Diagnosis of langerhans cell histiocytosis based on maxillofacial manifestations in an adult: case report

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ABSTRACT
Background: Langerhans cell histiocytosis (LCH) is a rare clonal disease that most commonly affects the pediatric population. In adults, its diagnosis is challenging due to its low prevalence and nonspecific clinical manifestations. The maxillofacial region may be the first site affected, making the dentist a key figure in early detection. Materials and Methods: We present the case of a 38-year-old male patient who consulted due to tooth mobility and difficulty chewing. Radiographic examination revealed osteolytic lesions in the mandible. The diagnosis was confirmed by biopsy with immunohistochemical positivity for CD1a, CD68, and S100. The patient was referred to the hematology-oncology team, where a systemic workup was completed. Treatment included chemotherapy with vinblastine, prednisone, and mercaptopurine, along with endocrine management and radiotherapy. Results and Discussion: The patient showed a favorable outcome, with no recurrence after four years of follow-up. The mandible was the most commonly affected site, with symptoms including pain, tooth mobility, and radiolucent lesions. Diagnosis was confirmed by immunohistochemistry in all cases. Treatment modalities varied and included surgery, radiotherapy, and chemotherapy. Discussion: This case highlights the role of dentists in identifying rare systemic diseases. Tooth mobility without evident periodontal disease may be the first sign of LCH. The literature supports a multidisciplinary approach and the need to consider LCH in the differential diagnosis of maxillofacial lesions. Conclusions: LCH can initially present in the maxillofacial region. Early recognition enables timely intervention, improving prognosis and reducing the risk of systemic complications.

Keywords: Mandible, Jaw, Maxillofacial, Immunohistochemistry.

1 INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare disease characterized by the clonal proliferation of immature dendritic cells expressing CD1a and Langerin (CD207), with a predilection for affecting bones, skin, lungs, and the pituitary gland (Allen, Merard, & McClain, 2018). Although it is more commonly observed in the pediatric population, diagnosing LCH in adults poses a clinical challenge due to its low prevalence and the heterogeneity of its clinical manifestations (Lin, Chu, Chang, & Liao, 2023). Oral and maxillofacial signs, such as tooth mobility, osteolytic lesions, or gingival swelling, may represent the initial and, in some cases, the only manifestations of the disease (Merglová et al., 2014).

Due to the nonspecific nature of these findings and their overlap with common odontogenic pathologies, the recognition of LCH by dentists and maxillofacial surgeons is crucial for early detection (Faustino et al., 2021). Timely identification through imaging studies and histological confirmation is essential to guide therapeutic decisions and prevent long-term consequences, particularly in cases with craniofacial involvement, which are associated with a higher risk of multisystemic disease and endocrine sequelae such as diabetes insipidus (Lin et al., 2023; Eckard & Schultze, 2003).

Although numerous reports of LCH exist in pediatric populations (Merglová et al., 2014; Zachariades, Anastasea-Vlachou, Xypolyta, & Kattamis, 1987; Loh & Quah, 1990; Mitomi, Tomizawa, & Noda, 2005; Wladis, Tomaszewski, & Gausas, 2008), the evidence in adults remains limited and

fragmented, especially regarding its maxillofacial presentation. Many of these adult cases are initially misdiagnosed as periodontal or infectious conditions (Uckan, Gurol, & Durmus, 1996; Xie, Wang, & Ding, 2021), resulting in delays in appropriate diagnosis and treatment. Therefore, it is essential to systematize the current knowledge regarding the clinical, radiographic, histopathological, and therapeutic characteristics of LCH in adults with mandibular and/or maxillary involvement, to facilitate early clinical suspicion and improve both functional and systemic outcomes.

The main objective of this study is to present a clinical case of LCH diagnosed in an adult based on oral signs and to conduct a review of the literature focusing on adult patients with maxillomandibular involvement, aiming to characterize the most relevant clinical, radiographic, histopathological, and therapeutic findings reported to date.

2 CASE REPORT

A 38-year-old male patient presented to a private dental clinic with complaints of “loose teeth” and difficulty chewing, with a one-year history of progressive symptoms. His family history included a mother who died of breast cancer and a father who died of gastric cancer. As a relevant medical history, the patient was undergoing treatment with zopiclone for depression.

Intraoral examination revealed gingival inflammation without bleeding, along with multiple teeth exhibiting increased mobility, but no pain. A panoramic radiograph revealed multiple osteolytic lesions in the mandible, prompting a biopsy and referral to the Oral Pathology Department at the Regional Hospital of Antofagasta.

