

Langerhans Cell Histiocytosis of the Mandible

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Abstract

The unusual disorder known as Langerhans cell histiocytosis, which is most frequently seen in children and young adults, is caused by the clonal proliferation of Langerhans cells. Even if clinical signs and radiographic evidence of destructive bone lesions may raise suspicion of the disease, a reliable diagnosis without a thorough pathological examination is challenging. This report describes a case of eosinophilic granuloma of the mandible in a nine-year-old child with characteristic radiological, histopathological, and immunohistochemical features.

Categories: Pathology, Other, Dentistry

Keywords: immunohistochemistry, radiolucency, mandibular swelling, lytic lesion, eosinophilic granuloma, langerhans cell histiocytosis

Introduction

Histiocytosis collectively refers to a group of uncommon diseases of the reticuloendothelial system. Langerhans cell histiocytosis (LCH) is characterized by aberrant growth of mature eosinophils and specialized bone marrow-derived antigen-presenting dendritic cells [1]. First, to identify the clinical and pathological traits shared by the numerous disease presentations, Lichtenstein recommended that they be categorized as histiocytosis X [1,2]. The word "X" was used to emphasize that there are still many questions about the nature and origin of the disease [1,3]. The three main components of LCH are eosinophilic granuloma, Hand-Schuller-Christian disease, and Letterer-Siwe disease. Eosinophilic granuloma is a localized condition affecting the bone [3]. Eosinophilic granuloma causes 60% to 70% of all cases of LCH and can manifest as solitary (50% to 75%) or multifocal bone abnormalities [4]. The Hand-Schuller-Christian disease is a subacute or chronic condition that is characterized primarily by the triad of "geographical skull" (caused by numerous calvarial lesions), diabetes insipidus, and exophthalmos [3]. The Letterer-Siwe disease is a widespread acute or subacute disease [3]. Nezelof et al. [5], reported in 1973 using the Birbeck granule as a marker that the lesions of histiocytosis X were caused by the growth and dispersion of aberrant histiocytic cells of the Langerhans cell system, leading to the change in nomenclature to Langerhans cell histiocytosis [1,3]. LCH can occur anywhere between 0.5 and 5.4 cases per million people per year [1]. The incidence in adults is one to two cases per million [6]. People of all ages, from the newborn to the elderly, can develop Langerhans cell histiocytosis; the highest incidence occurs between one and four years [7]. Less than 10% of children with the illness have jaw involvement [8]. Siwe proposed in 1933 that LCH was neither hereditary nor familial. However, there have been numerous reports, including three sets of identical twins, which suggest familial occurrence [9]. This article presents a rare case of unifocal eosinophilic granuloma of the mandible in a nine-year-old boy who presented with a gradually increasing swelling on the left side of his face over one month. We highlight the clinical and microscopic features of this rare case and stress the importance of histopathological examination in the diagnosis of this unusual condition.

Case Presentation

A nine-year-old male patient reported to the hospital with the complaint of swelling in the left lower jaw for the past one month (Figure 1). Clinical examination revealed a bony hard swelling in relation to the left body of the mandible, 2 X 0.5 cm in size, roughly round to oval in shape, non-tender, with a smooth surface, and ill-defined borders. The skin over the swelling appeared normal. Intraorally, the swelling was obliterating the buccal sulcus in relation to the 75 and 36 regions with grade III mobility of 75. The lesion was negative on aspiration.

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FIGURE 1: Swelling on the left side of the lower jaw

Orthopantomogram revealed a well-defined radiolucent lesion in relation to the left body of the mandible with discrete borders and no evidence of sclerosis. The associated teeth appeared normal (Figure 2). A computed tomography (CT) scan showed a solid lytic lesion in relation to the left lower jaw with both buccal and lingual cortical expansion and perforation (Figure 3). Based on the clinical and radiological findings, the differential diagnosis included ameloblastoma, keratocyst, lymphoma, and eosinophilic granuloma. The increase in volume with cortical bone growth and a radiolucent region typical of bone tissue breakdown often validated the predisposition to suspect these diseases. Furthermore, the involvement of tooth germ leads to the suspicion of the lesion being keratocyst or ameloblastoma.

