



Oncology

Management of primary Ewing sarcoma of the kidney with inferior vena cava (IVC) tumor thrombosis

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ABSTRACT

Ewing sarcoma (ES) is an entity which belongs to a spectrum of neoplastic diseases called the Ewing sarcoma family of tumors (EFT). EFTs of the kidney represent less than 1% of all renal tumors. Herein, we presented a case of primary renal ES with tumor thrombosis up to vena cava who underwent radical nephrectomy and IVC tumor thrombectomy followed by adjuvant chemotherapy. Histopathology showed that the tumor composed of small uniform, dark, round cells arranged in sheets, and rosetoid pattern. The diagnosis of ESFT was confirmed by detecting EWS/FLI-1 fusion gene using reverse transcription polymerase chain reaction (RT-PCR).

Introduction

Ewing sarcoma (ES) is an entity which belongs to a spectrum of neoplastic diseases called the Ewing sarcoma family of tumors (EFT). EFTs of the kidney represent less than 1% of all renal tumors. The diagnosis is based on the histology, immunohistochemistry, and molecular analysis. Standard of care in the case of localized and locally advanced diseases consists of local treatments (surgery/radiotherapy) in conjunction with systemic chemotherapy.¹

We present a case of a young man referred to our center with a left renal mass in association with a level 3 (retro-hepatic) inferior vena cava (IVC) tumor thrombus which turned out to be primary renal ES.

Case presentation

A 16-year-old male was evaluated with a history of 2 months-long abdominal pain in association with a single episode of gross hematuria. Physical examination revealed a palpable mass in left upper quadrant of the abdomen and a grade 3 non-reducible left testis varicocele. Computed tomography (CT) scan of abdomen showed a 14 cm solid heterogeneous mass in the middle and lower part of the left kidney with an IVC tumor thrombus up to the retrohepatic level (Fig. 1). Metastatic workup including chest CT and liver function tests were unremarkable. Intraoperative transesophageal echocardiography (TEE) revealed the upper limit of the thrombus to be beneath the hepatic veins. The patient underwent laparotomy using anterior midline incision. Following left

renal artery ligation, with the aid of a hepatic surgeon, the liver was mobilized and infrarenal IVC, right renal vein and retrohepatic IVC (below the hepatic veins) were clamped using Rummel tourniquets. Left radical nephrectomy and IVC thrombectomy was accomplished. Regional lymphadenectomy was performed (Fig. 2). Postoperative course was uneventful.

Histopathology showed that the tumor composed of small uniform, dark, round cells arranged in sheets, and rosetoid pattern. Cells had round to oval nuclei, dark clumped chromatin, inconspicuous nucleoli, and a small amount of vacuolated cytoplasm. Immunohistochemical (IHC) examination was positive for Vimentin and CD99 (Fig. 3). Chromogranin A, WT1, PAX8, CK7, TLE1, EMA were negative. The diagnosis of ESFT was confirmed by detecting EWS/FLI-1 fusion gene using reverse transcription polymerase chain reaction (RT-PCR) analysis. Regional lymph nodes were free from tumor. Following surgery the patient received several cycles of adjuvant chemotherapy as planned by a multidisciplinary team consisted of urologists, medical oncologists and radiation oncologists. Follow up examinations at 3, 6 and 12 months following surgery were unremarkable with no evidence of recurrence or metastasis.

Discussion

Renal ES is an aggressive neoplasm that predominantly affects young adults, with a slight male predominance.¹ Even though renal ES shares histologic, immunohistochemical, and molecular features with its

