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Case Report

Langerhans cell histiocytosis in the glenoid neck with rare mutation: A case report ☆

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disease that occurs mainly in children. It has several forms of clinical presentation. Early diagnosis is important for better results. A 17-year-old male patient presented with right sharp shoulder pain for 2 months. Magnetic resonance image (MRI) of the shoulder showed an expansile osseous lesion in the anterosuperior spine of the right scapula with significant edema that causes compression of the subscapular neurovascular bundle. A CT scan and X-rays were also performed. Overall, all the images suggested a lesion compatible with chondroblastoma; however, the pathology images documented a Langerhans cell histiocytosis with a mutation in the V600E/E2/D in the 15 exon of the BRAF gene. LCH is a difficult diagnosis, especially in cases where clinical presentation is not the most common. This case is unique as the lesion developed not only in the scapula which has a 3% prevalence in LCH, but also had radiographic and MRI characteristics of a chondroblastoma more than the typical LCH lesion. Additionally, it was accompanied by a BRAF V600E mutation which is uncommon in LCHs bone cases.

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Introduction

Langerhans cell histiocytosis (LCH) is a rare disease that arises when there is local hyperproliferation or deregulation of apoptosis in Langerhans cells. It is related to three clear etiologies: genetic, neoplastic, and immunological [1]. It occurs predominantly in children and in females more than males with a ratio of 8:1. There are clear presentations of the disease: the first one is an eosinophilic granuloma characterized by bone lytic lesions [2].

The second one is Hand-Schuller-Christian disease which is consistent with bone lesions, exophthalmos, and diabetes insipidus. The last one is Letterer Siwe disease in which the patient presents with lymphadenopathy, pancytopenia, hepatosplenomegaly, bone lesions, and skin rash [2]. LCH has a three-year mortality rate of 25%. It is highly important to detect LCH before changes appear on magnetic resonance imaging (MRI) in order to achieve a more successful recovery process [3].

Case presentation

A 17-year-old male patient presented with right sharp shoulder pain of 2 months of evolution, without association to trauma. The pain did not start after a certain type of specific movement or exercise. The pediatric orthopedic service decided to order an MRI of the shoulder. It reported an expansile osseous lesion in the anterosuperior spine of the right scapula of approximately 18 × 10 × 20 mm with significant edema that causes compression of the subscapular neurovascular bundle. These image findings were highly suggestive of scapular chondroblastoma (Fig. 1).

A right shoulder X-ray and computed tomography (CT) were recommended for better characterization of the lesion. The X-ray showed a radiolucent lesion in the neck of the right scapula of non-aggressive aspect and of non-specific characteristics in this imaging modality. CT reported the main imaging finding of an intraosseous lesion of rounded morphology of predominantly lytic aspect in the topography of the

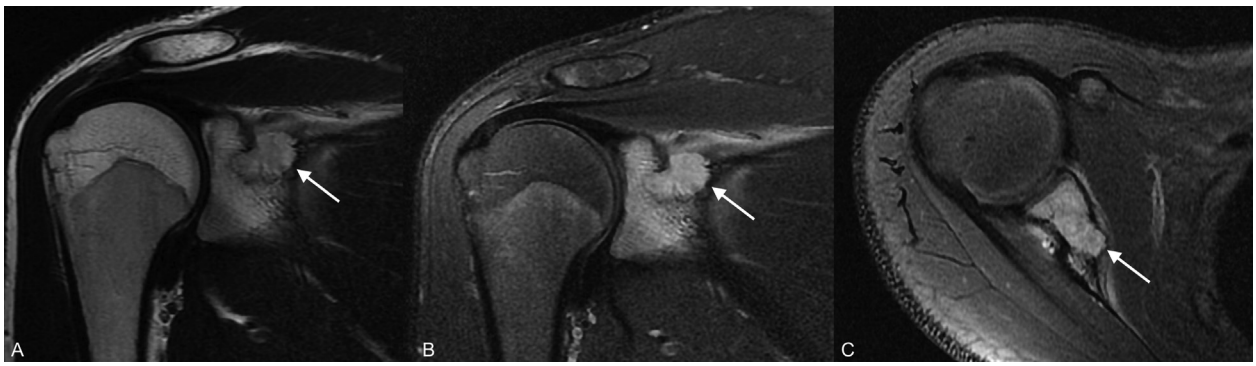

Fig. 1 – Coronal and axial view of MRI of the shoulder (A-C) expansile lesion that originates from the superior glenoid process, in the anterosuperior spine of the right scapula. the lesion shows high intensity on T2-weighted and low intensity on T1-weighted images. Important bone marrow edema is seen in the scapula, the lesion extends from the cortical bone to the adjacent soft tissues with compression of the suprascapular neurovascular bundle. The characteristic of the lesion and the extensive edema suggested a cartilaginous type lesion (chondroblastoma).

