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CASE STUDY

PRIMARY ADULT EWING SARCOMA OF THE KIDNEY: A RARE ENTITY

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ABSTRACT

Ewing sarcoma or primitive neuroectodermal tumor (ES/PNET) is an aggressive type of sarcoma that is rarely observed in the kidney. The diagnosis of primary renal EWS can be difficult; it mostly presents with non specific symptoms. The final diagnosis is based on combination of immunohistochemistry and fluorescence in situ hybridization (FISH). We review here in a case of Ewing Sarcoma of the kidney, and we review briefly the existing literature data.

INTRODUCTION

Ewing sarcoma or primitive neuroectodermal tumor (ES/PNET) a member of the family of small, round-cell tumors; are high-grade malignant tumours typically found in children and adolescents. They are the second most common form of bone malignancy and are rarely found in visceral organs. However, ES/PNET arising from the renal parenchyma is an extremely rare entity. No randomized studies have been published in the literature, and available data are limited to case reports or short case series (Riggi and Stamenkovic, 2007). In this case report, we present the clinical and histopathological features, management, and outcome of a case of renal ewing sarcoma, and we review the existing literature data about this rare entity.

Case report

A 31-year-old woman with no past medical history was admitted acutely to the emergency department with severe right flank pain and macroscopic hematuria started two weeks prior to her consultation. Associated symptoms included night sweats, nausea, and emesis. Physical examination revealed mild costovertebral angle tenderness. Results of his blood chemistry, routine blood tests, urine analysis, and urine culture were within normal limits. Abdominal computed tomography (CT) showed a huge tumor about 5.6 cm × 7.3cm involving the right kidney (Figure 1 and 2). The tumor had irregular, heterogeneous enhancement and some areas of necrosis. A bone scan and CT imaging of thorax, abdomen, and pelvis showed no evidence of metastasis.

The patient underwent right radical nephrectomy. Macroscopic examination showed a large mass in the right kidney, with lobulated contours, and white cut surface. Microscopic examination showed a small round cell tumor with a moderate degree of nuclear and cellular abnormalities and focal necrosis (Figure 1). Immunohistochemical analysis showed positive diffuse strong staining of cluster of differentiation 99 (CD 99), a focal staining of vimentin and epithelial membrane antigen and Ki-67(50%). The tumor cells were negative for Bcl-2, myogenin, GFAP, protein S-100, cytokeratin AE1/CKAE3 (Figure 4). The final pathological diagnosis was further confirmed by fluorescence in situ hybridization (FISH) which has shown the t(11;22) (q24;q12) translocation EWS gene consistent with Ewing's sarcoma (Figure 5). Adjuvant chemotherapy with vincristine (V), doxorubicin (A), ifosfamide (I) and etoposide (E): VIDE protocol was administered. The patient received a total of two chemotherapy cycles and refuses to continue chemotherapy at this time. Eighteen months after surgery, she has no evidence of recurrence.

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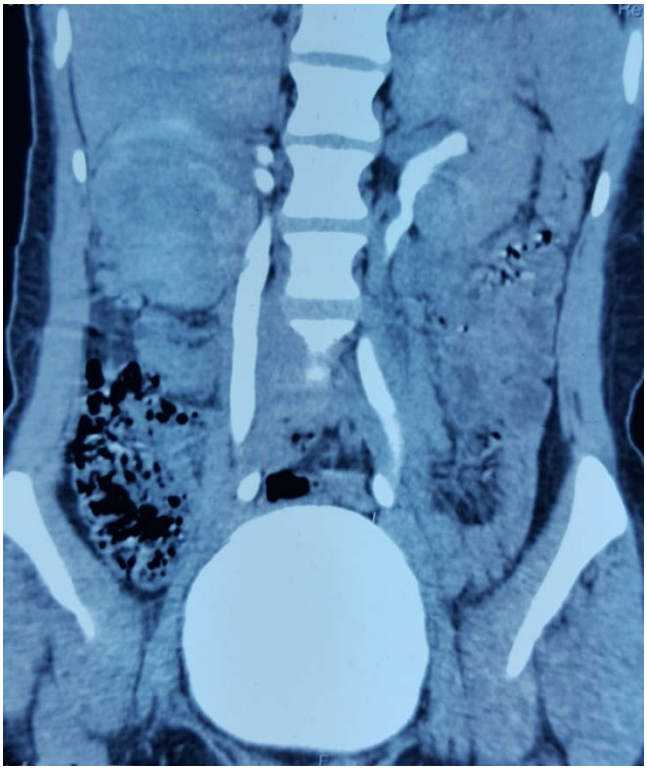

