renal tumors with Ewing's sarcoma type thrombus in the cava vein (10,11,12).

The treatment of choice varies depending on tumor stage at diagnosis. In patients with localized disease, radical nephrectomy followed by adjuvant chemotherapy is the treatment of choice. In patients with disseminated disease is used neoadjuvant chemotherapy followed by surgery for response.

Chemotherapy regimens are based on cyclophosphamide, actinomycin, vincristine, doxorubicin, ifosfamide and etoposide (10). Our center has been used chemotherapy regimen VAC-IE.

No consensus exists about the radiation of the nephrectomy bed. Some contributors (11) irradiate the surgical site with 50-60 Gys. Complete responses have been reported residual local disease with this treatment.

The cancer specific survival is short. In the series of Rodriguez-Galindo (1) only one of four patients remain free of disease at fourteen months of monitoring. In Jimenez's group (6), of the eight patients with follow-up, five die from disease progression at seventeen months of diagnosis. The three remaining patients are free of disease at 64 months after diagnosis. The best

documented series is Thyavihally (8), in which overall survival was 60% at forty months and 42% at five years. Survival was lower in patients with disseminated disease: fifteen months, compared to sixty months for patients with localized disease.

## CONCLUSION

In summary, renal Ewing's sarcoma is a rare condition, which affects preferentially young adults and is a subsidiary of a multimodal treatment.

The long-term survival is short.

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