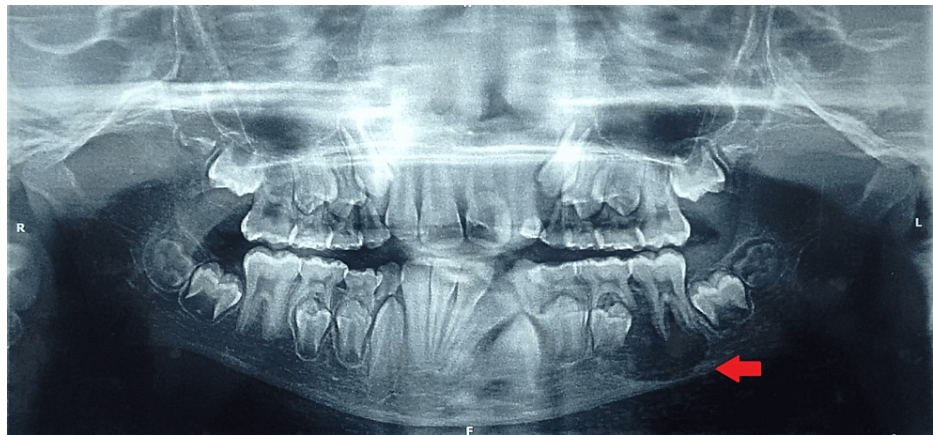


FIGURE 2: Orthopantomogram showing a well-defined radiolucent lesion in the left body of the mandible region

