Case Report

Intralesional Triamcinolone for Treating Mandibular Langerhans Cell Histiocytosis: A Case Report and Literature Review

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Abstract

Langerhans cell histiocytosis is a rare condition ranging in manifestation from a focal boney lesion to multisystem involvement. Several treatment modalities have been proposed including curettage, low-dose radiotherapy, chemotherapy and intralesional injection of corticosteroids. These treatment options can be used as a single or combined approach. Prognosis depends on the extent of systemic involvement, and solitary lesions respond favorable to treatment. Here, the authors report a case of a 10-year-old male patient with Langerhans cell histiocytosis affecting his right posterior mandible that was successfully treated with intralesional injection of triamcinolone in multiple sessions. Complete recovery was confirmed clinically and radiographically in 18 months from the time of diagnosis.

Keywords: Intralesional steroid, Langerhans cell histiocytosis, mandible, triamcinolone

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INTRODUCTION

Langerhans cells are macrophages (histiocytes) that arise from bone marrow precursor cells and are part of the monocytic series.[1] Langerhans cell histiocytosis (LCH) is an uncommon disorder characterized by proliferation of cells exhibiting phenotypic characteristics of Langerhans cells.[2] The incidence of LCH among pediatrics has been reported to vary from 2 to 5 cases/million/year.[3-5]

Clinical manifestation of this disorder ranges from a single system (unifocal or multifocal) to a disseminated disease affecting multiple organs, with the skull bone being involved in about 50% of the cases.[2,6] Although the cell of origin is known, the exact etiology and pathogenesis remain controversial. LCH is widely considered to be a neoplastic and monoclonal process.[2]

For confirming the diagnosis of LCH, histological examination of the affected organ is mandatory. Routine tissue sections reveal dense infiltrates of large atypical epithelioid cells with ample eosinophilic cytoplasm and the characteristic indented ovoid nuclei (Langerhans cells). Intermixed with these cells are a variable number of eosinophils, lymphocytes, plasma cells, benign-appearing multinucleated giant cells and histiocytes; hence, the old name "eosinophilic granuloma." In a well-controlled immunohistochemical examination of these atypical epithelioid cells, the usual characteristic immunoprofile

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includes expression of S100, CD1a and Langerin (CD207), which is the most specific.[7]

Ultrastructural examination of the proliferative cells shows the pathognomonic characteristic intracytoplasmic organelles, known as 'Birbeck granules.'[8] However, currently, the histological and immunohistochemical profiles alone are almost always adequate to make the correct diagnosis.[9] The most common clinical presentation of LCH in the maxillofacial region is as a solitary lesion in the jaw that is usually asymptomatic. LCH can be detected during routine dental examination or when the patients complain of mild pain, swelling and tooth mobility, as was the case with the patient in the case reported here.

CASE REPORT

A 10-year-old male patient presented to the Oral and Maxillofacial Surgery Unit at King Fahad Specialist Hospital, Dammam, Saudi Arabia, complaining of painless swelling in the right side of the face for a 6-week duration that was preceded by mild trauma to the right side of the mandible in the last 2 weeks. The patient was fit and well, with no other significant medical history. Extraoral examination showed facial asymmetry related to a diffuse swelling of the right mandibular region near the angle. Intraoral examination was positive for posterior mandibular swelling with buccolingual expansion. Further, the swelling was indurated and tender to palpation, and there was no teeth mobility.

Orthopantomogram X-ray revealed a large, radiolucent, irregular lytic lesion measuring 2.5 cm × 3.2 cm and extending from the retromolar area of the lower right first molar to the ramus of the mandible with a radiolucent line, suggesting a pathological fracture [Figure 1]. However, segments of the fracture were not mobile during the clinical examination. Interestingly, there were missing lower teeth buds of the second and third molars on both sides. The patient was taken to the operating room and an incisional biopsy was done under general anesthesia. The biopsy was sent for histopathological examination and its results revealed infiltration by numerous eosinophils and epithelioid histiocytes with ample cytoplasm and elongate coffee bean nuclei. The histiocytes were immunoreactive for S100 and CD1a proteins by standard immunohistochemical stains, thereby confirming the diagnosis of LCH [Figure 2].

A computed tomography scan of the chest, abdomen and pelvis with intravenous contrast was performed to rule out any systemic involvement and showed no evidence of metastatic lesions. Bone marrow aspiration revealed reactive hyperplasia with no evidence of infiltration.