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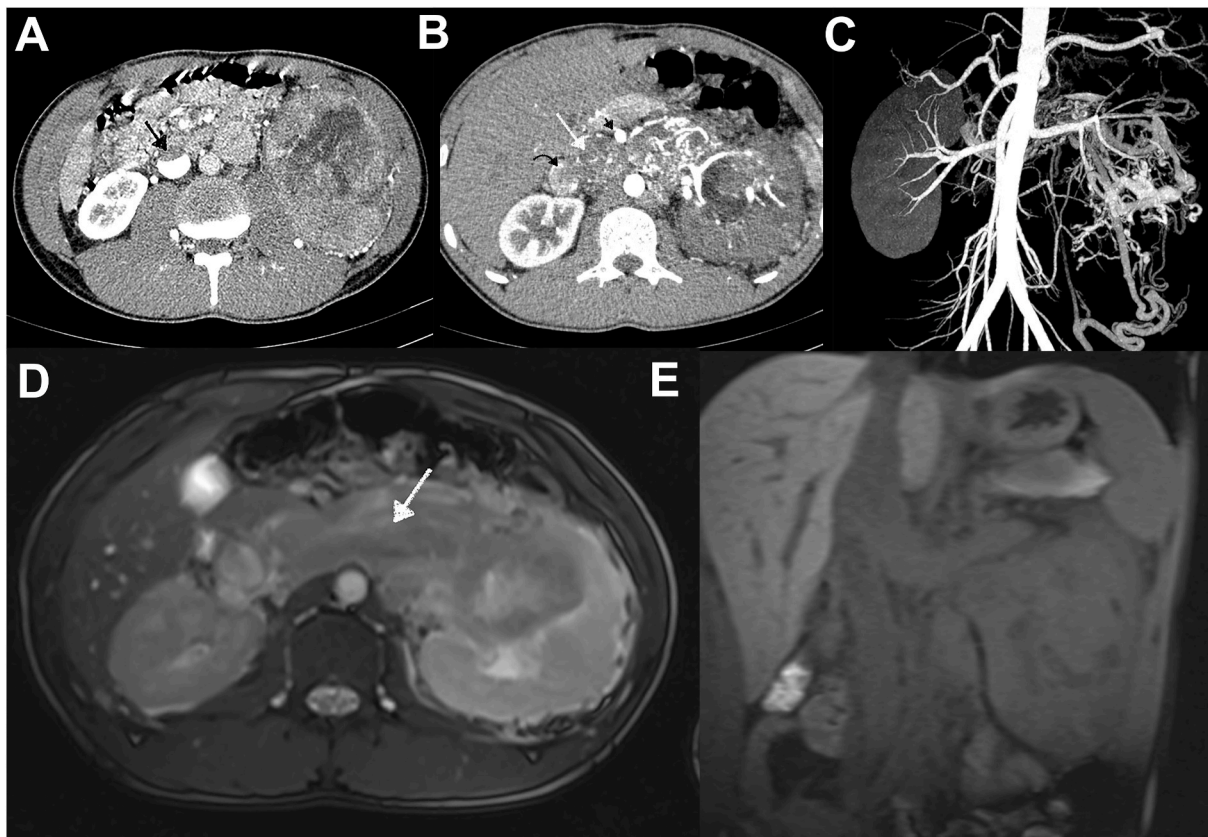


Fig. 1. A: Huge left renal mass. Filling defect within the IVC shows tumor thrombus (black arrow). B: Left renal vein is located between aorta and superior mesenteric artery (black arrow) and is involved by huge tumor thrombus (white arrow). A narrow rim of contrast agent is evident within IVC (curved arrow). C: Three-dimensional reconstruction of CT images shows significant neovascularization within the tumor. D: T2-weighted MR image shows huge tumor thrombus within left renal vein (white arrow). E: Coronal MR image shows the cephalad extent of tumor thrombus.

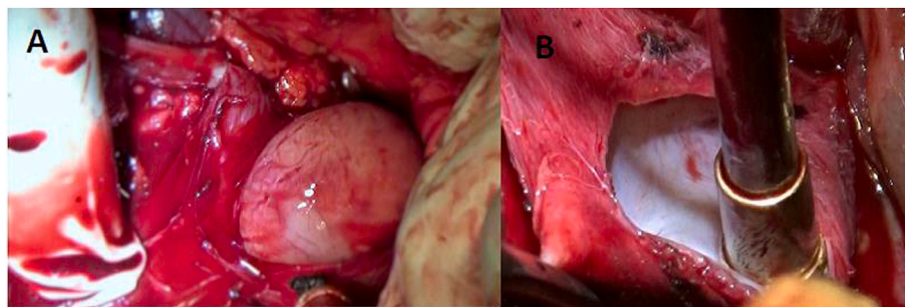


Fig. 2. A: Tumor thrombosis delivery after cavotomy. B: IVC lumen after thrombectomy.

counterparts in the bone and soft tissue, it seems to be more aggressive with poorer clinical outcome.²

Preoperative diagnosis of the disease is challenging as its clinical symptoms are nonspecific (including pain (54%), hematuria (29%) and renal mass (28%).¹ Moreover, radiologic modalities including CT and MRI are incompetent in discriminating renal ES from renal cell carcinomas (RCC). As a “small round blue cell tumor”, renal ES needs to be differentiated from other renal tumors such as blastemal Wilms tumor, small cell neuroendocrine carcinoma, neuroblastoma, rhabdomyosarcoma, synovial sarcoma, desmoplastic small round cell tumor, lymphoma and poorly differentiated renal cell carcinoma. Unfortunately, none of the immunohistochemical markers (including CD99) are specific for the diagnosis.

