case report

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Head and neck Langerhans cell histiocytosis: two case reports and review of the literature

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Summary Langerhans cell histiocytosis (LCH) is an inflammatory neoplasia of myeloid precursor cells driven by mutations in the mitogen-activated protein kinase (MAPK) pathway. It can present as single or multisystem LCH. It occurs in 0.5–5.4 per million people. While it can occur at any age, it is more common in children, predominantly males, under the age of 4 years. The unifocal single system variety is the most prevalent and least aggressive presentation, making up to 70% of cases. It can affect bone (80%), lymph nodes (5–10%) or lungs (15%). The mandible and sphenoid are the least common locations; therefore, when present, it could be easily mistaken for a variety of pathologies. Depending on the clinical features, treatment can range from simple observation to chemotherapy and/or radiation. We present 2 cases of unifocal single system LCH located at the mandible and skull base, and describe the diagnostic work up and treatment.

Keywords Bone · Lesion · Unifocal · Mandible · Sphenoid · Computed tomography

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Introduction

Langerhan's cell histiocytosis (LCH) is a rare disorder characterized by an abnormal accumulation of histiocytes. It was first described in 1893 and adopted the name Langerhan's cell histiocytosis in 1985 [1, 2]. The clinical classification of LCH includes: single-cel LCH (SS-LCH) with one organ/system involved (uni- or multifocal); and multisystem LCH (MS-LCH) with two or more organs/systems involved [3].

Its annual incidence has been reported to be 1–2 patients per million individuals with most patients presenting with single-system involvement (70%). Of patients with multisystem disease (30%), around 50% have equal or more than the one risk organ involved. It is more predominant in males (1.6–1.7 times more than females). It can occur at any age but is most common in the pediatric population. The majority of patients are younger than 15 years with a median age at diagnosis of 3.5 years [1, 2, 4]. We present two cases of SS-LCH located in the jaw and sphenoid bones in 2-year-old children and describe the diagnostic process and treatment.

