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

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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

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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includes expression of S100, CD1a and Langerin (CD207), which is the most specific.\cite{7}

Ultrastructural examination of the proliferative cells shows the pathognomonic characteristic intracytoplasmic organelles, known as ‘Birbeck granules.’\cite{8} However, currently, the histological and immunohistochemical profiles alone are almost always adequate to make the correct diagnosis.\cite{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.

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**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 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. 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. 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. The patient in the current case report did not follow routine dental examination, and thus the lesion was not addressed earlier.

From the literature, 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. Although the exact reason for this is unknown, some authors theorize that jaw lesions may spontaneously heal after biopsy.

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, 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 signs of disease progression or is at risk of developing disseminated LCH. For intervention, many treatment modalities have been proposed, but there is no controlled study demonstrating an advantage for one method over another. 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. Another approach is radiotherapy with or without chemotherapy. A radiation dose of 1200–1800 cGy 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. 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. Finally, intralesional injection of a corticosteroid, the treatment modality of the current case report, was first used in 1980 by Cohen et al. 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 cartilage.

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**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. | 5 years, 9 months, female | Right side mandible | Swelling, pain, fever | Methylprednisolone 150 mg, 2 injections | 11 |
| Jones et al. | 10 years, female | Right side mandible | Pain and swelling | Methylprednisolone 164 mg, 1 dosage | 8 |
| Watzke et al. | 39 years, male | Right and left side mandible | Swelling | Triamcinolone 25 mg, 6 injections | 15 |
| Putters et al. | 28 months, female | Left 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. | 10 years, male | Left side angle of mandible | Progressive, pressure-sensitive swelling | Methylprednisolone 200 mg, 1 dosage | 10 |
| 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 | Triamcinolone 120 mg as the initial dose, followed by three injections of 80 mg at 6-week intervals | 10 |
in contrast, osteogenesis stimulation by steroids.\textsuperscript{[27]} In addition, intralesional steroids can inhibit interleukin-1, and thus reduce bone resorption.\textsuperscript{[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.\textsuperscript{[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.