Figure 1. Parasagital view demonstrating the right lower pole renal mass

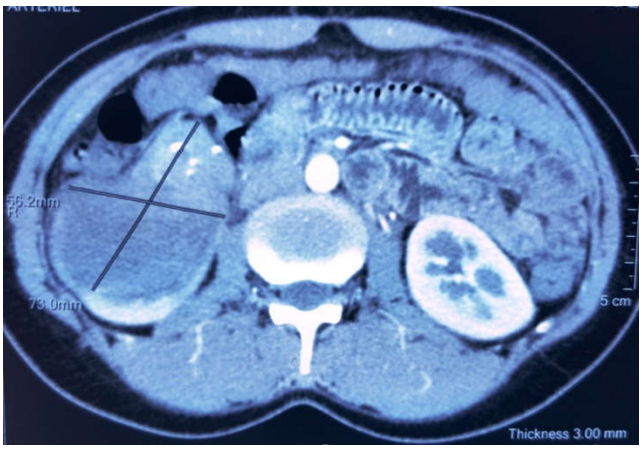

Figure 2. CT scan showing the 5.6 cm × 7.3 cm right lower pole renal mass

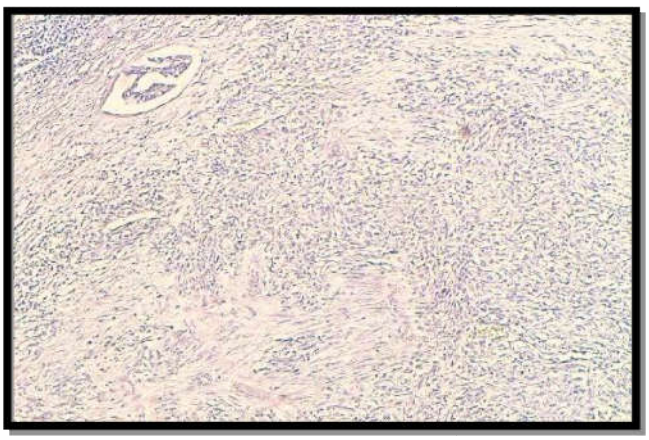

Figure 3. Small round cell tumor with a moderate degree of nuclear and cellular abnormalities (HESx20)

