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Case Report

Extraskelatal Ewing sarcoma: A case report [☆]

Siham Nasri, MD, Ranya Aqamour, MD, Leila Haddar, MD*, Imane Guerrouj, MD, Karim Haddar, MD, Narjisse Aichouni, MD, Imane Kamaoui, MD, Imane Skiker, MD

Department of Radiology, Mohammed VI University Hospital, Faculty of Medicine and Pharmacy, University Mohammed First, Oujda, Morocco

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ABSTRACT

Extraskelatal Ewing sarcoma is a rare tumor mainly affecting young people, of poor prognosis with very high mortality rates especially in metastatic forms. It can affect different locations, without specific clinical signs, which delays the diagnosis. Imaging plays an important role for diagnosis, staging, preoperative assessment and surveillance. The diagnosis should be set early to a better management. We report a case of a 30-year-old man with a large extraskelatal Ewing sarcoma of the left thigh. The patient was initially treated with chemotherapy. Unfortunately, the tumor has increased in size making surgery impossible. The patient ultimately died of pulmonary metastases.

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Introduction

Ewing sarcoma of the soft tissue is a rare tumor with a poor prognosis and high mortality rate especially in advanced and metastatic forms, which implies the need for early management in order to offer the best chances of survival. Faced with the absence of specific clinical and radiological signs, anatomopathological examination has a key role in the positive diagnosis. The therapeutic aspect is mainly based on surgery with total exeresis while preserving the maximum function of the affected organ.

Case presentation

We present the case of a 30-year-old man with no notable pathological history except for a chronic smoking habit of 10 packs per year. The history of the disease included joint pain in the inner part of the left thigh, radiating towards the pelvis, dating back three months, which motivated the patient to consult. The physical examination revealed a huge mass involving the inner side of the left thigh, without inflammatory signs or vascular or neurological abnormalities.

The patient underwent first an ultrasound (US) of the left thigh (Fig. 1), which revealed a heterogeneous lesion with hyperechoic areas, poorly limited with a long axis parallel to the skin, measuring 213 mm in long axis, associated with a

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* Corresponding author.

E-mail address: Leila.hdr33@gmail.com (L. Haddar).

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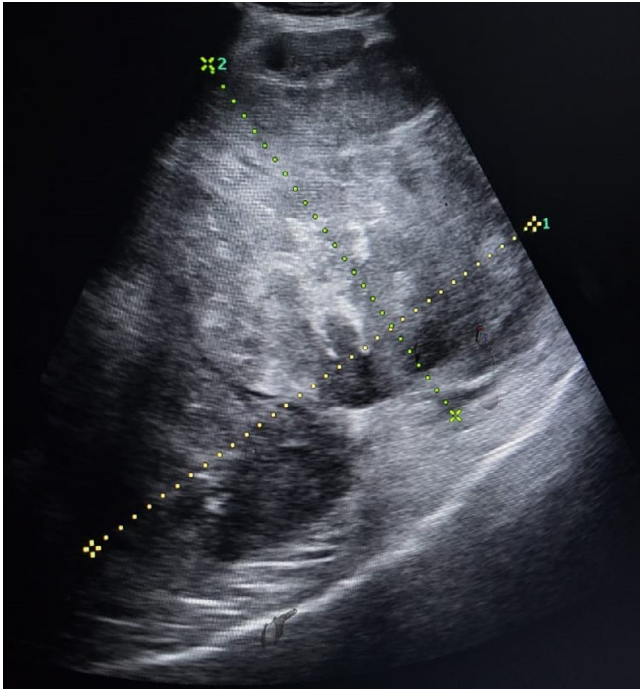


Fig. 1 – Ultrasound of the left thigh showing the tumor mass, which appears heterogeneous with hyperechoic areas.

significant infiltration of the soft tissues. The computed tomography (CT) with and without contrast of the left thigh (Fig. 2) revealed a huge soft tissue mass on the inner side of the left thigh measuring $215 \times 150 \times 132$ mm, containing multiple micro-calcifications and hyperdense hemorrhagic areas, and becomes heterogeneous after contrast. This tumor causes mass effect on surrounding vascular structures, without bone lysis. A magnetic resonance imaging of the left thigh was performed to better characterize the tumor. It showed (Fig. 3) a voluminous polylobulated mass involving the medial and posterior compartments of the left thigh, with irregular contours, with intermediate signal intensity on T1-weighted images, heterogeneous with high signal intensity on T2-weighted images, heterogeneously enhancing after injection of Gadolinium delineating areas of central necrosis, measuring 18.2×16.7 cm extended over 23.5 cm. It contains T1-hypersintense areas related to hemorrhagic zones. This mass occupies all the muscles of the internal and posterior compartments of the left thigh, with atrophy and T2-hyperintense signal of the muscles of the anterior compartment and the gluteus maximus muscle. The tumor is exposed to the bone cortex of the femur. The femoral vascular bundle remains separated from the mass by muscle fibers. It invades the sciatic nerve. It is associated with a significant infiltration of the subcutaneous soft tissues. There was a nodular mass with the same characteristics of the tumor described above, measuring 33×32 mm, located next to the semitendinosus muscle.