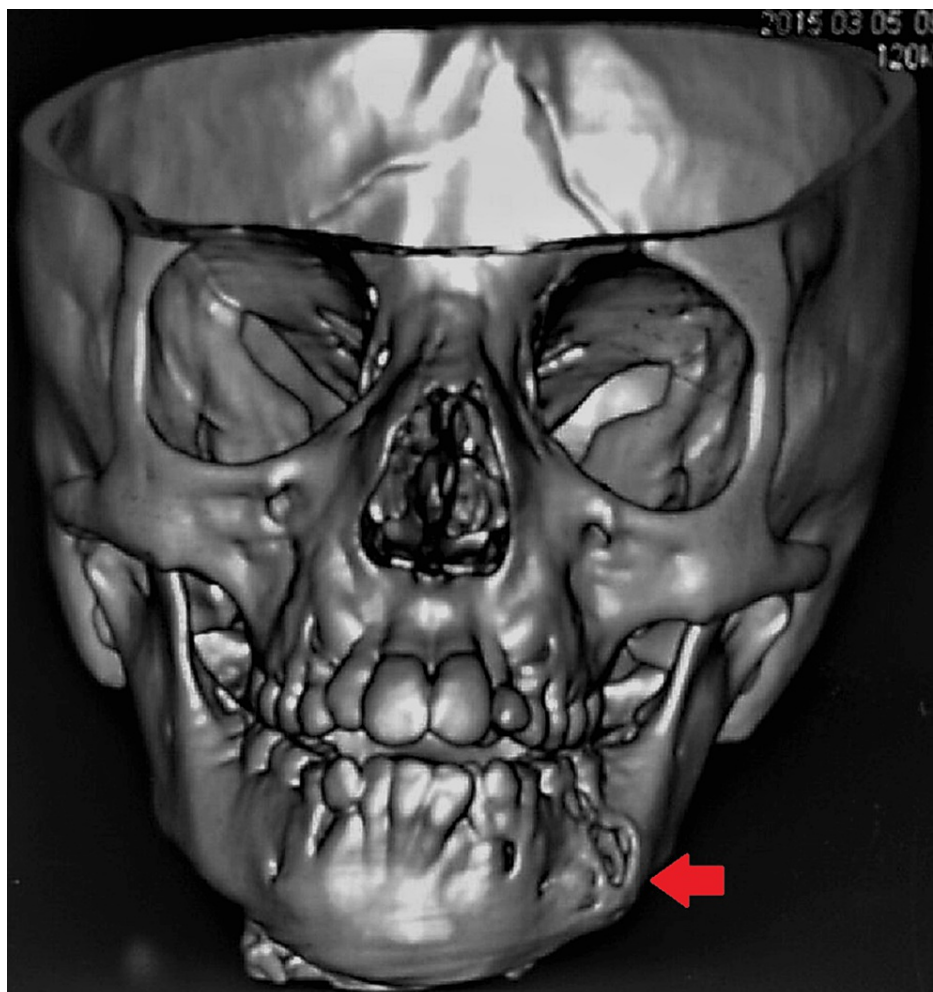


FIGURE 3: Computed tomography scan of facial bone showing a lytic lesion in the left mandibular region with buccal cortical expansion and perforation

An incisional biopsy was performed under local anesthesia. Histopathological findings of the biopsied specimen revealed hematoxylin-eosin-stained Langerhans cells typically having a moderate amount of homogeneous, pink, granular cytoplasm with distinct cell margins. There was profuse infiltration of eosinophils, plasma cells, and lymphocytes suggestive of Langerhans cell histiocytosis (Figure 4). Further,

the biopsied specimen was subjected to immunohistochemical staining and was positive for S100 and CD1a, confirmative of LCH (Figures 5-6). Hence, a systemic skeletal survey was carried out to rule out multifocal involvement, which yielded only negative clues, and thus it was concluded to be a case of restricted/localized Langerhans cell histiocytosis (eosinophilic granuloma of the mandible).

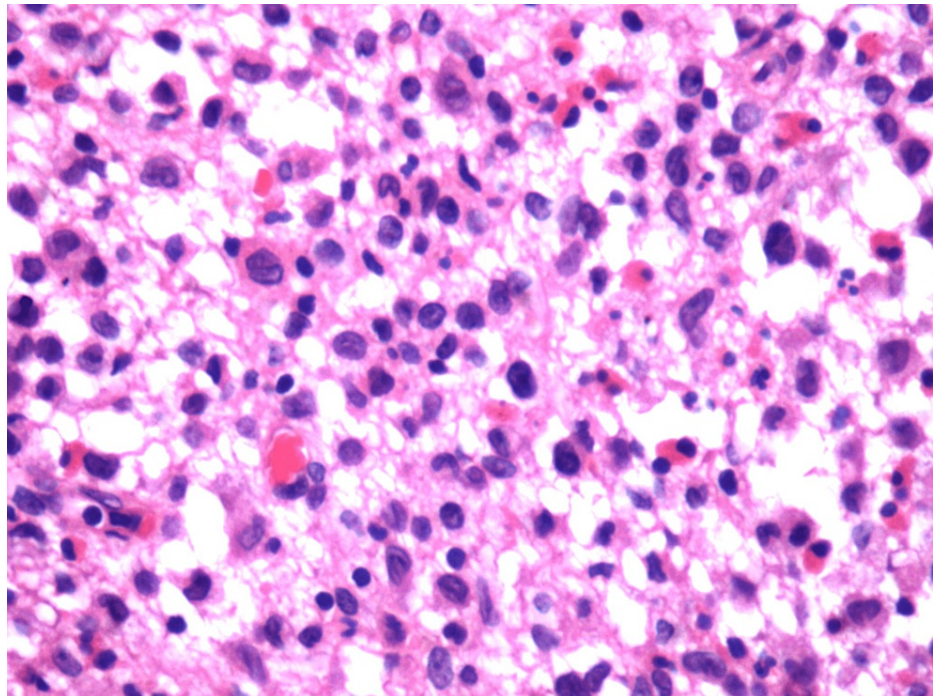


FIGURE 4: Photomicrograph of the biopsied specimen stained with hematoxylin and eosin