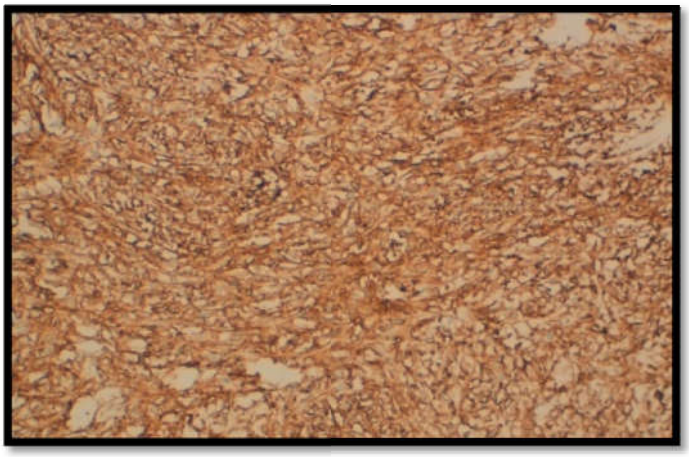

Figure 4. Positive diffuse strong staining of CD 99

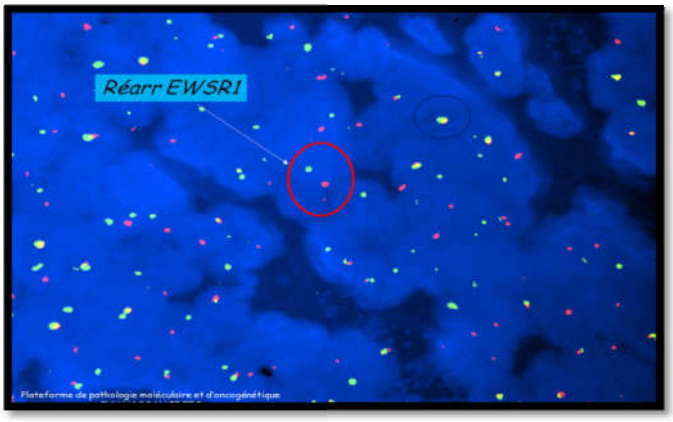

Figure 5. FISH : t(11;22) translocation EWS gene

DISCUSSION

ES/PNET is a part of the family of small round-cell tumors. It is mostly localized in bone or soft tissues surrounding the bone (Riggi and Stamenkovic, 2007). They occur rarely in visceral organs. Primary Ewing's sarcoma of kidney is a very rare entity that constitutes less than 1% of all malignant renal tumors, with an aggressive behavior and poor prognosis (Mani *et al*., 2009). The tumor affects predominantly young adults with a median age of 28 years (range 4–69 years), and a slight male predominance (Mani *et al*., 2009). The clinical presentation of renal sarcoma is not specific; it usually remains asymptomatic with a relatively short diagnostic delay, from a few weeks to a few months until they are large enough to produce symptoms; the loco-regional signs pain (85%) and palpable mass (75%) dominate the clinical picture. Hematuria is inconstant (25% of cases). The alteration of the general state, found in 25% of the cases reflects an advanced stage of the disease and correlates with a poor prognosis (Angel *et al*., 2010; Venkitaraman *et al*., 2009; Sheaff *et al*., 1997). The average size at the time of diagnosis varies from 5.5 to 23 cm (Bing *et al*., 2009) Furthermore, imaging characteristics can also be found in the case of other types of renal tumors (Bing *et al*., 2009). These tumors appeared as large areas of internal hemorrhage or necrosis, peripheral hypervascularity, and diffuse calcification. The differential diagnosis should be made with Wilms tumors, abscesses, lymphomas, renal cell carcinomas, metastases from a distant primary lesion, renal adenomas, sarcomas, and renal involvement by a primary retroperitoneal sarcoma (Zhihong

Liu *et al*., 2014; Nirmalya Chakrabarti *et al*., 2015; Maria Fernanda Arruda Almeida *et al*., 2014). The final Ewing's sarcoma diagnosis, is based on, the combination of morphological findings, immunohistochemical analyses, and cytogenetics studies. Macroscopically the tumor is tan-white with areas of hemorrhage and necrosis (Bing *et al*., 2009). Histologically, ES/PNET forms a monomorphic population of small blue cells that can be arranged as spherical grouping of dark tumor cells around a central area that called Homer–Wright rosettes (Bing *et al*., 2009; Tariq S. Hakky *et al*., 2013).