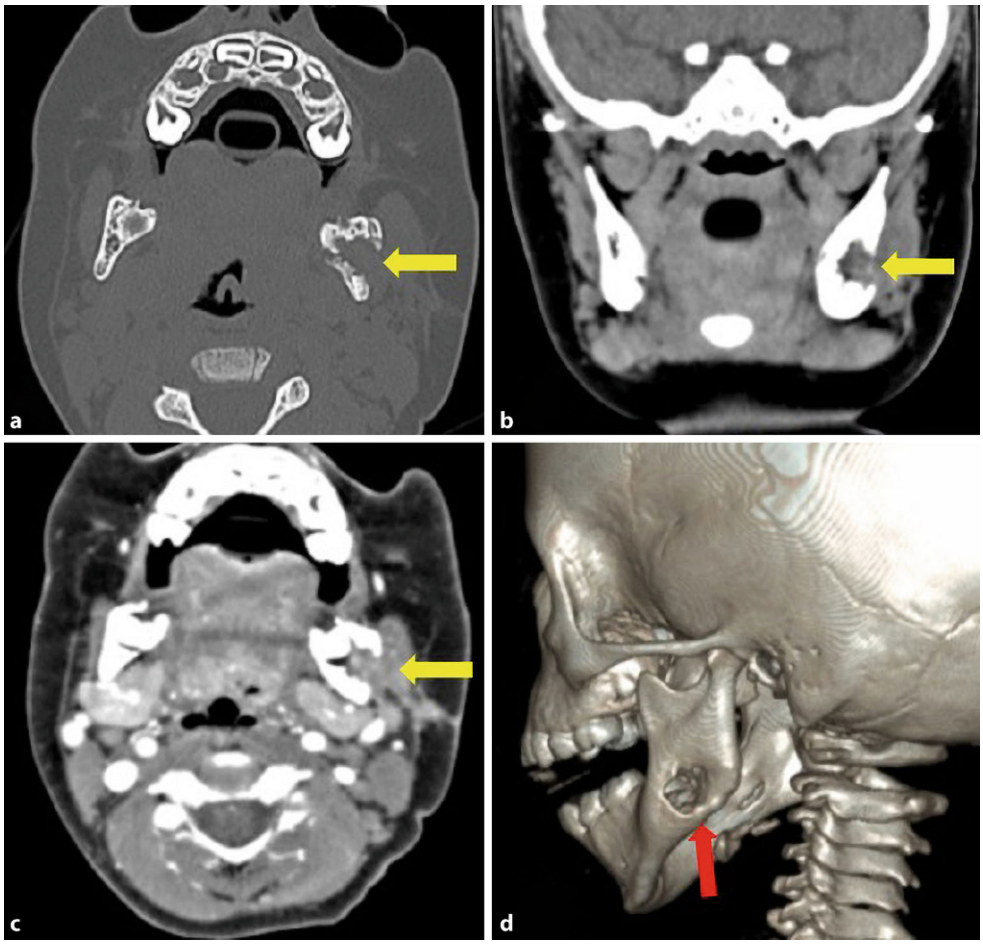


Fig. 1 **a** Axial computed tomography (CT) with bone window shows a destructive and expansive process eroding the left mandibular angle (*yellow arrow*). **b** Coronal CT with soft tissue window demonstrates infiltration of the left masseter muscle (*yellow arrow*). **c** Axial CT shows moderate enhancement post intravenous contrast administration (*yellow arrow*); **d** three-dimensional CT volume rendering shows osseous lesion (*red arrow*)

Case 1

A 2-year-old male child otherwise healthy, presented to his pediatrician's office with a fast-growing painless swelling on the left mandibular angle. The physical examination revealed a small firm mass measuring approximately 2 cm without skin erythema. The lesion was sensitive to palpation but painless to temporomandibular joint motion. A blood panel, coagulation studies and a fasting urine sample were performed as part of the work up and were all normal. However, a computed tomography (CT) study revealed an expansive-infiltrative mass in the left angle of the mandible with bone erosion. The lesion had irregular borders and invaded the masseter muscle measuring 1.9 × 2.4 × 1.5 cm in its greatest diameter. Following intravenous contrast administration, moderate enhancement with a central hypoattenuating area, suggestive of necrosis, was observed (Fig. 1).

Case 2

A 2-year-old female, with medical history of microcephaly, presented to the ear, nose and throat (ENT) clinic with a fast-growing painless swelling on the right preauricular region after trauma. The physical examination revealed a small firm mass, without skin erythema, which was sensitive to palpation and painful to temporomandibular joint motion.

A blood panel, coagulation studies and a fasting urine sample were performed as part of the work up and were all normal. CT and MRI (magnetic resonance imaging) revealed an expansive and infiltrative solid mass in the right medial skull base, with bone erosion in the sphenoid. The lesion had irregular borders and involved the temporomandibular joint, measuring 1.7 × 2.9 × 4.2 cm with avid enhancement following intravenous contrast administration (Fig. 2).

In both cases, biopsies of lesions were performed confirming the presence of LCH. Following the diagnosis, a myelogram and bone marrow biopsy were performed to assess systemic involvement. All the tests were normal except bone scintigraphy which showed abnormal osteoblastic activity in the involved sites. Given the results of the tests the final diagnosis of SS-LCH was made (Figs. 3 and 4).

The pediatric oncology tumor board recommended curettage of the affected area and the addition of methylprednisolone for case 1. Additionally, two cycles of chemotherapy, consisting of vinblastine and prednisone, were administered resulting in an excellent response.

