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MANDIBULAR LANGERHANS CELL HISTOCYTOSIS: DIAGNOSTIC AND THERAPEUTIC STRATEGIES: CASE REPORT

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ABSTRACT

Langerhans Cell Histocytosis (LCH) is a group of disorders generally presenting as a monostotic lesion affecting any of the flat or long bones. Soft tissue involvement might occur affecting mainly the lymph nodes, lungs, skin and mucous membranes subsequently. Bony lesions of the maxillomandibular area are also frequent, occurring in 30% of adult cases, it may affect any age group, but the peak incidence is at 1-4 years of age. A definitive diagnosis requires the presence of Birbeck granules or detection of CD1a glycoprotein and 100S protein for the lesional cells by Immunohistochemical staining. Conventional treatment of LCH is with surgery, radiotherapy, chemotherapy and steroid injections alone or in combination. In this case report we discuss diagnostic aspects and treatment modalities on the basis of clinical, radiological and histopathological findings in one and a half year old Libyan patient with LCH of the mandible.

KEY WORDS: Langerhans cell histocytosis, mandible. Immunohistochemicals (CD1a, S100)

INTRODUCTION

Langerhans Cell Histocytosis (LCH) is defined as neoplastic proliferation of Langerhans cells, and was formerly referred to as three overlapping lesions; eosinophilic granuloma of bone, Hand-Schuller-Christian disease and Letterer-Siwe disease.[1] Recently it has been classified by the World Health Organization based on the lineage of the specific histiocyte involved: Langerhans cell, undifferentiated cell, dendrocyte or macrophage.[2] LCH is primarily a paediatric disease: it may affect any age group, but the peak incidence is at 1-4 years of age. It is a rare disease with an incidence of 3 - 5 per million,[3] with a predilection to the males gender (52%).[4] LCH is a group of disorders generally presenting as a monostotic lesion affecting any of the

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flat or long bones.[5] Soft tissue involvement might occur affecting mainly the lymph nodes, lungs, skin and mucous membranes subsequently. However, on rare occasions, only soft tissue involvement mostly presenting as palatal or gingival ulcerations without the involvement of underlying bone have been reported.[6] It represents a spectrum of clinical disorders ranging from a highly aggressive and frequently fatal leukemia-like disease affecting infants to an easily cured solitary lesion of bone.[7] Osseous involvement is observed in 78% of patients, the cranium being the bone most commonly affected 49%. Bony lesions of the maxillomandibular area are also frequent, occurring in 30% of adult cases, particularly affecting posterior regions of the mandible. Pain and swelling of the mandible with mobility and loss of teeth may be the presenting symptoms of the disease.[8]The mandible is affected twice as often as the maxilla.[9] Destruction of lamina dura resulting in radiographic appearance "floating teeth".[10]A definitive diagnosis requires the presence of Birbeck granules or detection of CD1a glycoprotein and 100S protein for the lesional cells by Immunohistochemical staining.[11] A careful clinical examination, good diagnostic skill and awareness of characteristic cytological features of LCH leads to earlier diagnosis and treatment with minimal deformity.[12]Conventional treatment of LCH is with surgery, radiotherapy, chemotherapy and steroid injections alone or in combination.[13] Spontaneous regressions of localized disease has been reported.[14]

Case Report

A one and a half-year-old Libyan boy was attended to the outpatient clinic of oral and maxillofacial surgery department at faculty of dentistry, university of Tripoli with his parents had noticed a solitary, painless swelling in the left lower jaw two weeks back. On physical examination, the patient was well developed, well nourished, and in no acute distress. He was afebrile, and his vital signs were within normal limits. The general physical examination was normal, with the exception of head and neck area where it revealed a single, diffuse swelling measuring 2×4 cm in diameter extending beyond the lower border of the left mandible (Fig.1). On palpation, the swelling was tender, hard, immobile and attached to the underlying structures.

Intraoral examination revealed an expansion of the buccal cortical plate of the body of the mandible extending between the deciduous left lateral incisor to the retromolar region of the mandible with ill-defined margins. Oral mucosa was intact, with no ulcerations or proliferations, the skin over the swelling was smooth and did not show any secondary changes. The left submandibular lymph node was palpable, tender and mobile.

Computed tomography (CT) scan performed in multi-slices. An axial CT showed destruction of the buccal cortex and a focal bony destructive lesion in the left body of the mandible (Fig.2). 3-D CT image revealed multiple buccal osteolytic lesions in relation to the left mandibular body (Fig.3). With all these radiological investigations, the possible differential diagnosis were LCH, Ewing sarcoma, lymphoma and osteomyelitis.