However, ES/PNET of the kidney must still be differentiated from other small round cell tumors that can all form Homer–Wright rosettes. This group includes, renal neuroblastoma, Wilm's tumor, non-Hodgkin Lymphoma, alveolar rhabdomyosarcoma, monophasic synovial sarcoma, carcinoid tumors, desmoplastic small roumd cell tumor, clear cell sarcoma of kidney (Bing *et al*., 2009; Mihai Razvan Manescu *et al*., 2015). Even though this is sometimes difficult, an immunohistochemical analysis with a broad panel consisting CD99, Friend leukemia virus integration (FLI)-1, vimentin, neuron-specific enolase (NSE), S-100, and CK; is recommended to differentiating these unique entities (Jimenez *et al*., 2002). Moreover, CD99 is nearly expressed by all PNET tumors, with an incidence approximating 99%, but this is not specific for ES/PNET; whereas other markers show variable expression (Joel R. Angel and Anushayanthan Alfred, 2010) Approximately 85–90% of Ewing's sarcomas associate a functional oncogene resulting from the DNA translocation t(11;22)(q24;q12) (Mihai Razvan Manescu *et al*., 2015). Because the treatment is complex and includes surgery, chemotherapy, and radiotherapy, a multidisciplinary approach is recommended.

Molecular techniques can be used to confirm the diagnosis of ES/PNET; Approximately, 85% of Ewing's sarcomas associate a functional oncogene detected by FISH or reverse transcription-polymerase chain reaction resulting from the DNA translocation t(11;22)(q24;q12) (Hakky *et al*., 2013). Additionally, other chromosomal translocations include t(21;22) with analogous fusion of EWS to other partners have been reported in renal ES/PNET (Jinjing Zhong *et al*., 2015). Thus, FISH with negative EWS‑FLI1 fusion only cannot completely exclude the diagnosis of ES/PNET of the kidney (Berg *et al*., 2009). Management of ES/PNET has included surgery, chemotherapy, and radiation therapy (Zöllner *et al*., 2013). The EURO-E.W.I.N.G. 99 study recommends a multidrugs chemotherapy contained vincristine, doxorubicin, cyclophosphamide, ifosfamide and etoposide. That delivered prior and continued after local control (Mukkunda *et al*., 2009). No randomized studies have been published in the setting of the rarity of renal ES/PNET. Furthermore, in practice all Ewing's family tumors are treated in the same way using systemic chemotherapy in conjunction with surgery or radiotherapy or both modalities. Radical nephrectomy is an important method for local control of the disease and remained a valuable tool for the long-term survival of patients with renal Ewing's sarcoma. Local radiotherapy to the surgical bed must be added in the case of inadequate surgical margins (Ohgaki *et al*., 2010). According to some institutions, adjuvant chemotherapy in this group of patients shows a benefit while others find no clinical improvement (Wedde *et al*., 2011). Ewing's sarcoma is an aggressive tumor with a poor prognosis; adverse predictors of survival being non skeletal primary, older age, metastasis at diagnosis, incomplete resection, and bad response to chemotherapy (Zöllner *et al*., 2013). However among patients with local disease without metastasis at diagnosis, and who has taken aggressive multimodal treatment, the survival rate was 70%; while it has 9 to 41% for patients with metastatic disease (Maria Fernanda Arruda Almeida *et al*., 2014). All PNETs show a 5-year survival rate of 58–61% with a median survival of 120 months, whereas for renal Ewing' sarcoma 5-year disease-free survival is reported around 45–55% (Joel R. Angel *et al*., 2010). Mukkunda *et al*. have led a study of 7 patients with renal Ewing's sarcoma with a median follow-up of 36 months (range from 5 to 149), a median disease-free survival in patients with non metastatic disease of 30.35months (range from 5.1 to 149) with a 5-year overall survival rate of 42% (Mukkunda *et al*., 2009; Wedde *et al*., 2011).

Conclusion

Primary renal ES/PNET in adults is a very rare entity described by case reports in the literature. The treatment options are vastly different including radical nephrectomy and perioperative chemotherapy; postoperative radiotherapy may be indicated in some cases. Further, it remains an aggressive tumor with poor prognosis.

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The authors declare that they have no competing interests.

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