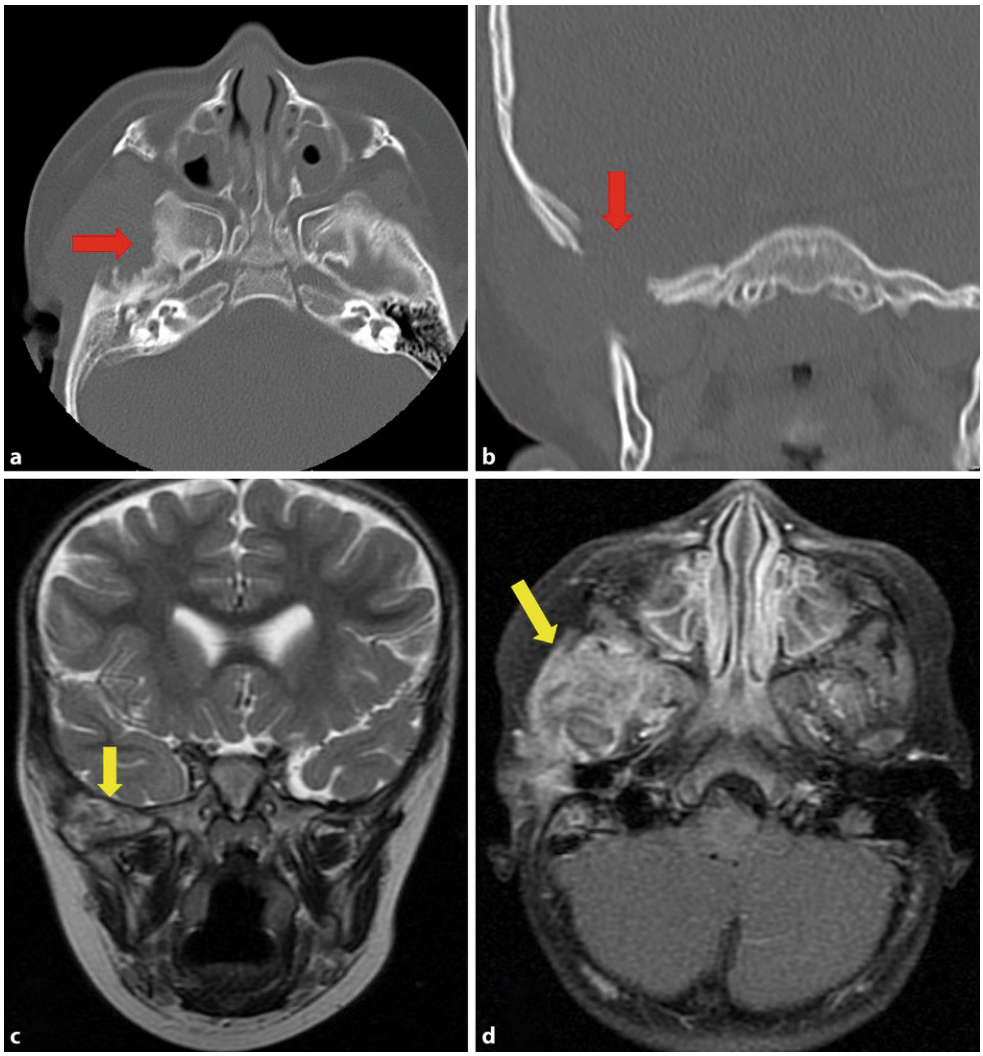


Fig. 2 **a**, **b** Axial and coronal computed tomography (CT) with bone window shows a destructive and expansive process eroding right greater wing of sphenoid bone (*red arrows*). **c** Coronal magnetic resonance imaging (MRI), T2 sequence shows solid mass with intermediate signal intensity without infiltration of temporal lobe (*yellow arrow*). **d** Axial MRI, T1 Fat Sat sequence, showing high enhancement post intravenous contrast administration (*yellow arrow*)

Follow-up examination accompanied by imaging studies failed to reveal any evidence of disease recurrence (Fig. 5).

For case 2, tumor board recommended chemotherapy with vinblastine and prednisone as a single modality for first-line treatment. At present, the patient is under second course without major complications (Fig. 6).

Discussion

The etiology and pathogenesis of LCH have been studied for many years but its etiology remains the subject of debate. Research advances during the last decade have revealed a clonal myeloid origin of the LCH cells and identified a number of activating mutations alongside the MAPK signal transduction pathway. However, the diagnosis of LCH is unequivocal in electron microscopy when Birbeck granules are observed and immunohistochemistry is positive for CD1a, CD 207 and S100 [4–8].