A complete blood count, erythrocyte sedimentation rate (ESR), creatinine and bone panel test were obtained and revealed an elevated ESR level of 29 mm/h and a low hemoglobin level of 11 g/dl, hematocrit 34%, mean corpuscular volume 23 fl, and mean corpuscular hemoglobin 24 pg, suggestive of iron-deficiency anemia.

Because of the size of the lesion, age of the patient and extent of surgery along with the expected morbidity with surgical resection, the planned treatment was a conservative approach. The patient received intralesional injections of 120 mg of triamcinolone as an initial dose followed by three injections of 80 mg at 6-week intervals. The patient was followed up on a monthly basis; the injections were well-tolerated and no side effects were reported. Four months after the first injection, there was a significant reduction in the size of the lesion [Figure 1b], and complete healing with normal bone trabeculation was appreciated 18 months after the first injection.

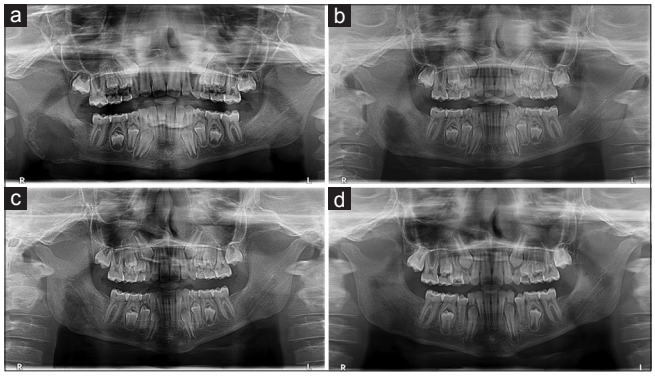

Figure 1: Serial panoramic radiograph monitoring the resolution of the lesion: (a) Orthopantomogram radiograph at the initial presentation; (b) 4 months after the first triamcinolone injection; (c) 8 months after the first triamcinolone injection; (d) 18 months from the initial injection

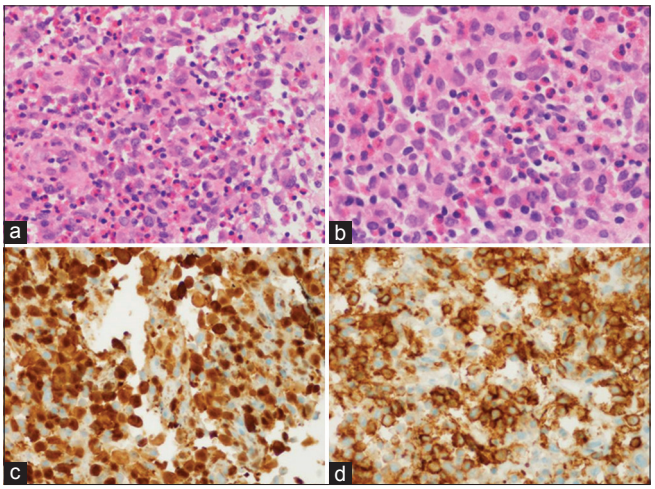

Figure 2: Histological sections stained by routine hematoxylin and eosin stains by routine hematoxylin and eosin stains at (a and b) medium power; (c and d) at high power

Contact with the patient was lost following the treatment. The Institutional Review Board at King Fahad Specialist Hospital, Dammam, provided ethical clearance for reporting this case report.

DISCUSSION

Clinical presentation of LCH in the maxillofacial region is usually asymptomatic, but it can be detected in regular dental examinations. Clinicians should note that LCH oral symptoms vary and include teeth loss, early exfoliation of primary teeth and jaw swelling.[10] In a case series of 50 patients with LCH, 36% were found to have had an oral involvement. Of these, dentists made the initial observation in 16% of the cases.[11] However, clinicians should note that jaw lesions may be encountered in the alveolus with a progressive bone loss and teeth mobility. It also presents in the inferior border of the mandible and ramus and may give the radiographic picture of osteomyelitis, sarcoma or odontogenic neoplasm.[10] The patient in the current case report did not follow routine dental examination, and thus the lesion was not addressed earlier.