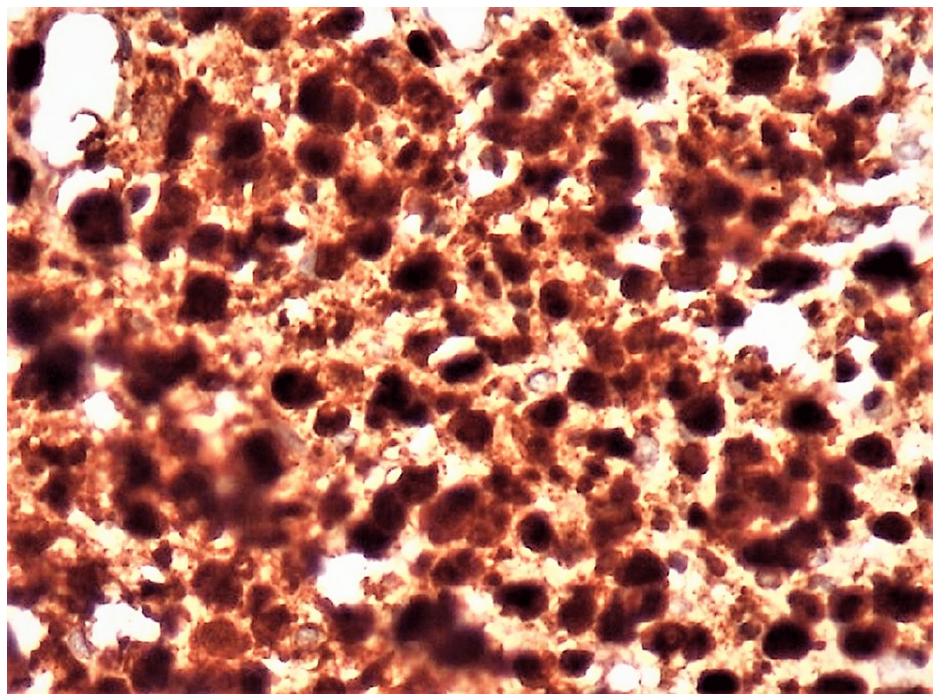


FIGURE 5: Immunohistochemical staining of the specimen showing positive staining with S100