LCH presentation is varied, ranging from SS-LCH: bone (unifocal or multifocal); skin, lymph node, lungs, hypothalamic-pituitary/central nervous system, other (thyroid, thymus) to MS-LCH: two or more organs/systems involved, with or without involvement of risk organs which include liver, spleen, and bone marrow. Risk organs involvement is usually responsible of the mortality associated with LCH [2, 3, 9].

The clinical course can vary from spontaneous resolution to death [6]. The main symptoms reported by patients diagnosed with LCH in descending order are, skin rashes, dyspnea or tachypnea, polydipsia, polyuria, bone pain, lymphadenopathy, weight loss, fever, gingival hypertrophy, ataxia and memory lapses [10] all that correlate with the sites that are usually affected [11].

SS-LCH is the most common (70% of cases) and less aggressive presentation. It can affect bone, lymph nodes or lungs (80% of the cases). Head and neck involvement is common in LCH ranging from 55 to 80% [2]. Bezdjian et al. [8] reported that the most common locations of the unifocal bone lesions are

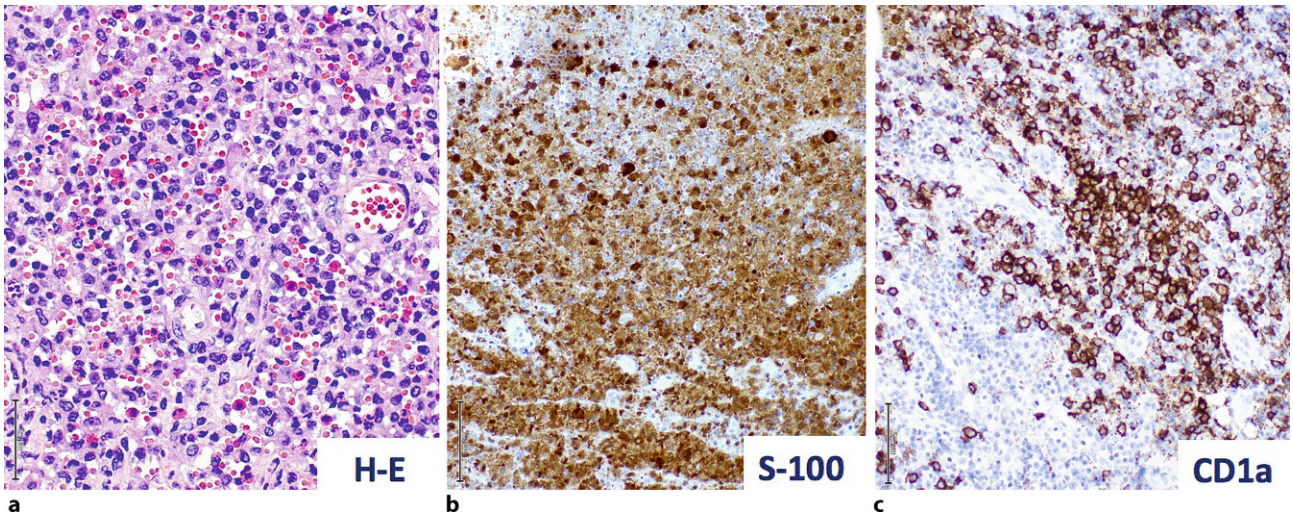


Fig. 3 Case 1. **a** Hematoxylin and eosin stain: widely tissue infiltrated by groups of Langerhans cells (irregular nucleus, abundant cytoplasm pink, kidney-shaped, with "coffee bean" folds), accompanied by inflammatory infiltrate where eosinophils are predominant (hence one of its synonyms: eosinophilic granuloma). Immunohistochemistry study showed positive antigens; **b** S-100 stain; **c** CD1 stain