A biopsy was performed, revealing fibrous connective tissue with areas of chronic lymphoplasmacytic inflammatory infiltrate. Notable findings included microgranuloma-like structures with hemorrhagic foci composed of histiocytic-like cells with pale cytoplasm and vesicular nuclei, accompanied by eosinophils and plasmacytoid cells. Immunohistochemical staining was positive for CD1a, CD68, and S100 (Figure 1). These histopathological findings confirmed the diagnosis of Langerhans cell histiocytosis.

The patient was referred to the hematology-oncology board, where further tests were performed. A bone scintigraphy revealed increased osteoblastic activity in the axial and appendicular skeleton (long bones, skull, ribs). Bone marrow aspiration showed myeloid hyperplasia with 5% plasmacytes. Additional tests included: urinary sodium 18 mmol/L; negative serology for hepatitis B, hepatitis C, and HIV; LDH 152 U/L; cortisol 2.38 µg/dL; and complete blood count with WBC 6,490/mm³, neutrophils 52.1%, hemoglobin 10.5 g/dL, hematocrit 32.2%, and platelets 251,000/mm³.

The maxillofacial surgery team performed dental defocalization of teeth 1.7, 1.6, 1.4, 2.4, 3.4, 3.7,

3.8, and 4.8. One month later, the medical board initiated chemotherapy with vinblastine, prednisone, and later mercaptopurine. The patient also received intranasal desmopressin (DDAVP) and hydrocortisone for adrenal insufficiency, as well as insulin, metformin, and sitagliptin (Januvia®) due to steroid-induced diabetes mellitus. Radiotherapy was administered to vertebra L1.

After four years of clinical follow-up, the patient remains in good general condition, with no oral abnormalities or radiographic evidence of mandibular bone recurrence (Figure 2).

Figure 1

(A,B,C) Hematoxylin and eosin staining, (D) CD1a, (E) CD68, (F) S100.

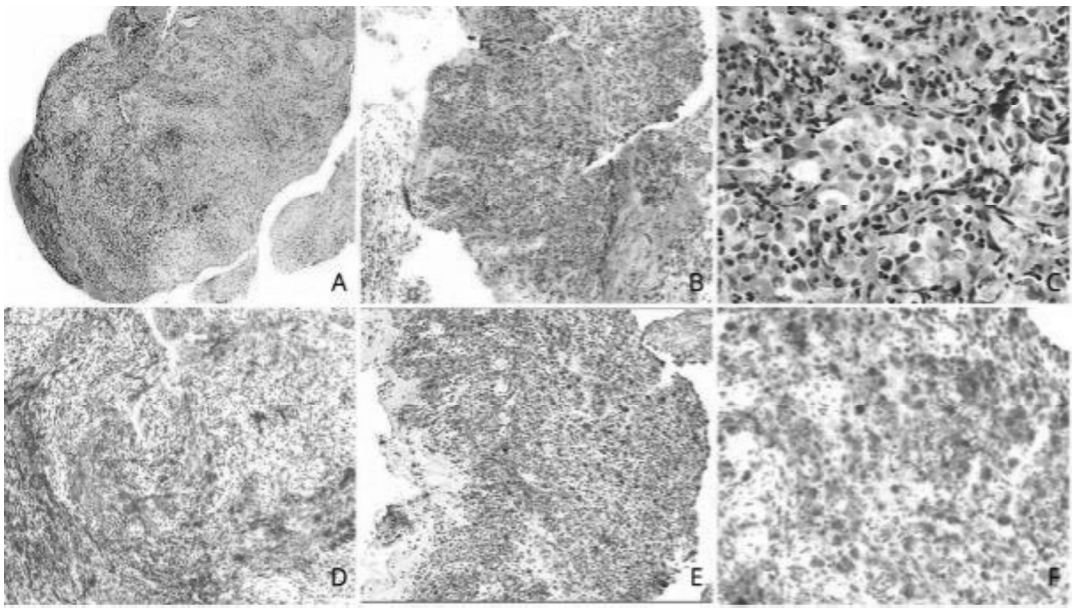
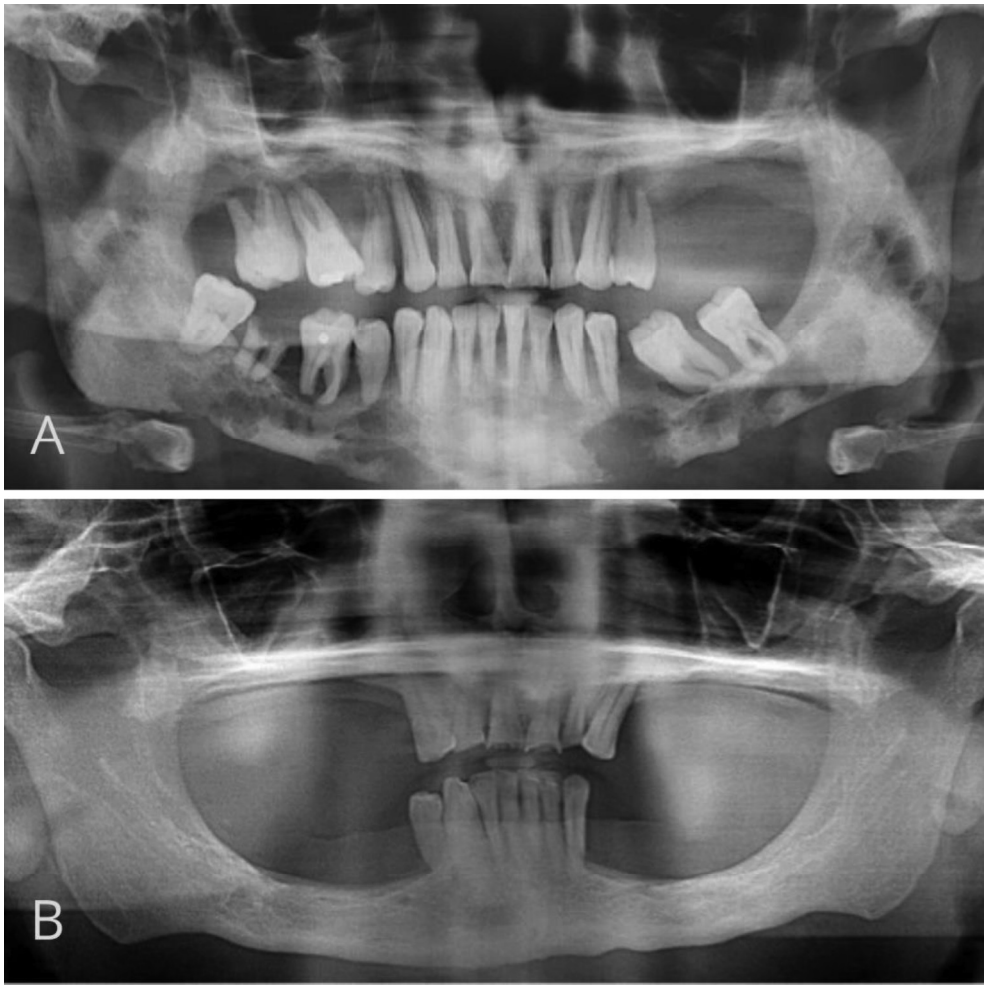