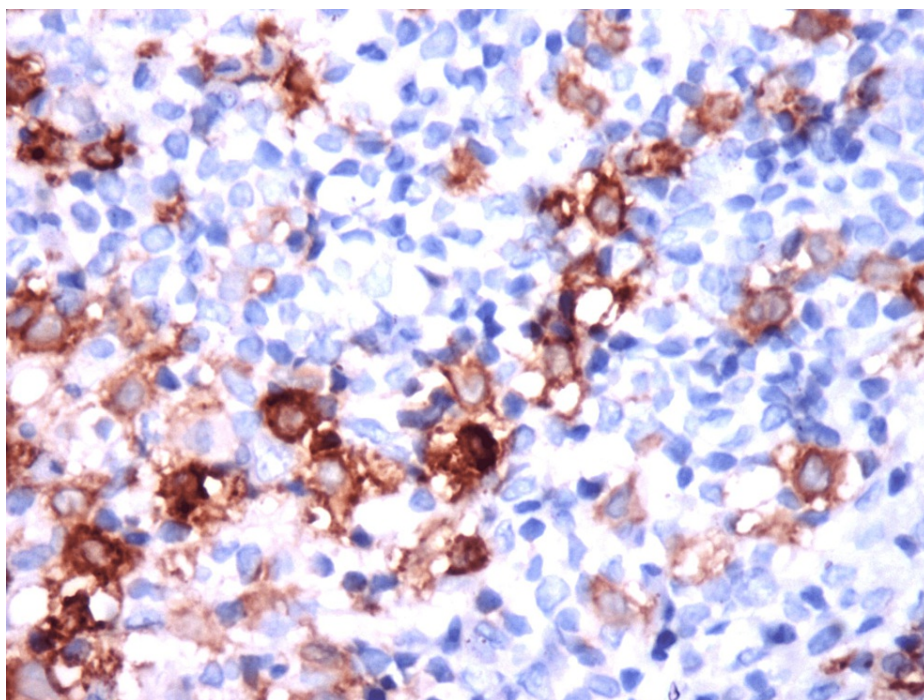


FIGURE 6: Immunohistochemical staining of the specimen showing positive staining with CD1a

The case was operated on under general anesthesia and the lesion was completely excised with thorough curettage of the surgical bed (Figures 7-9). Excisional biopsy confirmed the preoperative diagnosis. Adequate healing of the intraoral surgical site was observed postoperatively (Figure 10). The patient was followed up regularly for a period of three years and showed no signs of recurrence. Interestingly, the patient had a twin brother, and he was also subjected to clinical evaluation and orthopantomogram, which yielded no positive results.

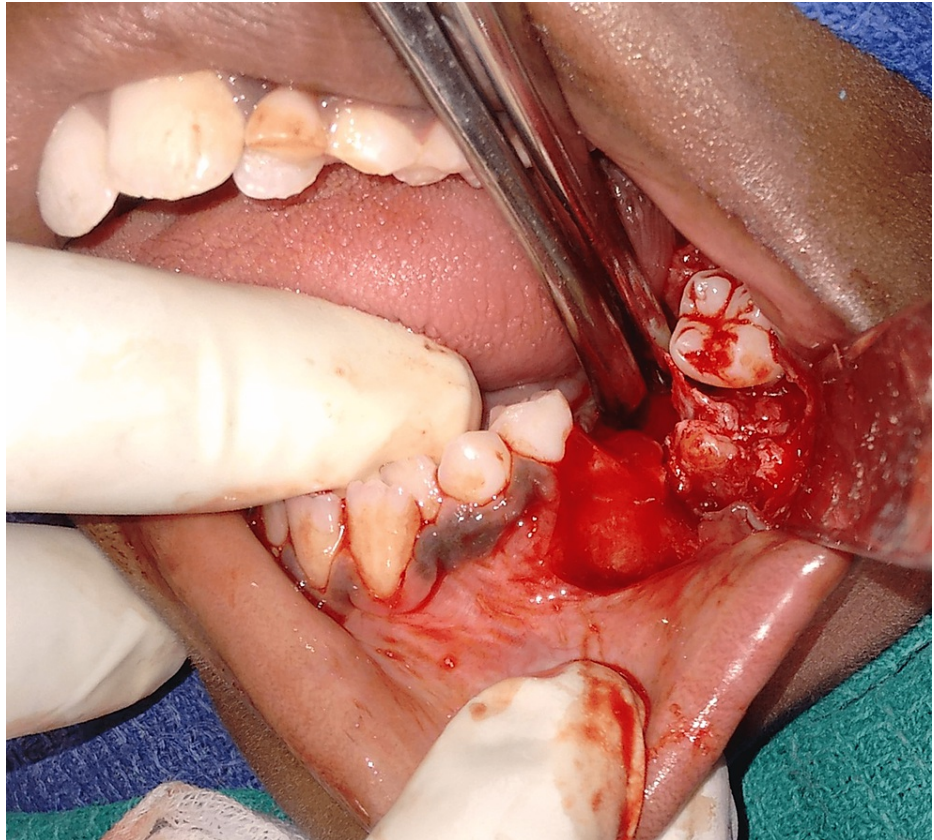


FIGURE 7: Exposure of the lesion



FIGURE 8: Lesion removed along with associated teeth



FIGURE 9: Closure done with 3-0 vicryl sutures



FIGURE 10: Postoperative healing of the intraoral surgical site

Discussion

Histiocytosis is a rare disease of the reticuloendothelial system characterized by the proliferation of specialized bone marrow-derived antigen-presenting dendritic cells [1]. The etiology of Langerhans cell histiocytosis (LCH) is unknown; however, it might be brought on by an infectious antigenic stimulation, a genetic anomaly, a dysregulated immunological response, a cytokine-mediated cellular growth of