From the literature,[6,12,13] the authors found that there are no controlled studies that provide an optimal approach for the treatment of LCH. Therefore, it is yet unclear if clinicians should intervene or adopt a more conservative approach with a close follow-up. It has been reported that monostotic lesions may spontaneously heal after biopsy.[14,15] Although the exact reason for this is unknown, some authors theorize that, as LCH is an inflammatory process, a biopsy and manipulation may cause decompression of the lesion and subsequently alter the inflammatory process and induce healing.[16,17]

The authors who support interventional treatment of LCH recommend it only when there is a risk for pathological fracture, limited jaw mobility and function and damaged vital structures (such as 'tooth germ') or if the patient shows sign of disease progression or is at risk of developing disseminated LCH.[18-20] For intervention, many treatment modalities have been proposed, but there is no controlled study demonstrating an advantage for one method over another.[6,12,21] One such treatment modality is the surgical curettage, which is considered a conventional treatment; however, a recurrence rate of 16% has been reported even after 11 years of surgical curettage treatment.[17,22] Another approach is radiotherapy with or without chemotherapy. A radiation dose of 1200–1800 cGys is advocated for lesions that are nonaccessible or when surgery poses a risk of damaging a vital structure, such as the optic nerve or a previously operated lesion.[16,21] The use of chemotherapy alone has also been reported, with 2-chloro-2'-deoxyadenosine being proven to be an effective treatment in patients with recurrent and multisystemic effects.[13,23] Finally, intralesional injection of a corticosteroid, the treatment modality of the current case report, was first used in 1980 by Cohen *et al*.[18] Since then, several authors have shown positive outcomes using this method, as detailed in Table 1. This method was adopted for our case because of these reported positive outcomes as well as the lesser invasive nature of intervention and risk of requiring major reconstruction after surgical cartage.

Although results of using intralesional corticosteroid injections for the treatment of LCH are promising, its mechanism of action is not well understood. Suggested mechanisms of actions include suppression of Langerhans cells, T-lymphocytes and eosinophils by steroids or,

Table 1: Summary of the reported Langerhans cell histiocytosis in mandible treated with steroid injection and its outcome

Author	Age and gender	Location	Symptoms	Corticosteroid and dosage	Resolution (months)
Cohen *et al*.[18]	5 years 9 months, female	Right side mandible	Swelling, pain, fever	Methylprednisolone 150 mg, 2 injections	11
Jones *et al*.[19]	10 years, female	Right side mandible	Pain and swelling	Methylprednisolone 164 mg, 1 dosage	8
Watzke *et al*.[24]	39 years, male	Right and left side mandible	Swelling	Triamcinolone 25 mg, 6 injections	15
Putters *et al*.[20]	28 months, female	Right side body mandible	Pain and swelling	Methylprednisolone 80 mg, 1 dosage	6
	9 years, male	Left side body mandible	Swelling and fracture	Methylprednisolone 40 mg, 1 dosage	3
	15 years, male	Left side body mandible	Pain and swelling	Methylprednisolone 80 mg, 1 dosage	6
Moralis *et al*.[25]	10 years, male	Left side angle of mandible	Progressive, pressure-sensitive swelling	Methylprednisolone 200 mg, 1 dosage	10
Esen *et al*.[26]	25 years, male	Anterior and right side of mandible	Pain and swelling	Methylprednisolone 3 injections of 80 mg, 80 mg and 60 mg	14
Present case	10 years, male	Right body and ramus of the mandible	Swelling right mandible associated with the right submandible, Palpable lymph node preceded with mild trauma to the affected area	Triamicinolone 120 mg as the initial dose, followed by three injections of 80 mg at 6-week intervals	10

in contrast, osteogenesis stimulation by steroids.[27] In addition, intralesional steroids can inhibit interleukin-1, and thus reduce bone resorption.[28]

As also demonstrated in the case described here, treatment with intralesional injection of steroids is generally safe and can be repeated within 4–6 weeks if no radiographic sign of improvement is appreciated.[26,29] But case selection is critical, as it is contraindicated in patients with a history of allergy or anaphylaxis to injectable pharmaceuticals, peptic ulcer, Cushing syndrome, renal failure, uncontrolled diabetes, anticoagulation therapy, varicella-zoster infection and fungal diseases.

CONCLUSION

There are different treatment modalities suggested for the management of LCH, and implementation of one approach versus the other varies depends on the extent, location and number of lesions. Injection of intralesional steroid is a safe and effective treatment modality for properly selected cases, with an average resolution time of 11 months. Based on the experience from the reported case, the authors suggest that intralesional steroid is a viable and less invasive treatment option that can be used as first-line therapy. However, larger studies should validate this effectiveness.

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Conflicts of interest
There are no conflicts of interest.

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