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A rare case of epithelioid hemangiothelioma of the quadriceps

Hemangioendotelioma is a group of rare vascular tumors with border-line behavior. They may involve internal organs, limbs, bones and soft tissue. The histological variant epitheliod hemangiothelioma is locally aggressive and has metastatic potential.
We present a case of a 41-years old woman affected by epitheliod hemangiothelioma of the right quadriceps. The patient complained of localized pain in the anterior region of the right thigh, which started about 3 months earlier during physical exercise. For the increasing size of the lesion, the patient was referred to our Department. On physical examination, the lesion appeared elastic, fixed to the surrounding tissues and painful under pressure. An ultrasound examination revealed a small avascular lesion and a MRI examination showed an oval formation measuring about 18 mm in diameter of nonspecific significance. A surgical removal of the lesion was performed and diagnosis of epithelioid hemangiothelioma was achieved. A complete removal of the quadriceps muscle was then accomplished.
In this paper, clinical and oncologic aspects of this rare tumor are discussed

KEY WORDS: Epithelioid hemangiothelioma, Lower limbs tumor, Rare tumors

Introduction

Epithelioid hemangiothelioma is a vascular tumor with unpredictable behavior. It occurs mainly in adult patients, and differently from other types of hemangiothelioma, it origins most frequently from the iliac and femoral veins of the lower limbs. Because of its rarity, many clinical aspects are still unclear.
In this paper, we present a rare case of a 41-years old woman with a solitary epithelioid hemangiothelioma of the right quadriceps, treated by surgical excision of the muscle. Based on our clinical case, we discuss on diagnostic and surgical strategies of this rare tumor.

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Case Report

A 41-year-old woman was referred to our Department of Surgery for the occurrence of localized pain in the anterior region of the right thigh. The patient complained of localized pain started about 3 months earlier after physical exercise. In the last weeks, a palpable lesion increasing in size was noted in the quadriceps region. On physical examination, the lesion appeared of elastic consistency and painful under pressure.
Ultrasound examination highlighted the presence of a slightly uneven lump of about 13 x 5 x 8 mm, that appeared avascular under power-Doppler ultrasound, in the front side of the distal third of femoral rectus muscle. This echographic pattern was comparable with a fibromatous lump.
After routine preoperative testing, which highlighted no alteration, patient went into surgery, during which a 4 cm long transverse incision was made on the front side of the leg. After intraoperative ultrasonographic assessment of the lesion, an incision in the muscle fiber was

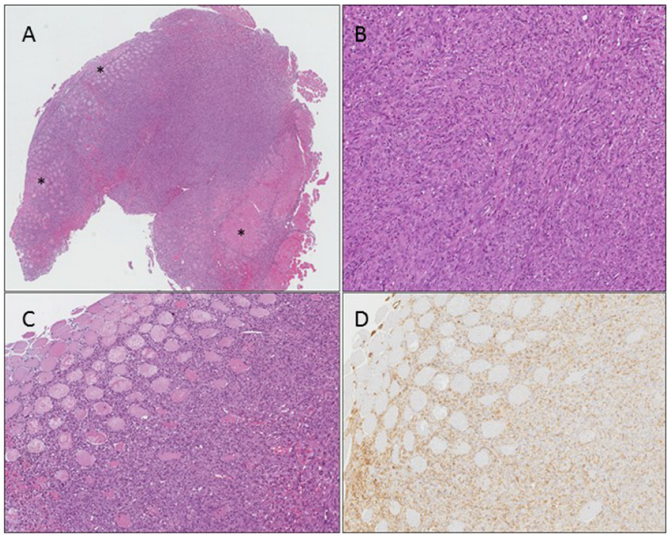

Fig. 1: **A**) At low magnification, a proliferation of neoplastic cells which infiltrates skeletal muscle (*) (H&E 20x). **B**) At high magnification, epithelioid cells with abundant eosinophilic cytoplasm and vescicular nuclei (H&E 300X). **C**) At high magnification, infiltration of skeletal muscle by epithelioid neoplastic cells (200X). **D**) Linear membranous staining for CD31 (200X).

made and the lump was removed while respecting its margins, although not clearly definable.
After placing the drain, the breach was closed at all levels. The day after surgery, the drainage pipe was removed without complications and the patient was discharged from the hospital.
Histological examination showed a proliferation of spindle-shaped and epithelioid cells with eosinophilic cytoplasm and vesicular nuclei. Neoplastic cells were embedded in sclerotic stroma and were arranged in multiple ill-defined nodules and short fascicles.
Immunohistochemical analysis revealed a strong, linear membranous positivity for CD31 and nuclear positivity for ERG which validated the diagnosis of epithelioid hemangioendothelioma (Fig. 1).
Further post-operative MRI failed to demonstrate other lesions in the quadriceps muscle or femoral bone involvement.
A total body – CT scan was also negative. Nevertheless, a complete removal of the quadriceps was accomplished. Histopathology was negative. No further therapy was required.