Langerhans cells, or even clonal origin [1,3]. Granulocyte-macrophage colony-stimulating factor, interleukin-3, and tumor necrosis factor-alpha have all been linked to the potential development of LCH, and more recently, cytogenetic studies have proposed the involvement of tumor suppressor genes (p53), oncogenes (c-myc, h-ras), growth factors, cell surface immunologic markers, and apoptotic factors in LCH as well [8]. LCH patients are categorized based on the extent of the disease as restricted Langerhans cell histiocytosis and extensive Langerhans cell histiocytosis [3]. Restricted Langerhans cell histiocytosis is characterized by isolated biopsy-proven skin lesions, monostotic lesions (with or without skin rash, lymph node involvement, or diabetes insipidus), or polyostotic lesions (with lesions in multiple bones or more than two lesions in a single bone, with or without skin rash, adjacent lymph node involvement, or diabetes insipidus). Extensive Langerhans cell histiocytosis is characterized by the involvement of visceral organs, with or without diabetes insipidus, bone lesions, skin rash, or adjacent lymph node involvement, without signs of dysfunction of the hemopoietic system, lungs, or liver [3].

Langerhans cell histiocytosis can present as anything from a solitary bone lesion that spontaneously regresses to a multisystem, potentially fatal disorder. Multiple organ systems may be involved in the extensive form of LCH, including the bones, skin, lymph nodes, bone marrow, liver, spleen, lungs, gastrointestinal tract, thymus, and endocrine and central nervous systems. Few forms of LCH require little to no treatment while other kinds necessitate aggressive therapy [9]. One hundred fourteen (114) cases (10%) out of the 1120 LCH cases that Hartman studied had oral involvement [10]. Fifty-three percent and 25%, respectively, of the entire group were made up of the monostotic and polyostotic forms of eosinophilic granuloma [4]. Eosinophilic granulomas of the skull have never been reported to occur in families before. Masaru Takahashi and Satoshi Kuwabara presented identical twins with eosinophilic granuloma of the skull [10]. The skull is the bone that is most frequently afflicted, followed by the long bones of the upper extremities and flat bones [11]. A plain radiograph generally shows one or more irregularly marginated lytic lesions of bone. The presentation might resemble mastoiditis when the mastoid process is affected while deafness and ossicle damage result from middle ear extension. In the spine, the lytic process may cause the vertebral body to compress and collapse, leading to vertebra plana [3].

Eosinophilic granuloma of the bone is a rare disease of the maxillofacial region, with an annual incidence rate ranging from one new case in 350000 to 2 million [8]. Around 76% of lesions are found in the mandible, with the mandibular ramus and body being involved in over 96% of cases, according to a recent review of the literature by Guruprasad & Chauhan et al. [12]. These statistics are strikingly similar to those of the case at hand. According to Aricó and Egeler, individuals with eosinophilic granuloma frequently seek consultation due to uncomfortable swelling [13]. There have also been reports of mouth opening limitations and facial asymmetry brought on by the lesion's growth [4]. LCH of the jaws is frequently accompanied by nearby soft tissue edema, "floating" teeth, gingival edema, fractures, or discomfort. Oral symptoms are often limited to a small number of teeth and frequently expose the roots of the teeth due to periodontal damage, severe gingival recession, and alveolar bone loss [14]. Common dental symptoms include teeth loosening and slow healing following tooth extraction [15]. After the breakdown of the alveolar bone, the lesion may produce a dull, constant discomfort, enlargement of the jawbone, soft tissue mass, pain, and ulceration [1]. The initial lytic process of the lesion is tiny, centrally situated, and has irregular, poorly defined boundaries. In the midphase, the boundaries usually get more clearly defined, but in the late phase, periosteal lamellations are resolved, the borders become more well-defined, and occasionally, a thick crust of sclerotic tissue forms. An uncommon clinical symptom is a pathological fracture [4]. A biopsy is advised because the radiographic appearance might resemble malignant tumors [15].