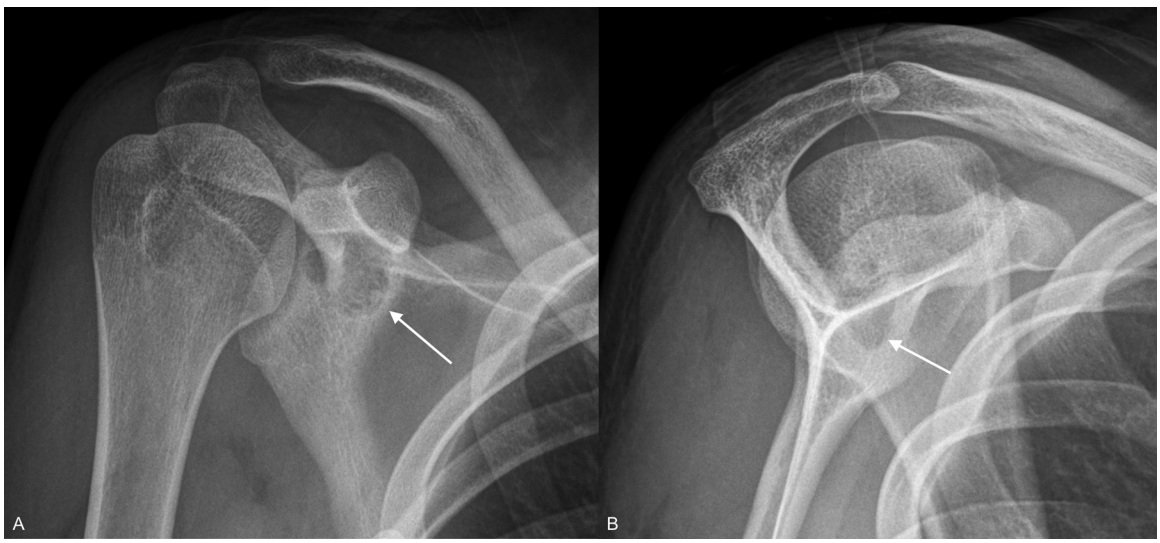

Fig. 2 – Shoulder X-ray AP and oblique view. (A-C) A lytic intraosseous lesion is observed in the neck of the scapula without periosteal reaction or soft tissue mass.

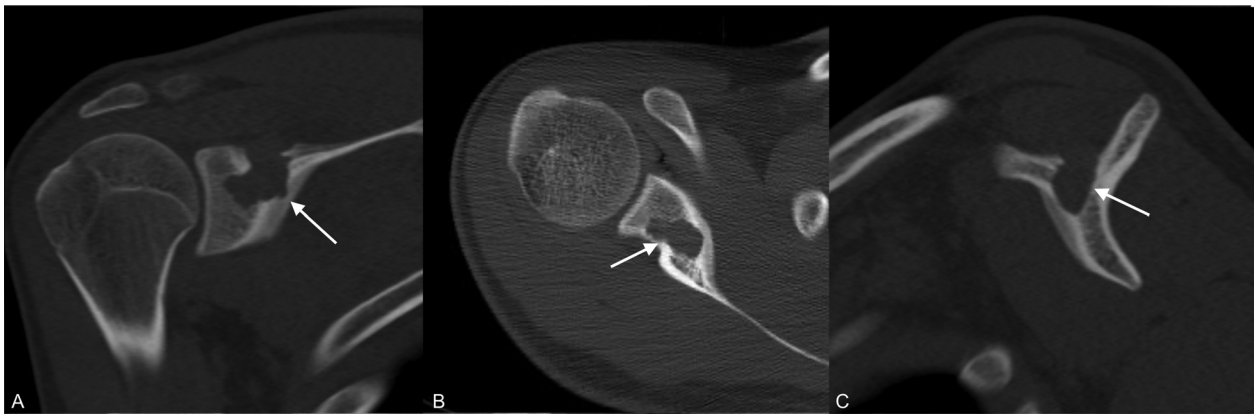

Fig. 3 – Shoulder computed tomography (A-C). An intraosseous round lesion of lytic characteristics, located on the right glenoid neck with approximate measurements of 20 x 21 x 8 mm (TXLXAP) and with a Hounsfield attenuation measurement of 125 HU is seen. No periosteal reaction is observed and no intralesional calcifications are seen. No compromise of soft tissues is reported.

glenoid neck with an approximate dimension of 20 × 21 × 8 mm (TX L X AP), with no internal calcifications, suggestive of a chondroblastoma, highlighting that definitive diagnostic is histopathologic (Figs. 2,3).