Discussion

Vascular tumors originating from the epithelioid (histiocytoid) endothelial cells include a variety of rare neoplasms with a wide biological behavior, ranging from benign hemangiomas to malignant angiosarcomas. Among them, there are the "hemangioendothelioma", group, which includes vascular neoplasms with a borderline behavior [1]. Hemangioendotheliomas seems to origin from abnormal growth of blood vessel cells. They are classified according to histopathologic features, into epithelioid hemangioendothelioma, papillary intralymphatic angioendothelioma (Dabska tumor), retiform hemangioendothelioma, kaposiform hemangioendothelioma, pseudomyogenic hemangioendothelioma (epithelioid sarcoma-like hemangioendothelioma), composite hemangioendothelioma [1].
Most of them have a low-grade differentiation, may locally recur and have a low metastatic tendency mainly to lymph nodes. It seems that epitelioid hemangioendothelioma, especially the large ones located at deep soft tissues, are the most aggressive [1].
All the type of vascular tumors can occur in soft tissues, skin, bone, thoracic and abdominal organs.
Epithelioid hemangioendothelioma's incidence is less than 1% of all vascular tumors [4]. It affects adult males [2-5] more than females, and usually appears in the second / third decade of life [3], with a range of 7 – 93 years and a mean age of 36 – 49 years [6-7]. It origins mainly from the iliac and femoral veins, while the main skeletal localization is the lower extremities [10]. Other localizations are described in the Literature are liver, lung [3-8], maxilla, spine region, head, neck, brain and meninges [9-12]. Liver solitary localization was described in 21% of total cases, and in 18% of cases was associated to lung lesion. Solitary lung involvement is reported in 12%. Localization in bone and limbs is reported respectively in 18% and 35% [13]. Very few cases of limbs' soft tissue are localization described in the Literature [6,14,15].
Multicentric presentation of epitelioid hemangioendothelioma has been described with involvement femur, tibia, phalange, cuneiform, tarsal navicular and metatarsal bone. However, it is not clear if they are multiple primitive or metastatical tumors [7,16-18].
Clinical presentation varies based on the localization. Generally, epitelioid hemangioendothelioma of limbs' soft tissue presents as a slowly increasing mass associated to pain and swelling [6]. Anesthesia and/or paresthesia in case of compressive neuropathy has been noted [6]. Cutaneous ulceration is also documented [6]. It can manifest as an osteolytic lesion [6,7,15], which may be responsible of fractures [7].
Diagnostic work-up, which US scan allows differential diagnosis between an arteriovenous malformation or an aneurysm [7], and X-ray examination to study the bone involvement. Contrast-enhanced MRI is useful to obtain morphological data, such as local extension, relations with the surrounding tissues, cleavage plan. CT scan is preferred for staging. PTE scan and bone scintigraphy are used to detect metastasis [7].
Histo-pathological examination is essential to diagnose epithelioid hemangioendothelioma. Microscopical features of epithelioid hemangioendothelioma are cords,

strands and solid aggregates of round, oval, spindle-shaped and polygonal cells, with abundant pale eosinophilic cytoplasm, vesicular nuclei, and inconspicuous nucleoli, embedded in a fibromyxoid or sclerotic stroma. Many neoplastic cells exhibit prominent cytoplasmic vacuolization as an expression of primitive vascular differentiation. Immunohistochemical markers that allow identifying peripheral epithelioid hemangioendothelioma are Fli-1 nuclear protein, EMA, CD68 and ERG. Fli-1 protein, if associated to CD31 reaches a higher sensitivity and specificity than CD31 and CD34 endothelial markers alone [7].
The majority of epithelioid hemangioendothelioma are locally aggressive and associated with low mortality [6], but progression to metastatic disease is possible, as it has been reported in the Literature [2].
Deyrup et al. proposed to classify EHE into low risk and high-risk behavior based on mitotic activity and tumor size [19].
Epithelioid hemangioendothelioma has a high incidence of multifocal lesions [6]; in such case, it seems that prognosis is better than in presence of unifocal lesion.
For the local aggressiveness, tendency to lymph nodes and distant metastasis, and possible multifocality of the tumor, therapeutic strategies remain controversial. Reported cases of spontaneous partial or total regression [15] of the tumor and a different classification of the aggressiveness lesions', are responsible for the not-well defined management of the affected patients.
Treatment options depend on the type, number, size and location [6]. Since epithelioid hemangioendothelioma may be locally aggressive, a wide local excision is recommended and adjuvant chemotherapy is sometimes required [6]. Generally, surgical excision is the first line and most effective therapy [6].
Metastatic patients should be submitted to chemotherapy and radiation therapy [6], although the role of chemotherapy has not been clarified.
Bisbinas et al. reported a case of multifocal bone EHE treated successfully with radiotherapy and a case of remission from single bone EHE in an old man after chemotherapy [15]. Saste et al. reported a case of metastatic EHE treated with remission by means of radiotherapy and chemotherapy.
Since the role and timing of adjuvant therapy has not been defined, close follow-up is recommended.

Riassunto

L'emangioendotelioma è un gruppo di rari tumori vascolari con comportamento border-line. Possono coinvolgere organi interni, arti, ossa e tessuti molli. La variante istologica detta "emangiotelioma epithelioide", è localmente aggressiva e presenta un potenziale metastatico.
In questo case report presentiamo un caso di una donna di 41 anni affetta da emangiotelioma epitelioide al quadricipite destro. La paziente lamentava un dolore localizzato nella regione anteriore della coscia destra, iniziato circa 3 mesi prima durante l'esercizio fisico. Per le dimensioni crescenti della lesione, la paziente è stata indirizzata al nostro Dipartimento. All'esame obiettivo, la lesione appariva elastica, fissa sui tessuti circostanti e dolorosa alla digitopressione. Un esame ecografico ha rivelato una piccola lesione avascolare e un esame RM ha mostrato una formazione ovale di circa 18 mm di diametro di significato non specifico. È stata eseguita una rimozione chirurgica della lesione ed è stata formulata diagnosi di emangiotelioma epitelioide. È stata quindi eseguita una rimozione completa del muscolo quadricipite.
In questo lavoro vengono discussi gli aspetti clinici e oncologici di questo raro tumore.

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