The morphologic, immunohistochemical, and clinical standards necessary for the diagnosis of LCH and other childhood histiocytic illnesses were established by the Writing Group of the Histiocytic Society in 1987. The sequence for the diagnosis of LCH includes the presumptive diagnosis (characteristic light microscopic features), designated diagnosis (light microscopic features plus two or more additional positive stains for S-100 protein, a-o-Mannosidase, peanut lectin, or adenosine triphosphatase), and definitive diagnosis (with electron microscopy, lesional cells with light microscopic properties, and Birbeck granules and/or lesional cells stained positively for CD1a antigen) [3].

The management of LCH depends on the level of involvement. In cases with restricted Langerhans cell histiocytosis involving only skin lesions, at first, therapy might not be required because the lesions frequently resolve on their own, especially in the newborn. Topical steroids are used as the initial line of treatment. If the lesions do not resolve, systemic chemotherapy is typically used to achieve resolution. Patients whose diseases have shown resistance to previous treatments have been treated successfully with topical nitrogen mustard or irradiation [3]. Depending on the location of the illness and the patient's age, low-dose radiation is useful in treating LCH with a total dosage of 3 to 10 Gy. Bone lesions presenting as localized painful lumps are preferably managed by surgical curettage. In cases with isolated lymph node involvement, resolution occurs without therapy [3].

The management of extensive Langerhans cell histiocytosis primarily involves chemotherapy. Due to the progressive nature of generalized LCH, systemic chemotherapeutic drugs have been used to treat the majority of patients. Short-course prednisolone is especially helpful for patients with severe illness but no organ failure since their prognosis is good [3]. According to Kelly and Pritchard, monoclonal antibody treatment is also very effective as a cytotoxin and an immunoregulator [16]. The specificity of a monoclonal

antibody directed against the CD1a antigen on Langerhans cells was utilized by these scientists [3]. Patients should be cautiously monitored for a long time since recurrence rates are reported to range from 1.6% to 25% depending on the treatment approach and location of the lesion [17].

Conclusions

Langerhans cell histiocytosis is an uncommon condition whose cause and pathophysiology are still unknown. The correct understanding of this diverse collection of illnesses may benefit from improvements in immuno-histochemistry, molecular biology, and radiodiagnostic procedures. Given that the disease can be unpredictable, it is important to consider the possibility that the unifocal disease could develop into multifocal. Due to the potential for the condition to worsen if left untreated, it is crucial to include an eosinophilic granuloma in the differential diagnosis of bone lesions in adult subjects. The unpredictable nature of Langerhans cell histiocytosis warrants early management and long-term follow-up.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