The biological workup showed hemoglobin 12.6 g/dl (Normal 12 – 16 g/dL), CRP 10 mg/l (Normal 0-6 mg/l), LDH 769 UI/l (Normal 125-143 UI/L). The patient was referred to the on-

cology hospital for specialized management. He underwent a surgical biopsy, which the anatomopathological and immunohistochemical study was performed in favor of Ewing's sarcoma. Thoracoabdominopelvic scan showed no signs of secondary localization.

The tumor was initially considered not metastatic but locally advanced and unresectable disease. The medical oncology team opted for neoadjuvant chemotherapy with surgical continuation if good response. The patient received three courses of chemotherapy with the VIDE protocol which is based on Vincristin, Ifosfamide, Doxorubicin, and Etoposide. The control CT scan, performed 6 months after the initial scan, showed an increase in tumor volume. The nonsurgical attitude was maintained due to the large volume of the tumor and the risk of loss of limb function, and the decision of the multidisciplinary team meeting was radiotherapy of which the patient benefited from 11 sessions.

Three months later, the patient is admitted to the emergency room for respiratory distress with an oxygen saturation of 40%. An emergency chest CT scan without and with contrast injection was performed showing pulmonary and bone metastases, and on the sections through the abdomen, there were multiple suspicious lesions in the liver, spleen, and pancreas. The patient died the following day despite the measures of reanimation.

Discussion

Ewing sarcoma (ES) is a malignant tumor that belongs to the Ewing sarcoma family of tumors (ESFT), mainly affecting bone structures. ESFT is a group of small round-cell tumors, which have the neural histology in common. This family of tumors includes the classical ES of bone (ESB), extraskeletal Ewing sarcoma (EES) which is our case, peripheral primitive neuroectodermal tumor (pPNET) and Askin tumor of the chest wall [1]. EES remains very rare, it is 10 times less than ESB, with an incidence of 0.4 per million [2]. It mainly affects young people between the ages of 10 and 30 years, without gender predominance [3,4]. EES can have different locations including the paravertebral region, the chest wall, the lower limbs and the pelvis. The nose, the orbit, the larynx, the nasopharynx, the scalp, the face, the neck, and the parotid gland remain extremely rare locations [5].

The absence of specific clinical signs often delays diagnostic and therapeutic management. The majority of patients present with a rapidly progressive swelling, associated with mild pain due to peripheral nerve or even spinal cord compression with motor and sensory disturbances, as well as the possibility of intratumoral hemorrhage. The tumor grows locally without any alarming inflammatory signs. This was the case with our patient, the tumor increased in size in a short time, without any inflammatory signs.

Even if the radiological features are nonspecific, imaging is essential for the diagnosis, the staging, the preoperative assessment and the surveillance of EES [6]. It also plays an important role to guide the optimal biopsy site. With Doppler US, ESS is usually a heterogeneous mass containing flow signals [6]. When CT is performed, it appears as a large mass with sim-