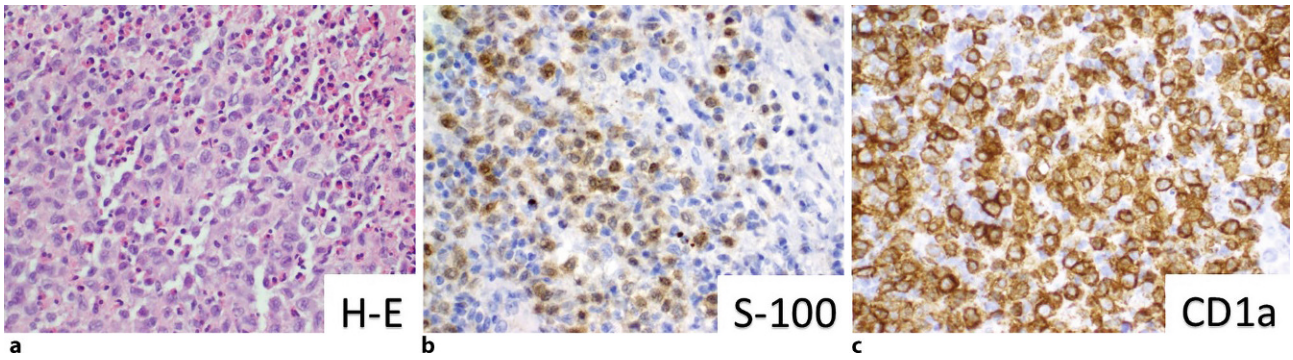
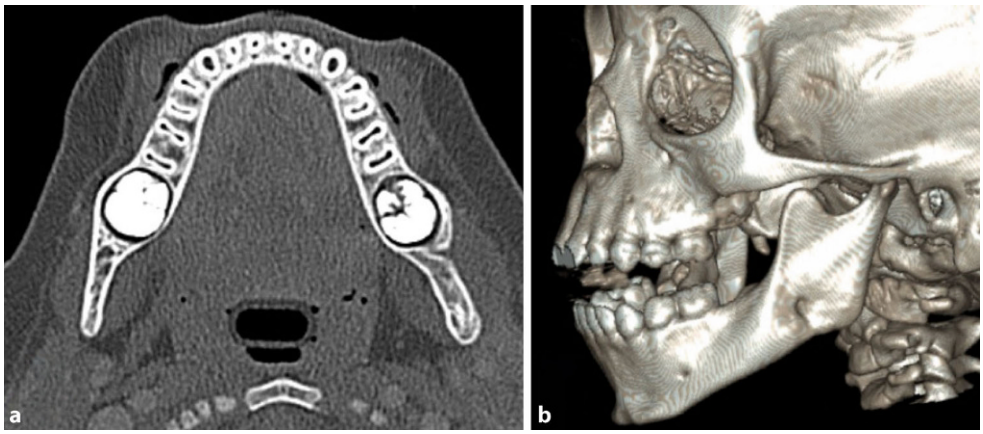


Fig. 4 Case 2. **a** Diffuse infiltration of the tissue by Langerhans cells: polygonal cells with eosinophilic cytoplasm, oval nuclei with longitudinal grooves resembling coffee beans. Minimal nuclear atypia. Accompanied by inflammatory cell infiltrate, mainly eosinophils (hematoxylin–eosin stain). **b** Nuclear and cytoplasmatic positive staining with S100. **c** Diffuse staining for CD1a

Fig. 5 **a** Axial bone window and **b** three-dimensional computed tomography volume rendering 8 months following treatment do not demonstrate residual lesion