- Jindal M, Sharma VK, Ahmed I, Agrawal A: Langerhans cell histiocytosis of maxilla and mandible in 6 years old child: a case report. *Int J Clin Pediatr Dent.* 2009, 2:45-9. [10.5005/jp-journals-10005-1029](https://doi.org/10.5005/jp-journals-10005-1029)
- Lichtenstein L: Histiocytosis X; integration of eosinophilic granuloma of bone, Letterer-Siwe disease, and Schüller-Christian disease as related manifestations of a single nosologic entity. *AMA Arch Pathol.* 1953, 56:84-102.
- Egeler RM, D'Angio GJ: Langerhans cell histiocytosis. *J Pediatr.* 1995, 127:1-11. [10.1016/S0022-3476\(95\)70248-2](https://doi.org/10.1016/S0022-3476(95)70248-2)
- dos Anjos Pontual ML, da Silveira MM, de Assis Silva Lima F, Filho FW: Eosinophilic granuloma in the jaws. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2007, 104:e47-51. [10.1016/j.tripleo.2007.07.006](https://doi.org/10.1016/j.tripleo.2007.07.006)
- Nezelof C, Basset F, Rousseau MF: Histiocytosis X histogenetic arguments for a Langerhans cell origin. *Biomedicine.* 1973, 18:365-71.
- Allen CE, Merad M, McClain KL: Langerhans-cell histiocytosis. *N Engl J Med.* 2018, 379:856-68. [10.1056/NEJMra1607548](https://doi.org/10.1056/NEJMra1607548)
- Raney RB Jr, D'Angio GJ: Langerhans' cell histiocytosis (histiocytosis X): experience at the Children's Hospital of Philadelphia, 1970-1984. *Med Pediatr Oncol.* 1989, 17:20-8. [10.1002/mpo.2950170106](https://doi.org/10.1002/mpo.2950170106)
- Shah PD, Mukherji S: Langerhans cell histiocytosis presenting as a unifocal eosinophilic granuloma in the body of the mandible: a rare report. *Int J Otorhinolaryngol Clin.* 2015, 7:16-8. [10.5005/aijoc-7-1-16](https://doi.org/10.5005/aijoc-7-1-16)
- Kuwabara S, Takahashi M: Eosinophilic granuloma of the skull in identical twins--case report. *Neurol Med Chir (Tokyo).* 1990, 30:1043-6. [10.2176/nmc.30.1043](https://doi.org/10.2176/nmc.30.1043)
- Hartman KS: Histiocytosis X: a review of 114 cases with oral involvement. *Oral Surg Oral Med Oral Pathol.* 1980, 49:38-54. [10.1016/0030-4220\(80\)90030-4](https://doi.org/10.1016/0030-4220(80)90030-4)
- Egeler RM, Nesbit ME Jr: Langerhans cell histiocytosis and other disorders of monocyte-histiocyte lineage. *Crit Rev Oncol Hematol.* 1995, 18:9-35. [10.1016/1040-8428\(94\)00117-c](https://doi.org/10.1016/1040-8428(94)00117-c)
- Guruprasad Y, Chauhan DS: Solitary eosinophilic granuloma of mandibular condyle: literature review and report of a rare case. *J Maxillofac Oral Surg.* 2015, 14:209-14. [10.1007/s12663-012-0438-7](https://doi.org/10.1007/s12663-012-0438-7)
- Arico M, Egeler M: Clinical aspects of Langerhans cell histiocytosis. *Hematol Oncol Clin North Am.* 1998, 12:247-57. [10.1016/s0889-8588\(05\)70508-6](https://doi.org/10.1016/s0889-8588(05)70508-6)
- Piattelli A, Paolantonio M: Eosinophilic granuloma of the mandible involving the periodontal tissues. A case report. *J Periodontol.* 1995, 66:731-6. [10.1902/jop.1995.66.8.731](https://doi.org/10.1902/jop.1995.66.8.731)
- Uckan S, Gurol M, Durmus E: Recurrent multifocal Langerhans cell eosinophilic granuloma of the jaws: report of a case. *J Oral Maxillofac Surg.* 1996, 54:906-9. [10.1016/s0278-2391\(96\)90546-7](https://doi.org/10.1016/s0278-2391(96)90546-7)
- Kelly KM, Pritchard J: Monoclonal antibody therapy in Langerhans cell histiocytosis--feasible and reasonable?. *Br J Cancer Suppl.* 1994, 23:S54-5.
- Can IH, Kurt A, Özer E, Sari N, Samim E: Mandibular manifestation of Langerhans cell histiocytosis in children. *Oral Oncology Extra.* 2005, 41:174-7. [10.1016/j.ooe.2005.04.007](https://doi.org/10.1016/j.ooe.2005.04.007)