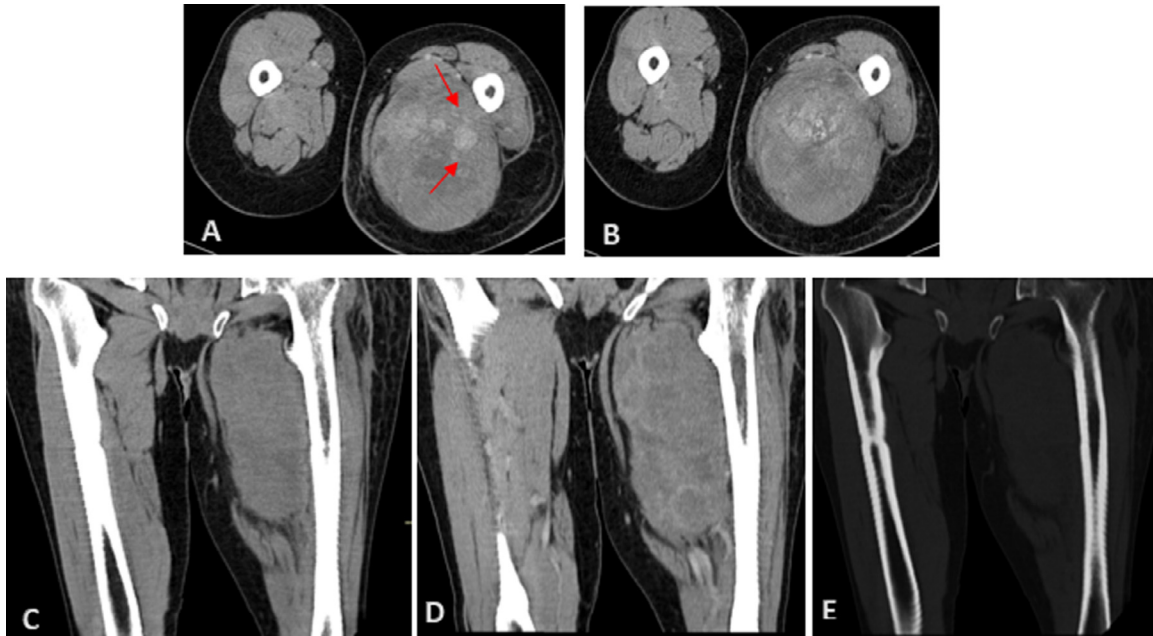


Fig. 2 – CT scan: axial plane without (A) and with contrast (B), coronal plane without (C) and with contrast (D) and bone window (E) revealing the huge soft tissue mass on the inner side of the left thigh, containing multiple micro-calcifications (arrow).

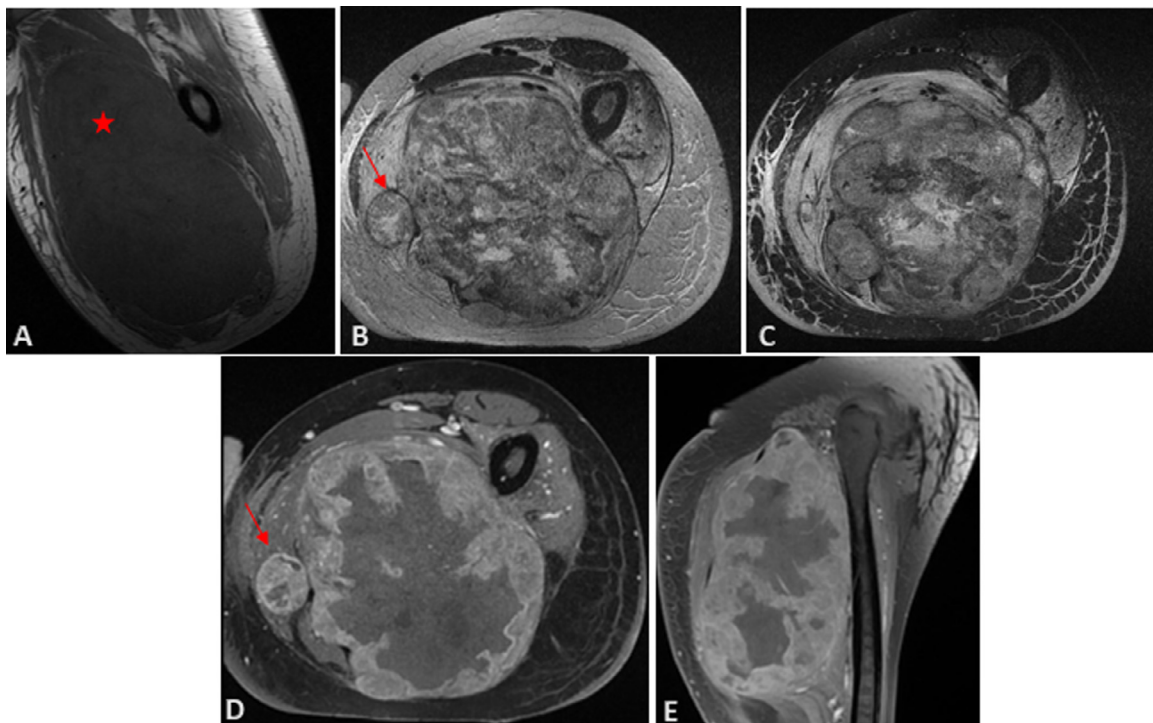


Fig. 3 – MRI: T1-weighted (A), T2-weighted (B), T2-weighted with fat suppression (C) images and after injection of Gadolinium in axial (D) and coronal (E) planes: the voluminous polylobulated mass involving the medial and posterior compartments of the left thigh, with irregular contours, with intermediate signal intensity on T1-weighted images, heterogeneous with high signal intensity on T2-weighted images, heterogeneously enhancing after injection of Gadolinium delineating areas of central necrosis and T1-hypersintense areas related to hemorrhagic zone (*). Nodular mass with the same characteristics of the tumor described above (red arrow).