REFERENCES

1. Marx RE, Stern D. Oral and Maxillofacial Pathology. Chicago: Quintessence, 2003.
2. Alabajq I, Boras VV, Femenic R, Cekic-Arambasin A, Antic M, Kelecic J, et al. Unrecognized oral manifestations of Langerhans cell histiocytosis which progressed to systemic disease. Oral Oncol Extra 2006;42:10-3.
3. Carstensen H, Orvold K. The epidemiology of Langerhans cell histiocytosis in children in Denmark, 1975–1989. Med Pediatr Oncol 1993;21:387-8.
4. Müller J, Garami M, Hauser P, Schuler D, Csóka M, Kovács G, et al. Hungarian experience with Langerhans cell histiocytosis in children. J Pediatr Hematol Oncol 2006;23:135-42.
5. Alston RD, Tatevossian RG, McNally RJ, Kelsey A, Birch JM, Eden TO, et al. Inocence and survival of childhood Langerhans cell histiocytosis in Northeast England from 1954 to 1998. Pediatr Blood Cancer 2007;48:555-60.
6. García de Marcos JA, Dean Ferrer A, Alamillos Granados F, Ruiz Masera JJ, Barrios Sánchez G, Romero Ortíz AI, et al. Langerhans cell histiocytosis in the maxillofacial area in adults. Report of three cases. Med Oral Patol Oral Cir Bucal 2007;12:E145-50.
7. Leong AS. A Pattern Approach to Lymph Node Diagnosis. New York: Springer Science & Business Media, 2010.
8. Mierau GW. Intranuclear birbeck granules in Langerhans cell histiocytosis. Pediatr Pathol 1994;14:1051-4.
9. Harman CM, Brown N. Langerhans cell histiocytosis: A Clinicopathologic review and molecular pathogenetic update. Arch Pathol Lab Med 2015;139:1211-4.
10. Can IH, Kart A, Özer F, San N, Samim E. Mandibular manifestation of Langerhans cell histiocytosis in children. Oral Oncol Extra 2005;41:174-7.
11. Sigala JL, Silverman S Jr. Brody HA, Kushner JH. Dental involvement in histiocytosis. Oral Surg Oral Med Oral Pathol 1972;33:48-2.
12. Bartrick A, Friedrich RE, Roesser K, Schmelzle R. Oral Langerhans cell histiocytosis. J Cranio maxillofac Surg 2002;30:91-6.
13. Singh A, Prieto VG, Czelusta A, McClain KL, Duvic M. Adult Langerhans cell histiocytosis limited to the skin. Dermatology 2003;207:157-61.
14. Namai T, Yusa H, Yoshida H. Spontaneous remission of a solitary eosinophilic granuloma of the mandible after biopsy: A case report. J Oral Maxillofac Surg 2001;59:1485-7.
15. Key SJ, O’Brien CJ, Silvester KC, Crean SJ. Eosinophilic granuloma: Resolution of maxillofacial bony lesions following minimal intervention. Report of three cases and a review of the literature. J Cranio maxillofac Surg 2004;32:170-5.
16. Hartman KS. Histiocytosis X: A review of 114 cases with oral involvement. Oral Surg Oral Med Oral Pathol 1980;49:38-54.
17. Roychoudhury A, Shah N, Parkash H, Mukhopadhyay S, Chopra P. Eosinophilic granuloma of the jaws. Br J Oral Maxillofac Surg 1998;36:380-3.
18. Cohen M, Zornoza J, Cangir A, Murray JA, Wallace S. Direct injection of methylprednisolone sodium succinate in the treatment of solitary eosinophilic granuloma of bone: A report of 9 cases. Radiology 1980;136:289-93.
19. Jones LR, Toth BB, Cangir A. Treatment for solitary eosinophilic granuloma of the mandible by steroid injection: Report of a case. J Oral Maxillofac Surg 1989;47:306-9.
20. Putters TF, de Visscher JG, van Veen A, Spijkervert FK. Intralesional infiltration of corticosteroids in the treatment of localised Langerhans’ cell histiocytosis of the mandible: report of 3 cases. Int J Oral Maxillofac Surg 2005;34:571-5.
21. Scegenschmiedt H, Mecke O, Olsewowski T, Bruns F, Heyd R, Schaefer U, et al. Radiotherapy is effective in symptomatic Langerhans cell histiocytosis (LCH): Long-term results of a multicenter study in 63 patients. Int J Radiat Oncol Biol Phys 2003;57:S251.
22. Zuendel MT, Bowers DF, Kramer RN. Recurrent histiocytosis X with mandibular lesions. Oral Surg Oral Med Oral Pathol 1984;58:420-3.
23. Hicks J, Flaitz CM. Langerhans cell histiocytosis: Current insights into infiltrative corticosteroid treatment for recalcitrant lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2005;100:S42-66.
24. Watzke IM, Millesi W, Kermer C, Gisslinger H. Multifocal eosinophilic granuloma of the jaw: Long-term follow-up of a novel intraosseous corticoid treatment for recalcitrant lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000;90:317-22.
25. Key SJ, O’Brien CJ, Silvester KC, Crean SJ. Eosinophilic granuloma: Resolution of maxillofacial bony lesions following minimal intervention. Report of three cases and a review of the literature. J Cranio maxillofac Surg 2004;32:170-5.
26. Driemel O, et al. Radiotherapy is effective in symptomatic Langerhans cell histiocytosis (LCH): Long-term results of a multicenter study in 63 patients. Int J Radiat Oncol Biol Phys 2003;57:S251.
27. Huiskes MM, Toth BB, Cangir A. Treatment for solitary eosinophilic granuloma of the mandible by steroid injection: Report of a case. J Oral Maxillofac Surg 1989;47:306-9.
28. Putters TF, de Visscher JG, van Veen A, Spijkervert FK. Intralesional infiltration of corticosteroids in the treatment of localised Langerhans’ cell histiocytosis of the mandible: report of 3 cases. Int J Oral Maxillofac Surg 2005;34:571-5.
29. Scegenschmiedt H, Mecke O, Olsewowski T, Bruns F, Heyd R, Schaefer U, et al. Radiotherapy is effective in symptomatic Langerhans cell histiocytosis (LCH): Long-term results of a multicenter study in 63 patients. Int J Radiat Oncol Biol Phys 2003;57:S251.