Blood investigations showed no significant finding, the differential leukocytes, liver function and renal function tests were normal.

Aspiration biopsy of the lesion was performed with a wide bore 18G needle to rule out vascular component. To evaluate the possibility of systemic involvement, a radiographic skeletal survey for the skull, whole spine, pelvis and both lower limbs was done, but did not reveal any abnormality (Fig.4). Ultrasound of the abdomen did not reveal any organomegaly.

Surgery in the form of curettage and excisional biopsy of the jaw lesion and the involved left submandibular lymph node was done under general anesthesia through an intraoral approache as diagnosis and a part of the case treatment.

Fig. (1) Photograph of the case showing a diffuse swelling over the left side of the body of the mandible

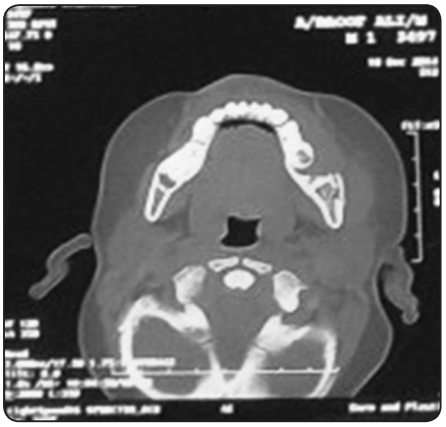

Fig. (2) An axial CT image, showing a wide destructive lesion in the left mandibular body

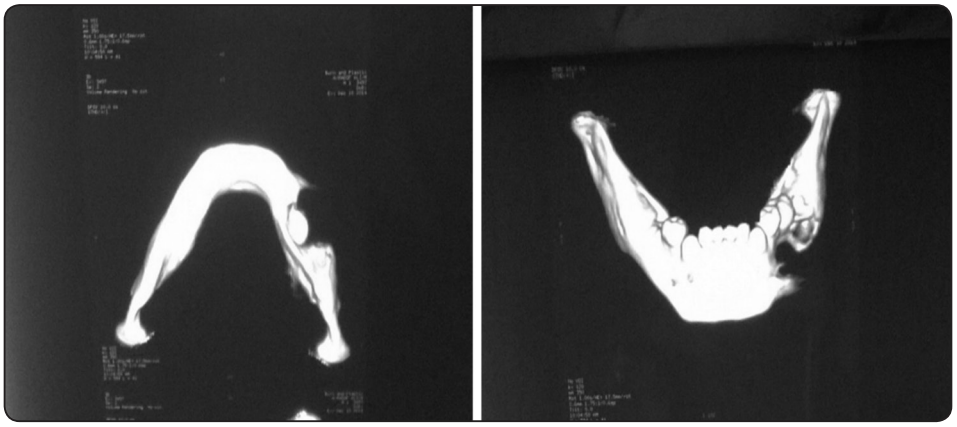

Fig. (3) 3-D CT image showing destruction of the buccal cortex & intact lingual cortex

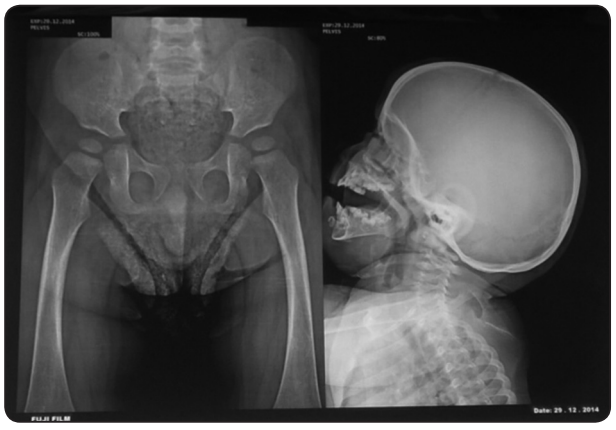

Fig. (4) X-ray of the skull, spine, pelvis & lower extremities showing no any lesion

Histopathological examination of the soft tissue mass of the left mandible obtained by excisional biopsy with H &E stain showed diffuse proliferation of the intermediate size cells, with eosinophilic to clear cytoplasm and oval nuclei with indentation and grooves, and dense eosinophilic infiltration in the background (Fig.5). Immunohistochemical staining showed that the histiocyte cells were strongly positive for CD1a and S-100 protein. These features were most consistent with LCH (Fig. 6 a&b). One lymph node was identified and was focally involved by the proliferation (Fig.7a&b).

The patient was diagnosed with LCH based on clinical, radiological, histopathological and Immunohistochemical investigations.