Taking into account these findings, the patient was seen by an orthopedic oncologist, who suggested surgical excision of the lesion. Surgery, consisting of complete resection of the lesion, curettage, and local flap, was performed without any complications. The specimen was sent to pathology for further characterization. The pathology reported multiple irregular fragments of soft and firm tissue of brown color, the larger one measures 1 × 1 × 1 cm and the smallest one has approximately 0.2 × 0.2 cm. Immunohistochemical studies showed intense and diffuse reactivity of tumoral cells for the markers CD1A, CD68, and S100 protein, with a proliferation cellular index (KI67) of 30%, The specimen was not reactive for P63 (Fig. 4).

Morphologically fragments of bone and fibrous tissue can be observed encompassed in a neoplasm of mononuclear cells of intermediate size with nuclei of irregular borders associated with lymphocyte and eosinophilic infiltrate. These morphological and immunohistopathological findings were consistent with Langerhans cell Histiocytosis. After histochemical diagnosis, studies for the BRAF gene were made and processed on the same sample which turned out mutated in the V600E/E2/D in the 15 exon of the BRAF gene.

The patient is now displaying additional symptoms, including papular lesions on the thorax, arms, and back, pain in the lateral condyle of the left arm, and other signs that are not consistent with his initial diagnosis of LCH.

Discussion and conclusions

Assessing imaging techniques in LCH depends on the disease's phase and the lesion's location. Early onset lesions tend to have an aggressive pattern of osteolysis and have a wide zone of transition sometimes accompanied by a lamellar periosteal reaction. Differential diagnosis tends to include osteomyelitis, Ewing's sarcoma, leukemia, and lymphoma [4]. Late-onset lesions have well-defined, sclerotic margins and a narrow zone of transition with or without periosteal reaction [4]. Differential diagnoses include healing metastases, intraosseous hemangioma, fibrous dysplasia, giant cell tumor, and enchondroma [4].

CT is useful for determining cortical disruption and examining osseous destruction. On the other hand, MRI is the best imaging method to evaluate the extent of the lesion, marrow edema, and assess soft-tissue involvement. It can affect any bone but predominantly affects flat bones in the following order of predilection: skull, mandible, ribs, pelvis, and spine [5].

Skull lesions tend to have a well-defined lytic "punched-out" appearance caused by asymmetric destruction of the inner and outer cortices. On MRI, the soft-tissue component is hyperintense on T2-weighted images with enhancement after contrast administration [5]. In relation to the spine, the vertebral body is the most commonly affected, in radiography and CT lytic lesions appear. MRI shows an increased T2 signal with areas of enhancement and T1 shows decreased intensity [6].

In children, long bone involvement is the predilection pattern accompanied by symptoms such as focal pain and swelling. The femur, humerus, and tibia are the most commonly involved long bones, specifically the diaphysis and/or metaphysis. Lesions seem lytic, expansile, and aggressive on CT and X-ray. On an MRI, intramedullary lesions with extramedullary soft tissue components are visible. Hypointense on T1-weighted sequences and hyperintense on T2-weighted sequences. A clearly defined sclerotic border is present in late or more mature lesions [6].

Various studies have reported a prevalence of BRAF V600E gene mutation from 33% to 69% in patients varying from young children to young adults with LCH. Highlighting that BRAF mutation in LCH of bone, like our case, is uncommon with an 11% prevalence [7]. Another mutation of MAPK2K1 has been reported and it mainly occurs in bone LCH [8].