ilar density to the muscles, often with regular contours, forming a pseudo capsule, but sometimes with less defined contours, invading adjacent nerve and vascular structures. There may be extrinsic bone erosions, cortical thickening or aggressive periosteal reaction. The injection of contrast medium shows areas of necrosis; calcifications may be present [6]. On magnetic resonance imaging, the tumor has low to intermediate signal intensity on T1-weighted images, high signal intensity on T2-weighted sequences, and enhances heterogeneously after Gadolinium injection [6]. As it is a malignant tumor, EES can be diffusely metastatic; the most common distant locations involve the lungs, bone and brain. PET/CT plays a complementary role in assessing the presence of metastatic disease [6].

Given the nonspecificity of the clinical and radiological signs, anatomopathology plays an important role in the positive diagnosis with histological characteristics similar to those of ESB [7].

The low frequency of this entity explains the lack of data on optimal management. Surgery with complete excision represents the cornerstone in the treatment of localized EES [5]. The quality of the initial excision has an important effect on both local and distant recurrence, but surgery alone is never sufficient and it is recommended to combine surgery with chemotherapy and/or radiotherapy depending on the location, resectability and stage of the tumor [8]. Local control of malignancy is largely dependent on resection margins. When chemotherapy is not effective, wider resection margins are required [9,10]. In cases where wide negative margins is not possible, for example because of vascular or nerve structures, postoperative radiotherapy is recommended to achieve better local control [9,10]. If the tumor is unresectable, radiation therapy becomes the only possible treatment [11,12]. In metastatic disease, chemotherapy remains an option, with the aim of prolonging progression-free survival [13]. In such situations, the prognosis is very poor [10]. In our case, the patient initially had nonmetastatic disease. He received three courses of neoadjuvant chemotherapy and yet a CT scan showed an increase in tumor size which was unexpected, and the decision was surgical abstention with a switch to radiotherapy. The patient ultimately died of metastases, which reflects the aggressiveness of his tumor.

Because of the relative rarity of EES, a specific staging system does not yet exist. For this reason, the use of the American Joint Committee on Cancer (AJCC) system for all soft tissue sarcomas is suggested [14]. But the problem is that this system is based on lymph node metastases, which are rare in EES [14]. In addition, EES is usually diagnosed at an advanced stage [14,15]. For these reasons, Ludwig et al. suggested an alternative approach, which consists of staging patients according to whether they have resectable or unresectable disease, and considering that all patients have micrometastatic disease [15].

Compared to ESB, EES have a better prognosis [16]. However, there are poor prognostic factors associated with EES that one should be aware of, these include advanced age, pelvic involvement, as well as the initial tumor size, which represents the strongest factor in localized EES [17,18]. The laboratory workup at the time of diagnosis also plays a role, as studies have shown that an elevated white blood cell count,

low hemoglobin, and elevated LDH at diagnosis are associated with a poor prognosis [19,20]. Another important prognostic factor is the histologic response to neoadjuvant chemotherapy [12]. Metastatic or recurrent forms represent forms of very poor prognosis, and are almost always fatal [21]. The introduction of chemotherapy in the treatment of EES has remarkably improved survival rates for patients with the localized form of the disease, from 10% five-year survival for patients without chemotherapy to 70%-80% with appropriate chemotherapy [14]. In terms of survival for patients with metastatic disease, despite chemotherapy, results remain poor, with minimal improvement in 5-year survival from 15% to 32% [14].

Our patient unfortunately progressed from a localized advanced form to a metastatic form despite appropriate treatment. The major contributing factor would be the large size of the tumor that compromised vascular and nervous structures, making it unresectable. The lack of response to treatment has unfortunately contributed to the development of multiorgan metastases.

Conclusion

EES remains a rare tumor. It should be considered in young adults who present with a large heterogeneous mass, especially in the trunk and extremities. Imaging plays an essential role in every step of the management. Immunohistochemical analysis confirms the diagnosis. The treatment for localized disease is neoadjuvant chemotherapy that is followed by surgery. Radiation therapy has its place in unresectable disease.

Patient consent

Informed consent was obtained from the patient.

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