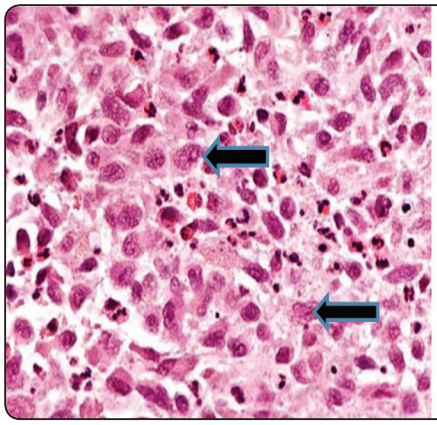

Fig. (5) Photomicrograph showing a diffuse infiltrate of Pale-staining Langerhans cells (arrows) intermixed with few granular eosinophils H&E stains

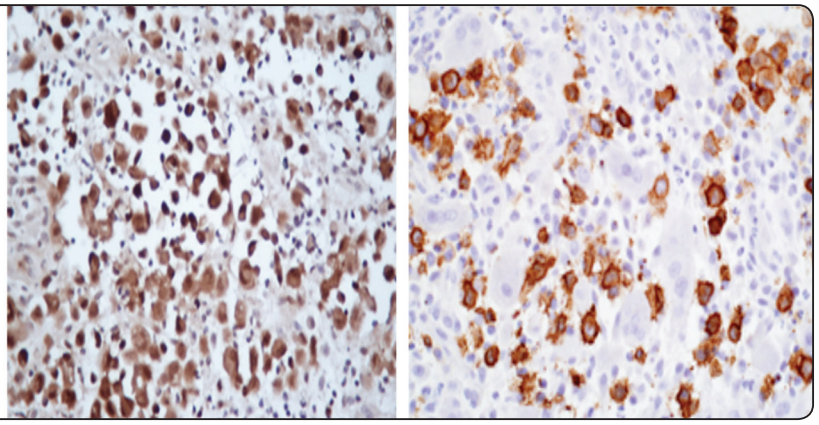

Fig. (6) **a)** Photomicrograph showing S100 immuno-Positivity for Langerhans cells, X200 magnification X200 magnification. **b)** Photomicrograph showing CD1 immuno-Positivity for Langerhans cells, X200 magnification

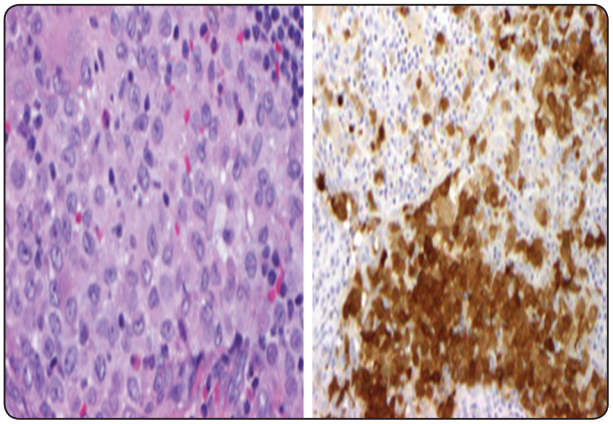

Fig. (7) **a)** Photomicrograph showing left submandibular lymph node biopsy Involved by Langerhans cells and eosinophils. H&E, X400. **b)** Photomicrograph of the same lymph node showing S 100 immunopositivity reaction for Langerhans cells, X200.

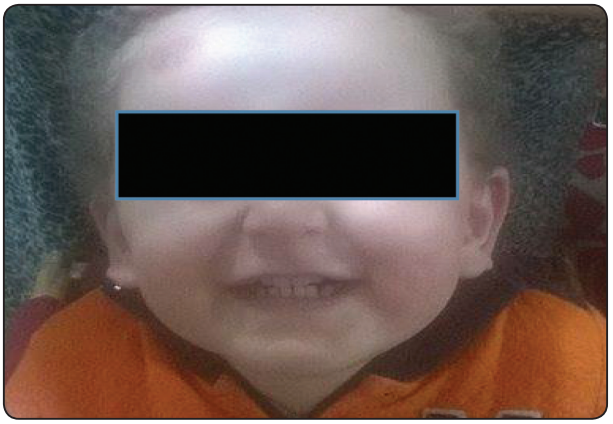

Fig. (8) Three months postoperatively regression of left mandibular swelling with eruption of left lower deciduous canine.