This family of tumors harbors a characteristic nonrandom chromosomal translocation (11; 22) (q24; q12) in more than 90% of the cases

which results in the production of the EWS/FLI-1 fusion gene. As differentiating ES from the other pathologies can affect our management dramatically, it is necessary to confirm the diagnosis by finding this translocation through cytogenetics or Polymerase chain reaction (PCR) assays.

Survival analyses are suggestive of an aggressive nature of the disease. In a study which was conducted by Murugan et al., 57% (4/7) of the patients with localized or locally advanced disease developed metastasis in a mean of 14 months despite surgical treatment in combination with systemic chemotherapy.² Moreover, several studies suggest even a higher level of aggressiveness of renal ES in comparison to its nonrenal counterparts. It has been shown that more than 65% of the patients with renal ES present with metastatic disease.^{1,2} In contrast, 25% of patients with nonrenal ES have metastasis at presentation. In fact, it seems reasonable to assume that a large number of patients with

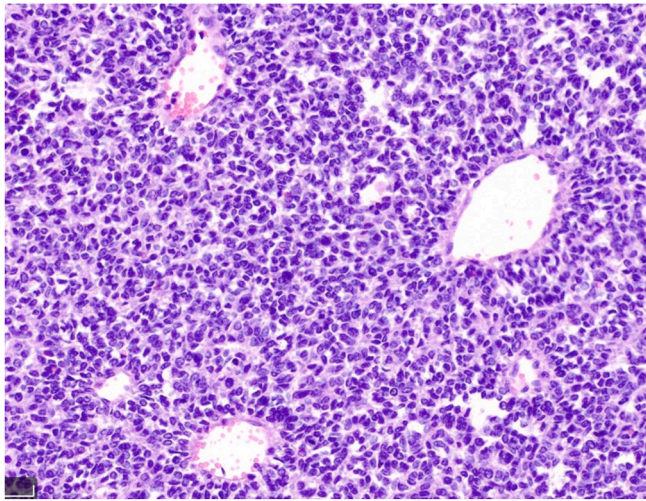


Fig. 3. Histopathologic examination of tumor revealed that it composed of small round uniform cells arranged in sheet and Rossetoid pattern. Cells had dark chromatin and round to oval nuclei.

localized disease harbor subclinical metastasis as up to 90% of patients with nonmetastatic bone ES, experienced relapse of the disease following local treatment.³

Based on the previously mentioned points and an overall response rate of 66% to chemotherapy in metastatic setting,¹ a combination of local and systemic (in the shape of neoadjuvant/adjuvant setting) treatments has been adopted as the standard of care. The current systemic treatment of ESFT includes cycles of Vincristine, Doxorubicine, Cyclophosphamide (VDC) plus Ifosfamide and Etoposide (IE). Ideally, Local treatment (in the form of radical nephrectomy or radiation therapy) is preceded by neoadjuvant chemotherapy and followed by additional cycles of chemotherapy. Unfortunately, management of most of the renal ES cases is far from excellence as only one third of patients with primary renal ES underwent biopsy prior to surgery and less than 70% (19/28) of biopsied patients received neoadjuvant therapy before nephrectomy.⁴ Much of this flawed management is related to inability to discriminate ES from common malignant pathologies (i.e. RCC) based on noninvasive preoperative evaluations. Therefore, at the very least, it is reasonable to perform percutaneous biopsy in young patients

presenting with large renal tumors.⁴

Herein, we presented a case of primary renal ES with tumor thrombosis up to vena cava who underwent radical nephrectomy and IVC tumor thrombectomy followed by adjuvant chemotherapy due to the lack of suspicion of such a rare pathology to perform preoperative percutaneous biopsy.

Conclusion

Preoperative diagnosis of the disease is challenging as the clinical symptoms of the disease are nonspecific. However, with the extensive availability of both histopathological methods and molecular markers, these cases can be diagnosed.

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None.

Declaration of competing interest

There is no conflict of interest.

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