LCH has in general a favorable prognosis with an overall survival rate of 98% and a recurrence rate ranging from

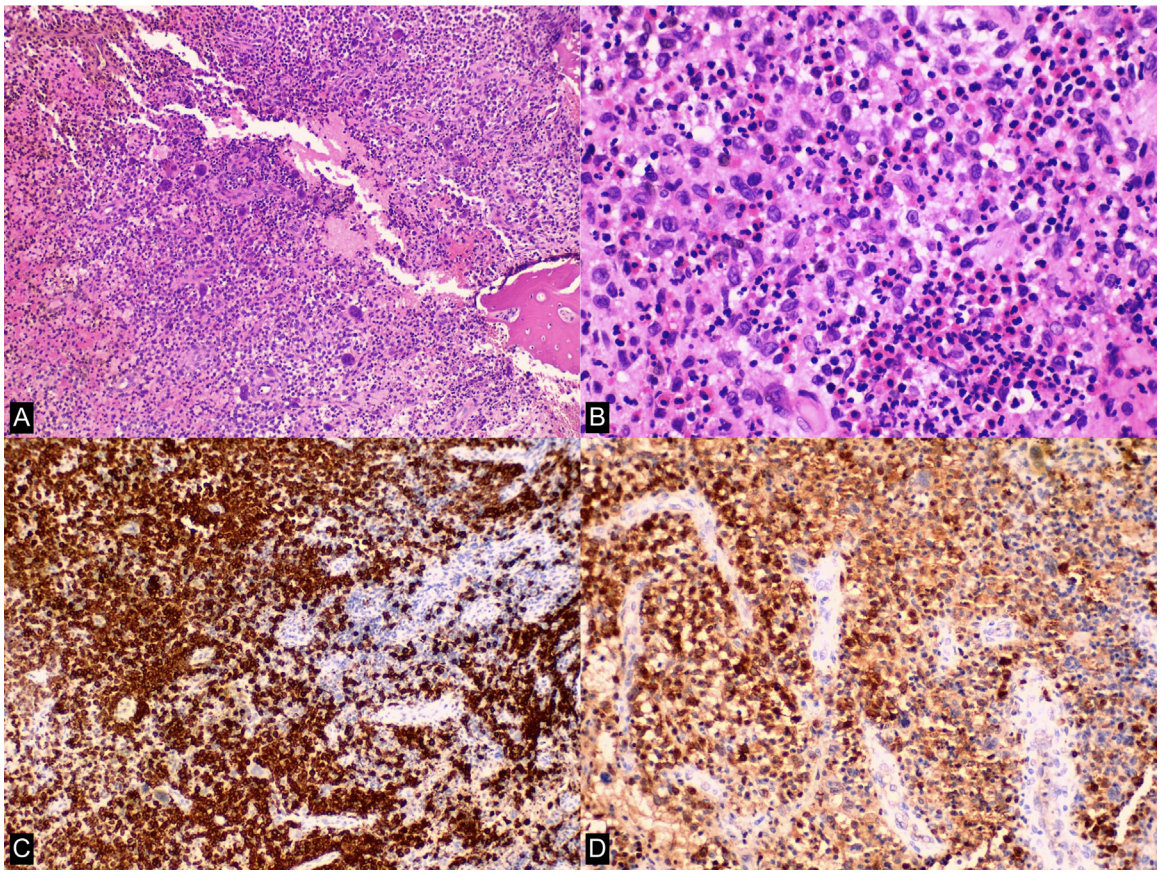

Fig. 4 – (A) Low-power image of bone Langerhans cell histiocytosis with clusters of Langerhans cells osteoclast-like cells (H&E). (B) High-power image of Langerhans cell histiocytosis showing distinctive morphology of intermediate-sized cell with nuclear grooves, irregular nuclear contours, and eosinophilic cytoplasm and large numbers of eosinophils (H&E). (C and D) Langerhans cell histiocytosis show immunoreactivity in most of the cells with CD1a (C) and S100 protein (D).

20-50%. Given that prognosis and treatment options are based on the disease's severity, it is crucial to do a systematic survey of lesions as soon as a lesion is identified in images. A whole-body MRI and radiographic screening of the chest and skeleton are advised. Even a full-body PET-CT scan is thought to be extremely helpful [9].

Pathologic findings are considered the most important in order to confirm the diagnosis of LCH. Immunocytochemistry is also quite useful, as Langerhans cells express CD1a, S100 and CD68 [9].

The preferred treatment of unifocal bone lesions, like our patient, usually consists of surgical removal of the lesion and systemic chemotherapy, in occasions a corticosteroid injection can be used to manage pain and local symptoms in the postoperative period. Our patient had surgical removal of the lesion and intralesional curettage with a local closure flap. Nonetheless has not started chemotherapy so far [10].

LCH is a rare disorder that commonly affects young children. The case presented is unique as the lesion developed not only in the scapula which has a 3% prevalence in LCH, but also had radiographic and MRI characteristics of a chondroblastoma more than the typical LCH lesion. Additionally, it was accompanied by a BRAF V600E mutation which is uncommon in LCHs bone cases [6,8].

Patient consent

Informed consent was obtained from the patient.

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