A pediatric oncologist recommended treatment with systemic chemotherapy. The patient was given Vinblastine weekly for 7 doses and prednisolone for 4 weeks as induction, then maintenance therapy Vinblastine every 3 weeks plus 5 days prednisolone, 6 Mercaptopurine as daily and Methotrexate weekly for the period of 6 months. Three months after surgery and chemotherapy the left mandibular lesion showed complete clinical remission with eruption of the left lower deciduous canine (Fig.8).

DISCUSSION

LCH, a disorder of antigen presenting cells, is the commonest disorder of the mononuclear phagocytic system.[15] LC histiocytes are immature dendritic cells that are responsible for a rare, unique disease process due to its cells of origin called LCH[16]of unknown etio-pathogenesis.[17]

Different hypothesis have been proposed, which include a disorder of immune regulation with deficiency of T suppressor lymphocytes, a neoplastic proliferation of Langerhans cells or other

etiological factors like viruses, bacteria and genetic components.[18]

In 90% of reported cases, it appears in children under the age ten with peak incidence between one and four years of age.[19]In our patient, site of occurrence, age, sex, and manifestations of the disease were coincide with those written in previous studies. Radiographs, blood testing, clinical signs, and tissue biopsy are the primary methods for establishing a diagnosis for LCH. Only a biopsy can establish a definitive diagnosis, but this is not always an immediate option.[20]Jaw involvement has basically two forms: one is the focal osteolytic lesion in the vertical tubular portions of the mandible, and in the horizontal portion with resorption of the alveolar ridge, producing the radiographic appearance of "floating teeth".[21] As radiographic findings of the present case, lytic and destructive bone lesions are seen, and bone lesions are associated with adjacent soft tissue masses.[22]

Final diagnosis of LCH can be made only by histopathological examination. Therefore, until the lesion is removed surgically and examined by biopsy, which is not always practical to perform depending on the anatomical location, LCH must always be a consideration in the differential diagnosis.[10,23] However, the presence of Langerhans cells with characteristic cleaved or coffee bean shaped nuclei is hallmark of LCH and the positivity with CD1a and S100 protein would have helped in confirming the diagnosis.[6] which was evident in our case.

For this patient clinically, radiographically as well as histopathologically had the features of Langerhans cell histiocytosis. Our case showed only destructive bone lesion in the left posterior mandibular region which exhibited as hard, tender swelling.[24]

Differential diagnosis of unifocal LCH presenting in the maxillofacial region include: severe periodontal disease, periapical infection. Other differential diagnosis include osteomyelitis, primary or secondary malignant disease, ameloblastoma and odontogenic myxoma. Osteoradionecrosis or bisphosphonate osteonecrosis of the jaws should be considered if medical or drug history suggested.[25] All these diagnostic possibilities ruled out in the present case as there was no history of trauma to the jaws nor odontogenic infections. Furthermore, there was negative bone involvement in skeletal bone survey.

A wide spectrum of treatment modalities have so far been adopted ranging from surgical curettage to radio and / or chemotherapy as well as cortisone therapy.[26]Accessible lesions are best managed by surgical excision or curettage, since it promotes healing in most of the cases.[27]

In cases of LCH with oral manifestations, it is stated that not all teeth involved by the disease require removal but teeth with marked mobility or with periapical lytic lesion should be sacrificed.[28] In our present case the left lower deciduous canine tooth crypt which preserved during surgery has been erupted.

Prognosis is associated with age of patients. In general, the prognosis is poorer for LCH patients in whom the first sign of the disease develops at very young age and better for LCH patients who are older at the time of onset.[22]

The prognosis of unifocal LCH lesion is generally excellent, but in very rare instances, the lesion may recur rapidly within a short period and lead to a fatal outcome,[10] because the exact cause is unknown and treatment cannot directly stop the disease.[20]

CONCLUSION

Langerhans cell histiocytosis may be a benign or self-limited disease. However, in very rare instances, a solitary LCH may recur rapidly within a short duration and become a fatal. Furthermore, the etio-pathogenesis of LCH remains obscure.

According to Histiocyte society 2009, the diagnosis of LCH is based on histological and immunophenotypic examination of lesional biopsy. Moreover, positive staining of the lesional cells with CD1a, and S100are required for definitive diagnosis.

The optimal treatment for LCH has not been established. Curettage of the center of a bone lesion is usually sufficient for pathologic diagnosis and also may trigger the initiation of a healing process. Complete excision of bone lesion is not indicated and may increase the size of the bone defect, the healing time, and result in late skeletal deformity. Consequently, all patients with LCH require long term follow up to identify disease recurrence or late stage complications.

Dental professionals are in a unique position to identify and refer patients for LCH therapy. Dental professionals must also have an understanding of oral lesions to avoid misdiagnosing this disease.

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