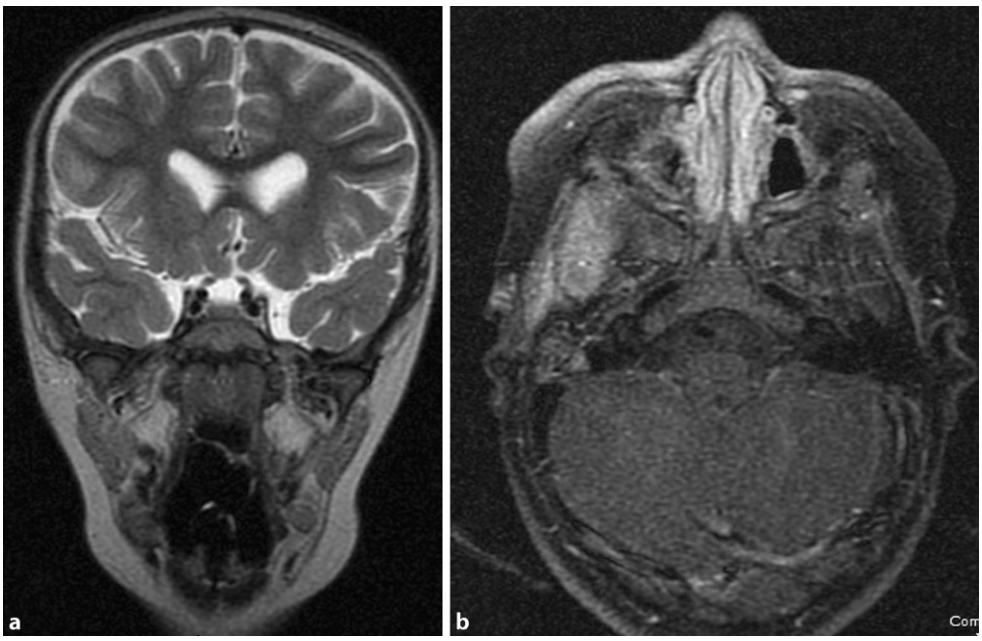


Fig. 6 **a** T2-weighted magnetic resonance imaging (MRI) sequence; **b** T1 Fat Sat post gadolinium-based contrast MRI sequence. Imaging follow-up after completion first course of chemotherapy. Figure 6**b** compared to pre-treatment MRI Fig. 2**d** demonstrates partial response with interval decreased size in residual enhancing mass

the skull (frontal and parietal 64%), orbit (24%), cervical spine (8%) and mandible (4%). In the mandible, LCH can mimic several pathologies ranging from apical cysts, odontogenic tumors, ameloblastomas, non-odontogenic tumors such as giant cell granulomas, inflammatory diseases (osteomyelitis), vascular malformations and certain neoplasms [12].

CT and MRI are useful in the diagnosis of LCH by delineating the extent of the disease [13]. LCH bone involvement is identified on plain radiographs and computed tomography as an osteolytic process with a "punched out" appearance [14]. Postgadolinium MRI, due to its higher soft tissue contrast resolution, is the imaging modality of choice to delineate the extraosseous extent of disease to adjacent soft tissues such as muscle, dura, brain, facial nerve, and vascular structures/venous sinuses, which may have important prognostic implications. LCH lesions are iso- to hypointense on T1-weighted MR images with avid enhancement following intravenous gadolinium administration; they are iso- to hyperintense on T2-weighted MR images [12, 14].

Treatments protocols for low-risk LCH of the unifocal variety range from simple observation to curettage and chemotherapy with or without coadjuvant radiotherapy [6]. When there are injuries that involve only the skin, LCH can resolve spontaneously. If these lesions persist, the use of topical corticosteroids may suffice. In cases involving the head and neck region affecting more than one bone site or affecting the sphenoid, ethmoid, temporal bone or the orbital bones, the use of chemotherapy with vinblastine and corticosteroids is recommended [12]. This latter treatment is endorsed by the Society of Histiocytosis and yields successful results in the majority of the cases of the unifocal and single system variety. Radiation therapy is not recommended as the first line of treatment; some authors propose to give low doses (6–10 Gy) to reduce the risk of secondary tumors or disease recurrence or for those cases with involvement of vital structures and to conserve function when intralesional therapy is not feasible [8, 12, 15]. In general, most cases are resolved satisfactorily. The unifocal variety has a 5-year survival rate of 90%, while the 5-year survival rate in the multifocal variety is 58% [16].

Conclusions

LCH is a rare inflammatory neoplasia of myeloid precursor cells being most prevalent in children. The unifocal SS-LCH is the most common, affecting mainly bony structures and presenting the best prognosis. Treatment is often dictated by the clinical presentation and the degree of head and neck involvement.

Conflict of interest I. Sepúlveda, I. Mendoza, R. Novoa, G. Ayres, N. Inostroza, J.P. Ulloa, and F. Rivas-Rodriguez declare that they have no competing interests.

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