Figure 2

(A) Initial panoramic radiograph. Multiple teeth lacking bone support and osteolytic lesions throughout the mandible. (B) Follow-up panoramic radiograph, year 2024.



3 RESULTS AND DISCUSSIONS

LCH in adults with oral manifestations represents a significant diagnostic challenge due to its low prevalence and nonspecific clinical presentation (Kim et al., 2019; Sabrine et al., 2020). This study reports a clinical case of LCH diagnosed in an adult patient based on maxillofacial signs. In terms of anatomical distribution, mandibular involvement was the most frequent (71.43%) (Uckan et al., 1996; Xie et al., 2021; Terada, 2013; Siessegger, Klesper, Kasper, & Zoeller, 2002; Sabrine et al., 2020), while combined maxillary and mandibular involvement was reported in 28.57% of cases (Salam, Shahid, & Mirza, 2017; Annibali et al., 2009). The most common clinical findings included gingival inflammation and advanced periodontal signs such as tooth mobility (71.43%), pain (57.14%), and trismus (14.28%). Facial swelling

or submandibular lymphadenopathy was noted in two cases (28.57%) (Uckan et al., 1996; Sabrine et al., 2020).

Radiographic studies, usually panoramic imaging, revealed multiple osteolytic or radiolucent lesions, most of them poorly defined and occasionally presenting the characteristic "floating teeth" appearance (Uckan et al., 1996; Xie et al., 2021; Terada, 2013; Salam et al., 2017; Siessegger et al., 2002; Annibali et al., 2009; Sabrine et al., 2020). In all cases, diagnosis was confirmed by immunohistochemistry, with positivity for CD1a and/or S-100 (Uckan et al., 1996; Xie et al., 2021; Terada, 2013; Salam et al., 2017; Siessegger et al., 2002; Annibali et al., 2009; Sabrine et al., 2020); some reports also described positivity for Langerin, CD45, or other immunologic markers (Xie et al., 2021; Salam et al., 2017).

Consistent with the literature, the initial manifestation in our patient was tooth mobility in the absence of evident periodontal disease, a common finding in the reviewed series (Xie et al., 2021; Annibali et al., 2009). This mobility, combined with radiographically evident mandibular osteolytic lesions (Uckan et al., 1996; Xie et al., 2021; Terada, 2013; Salam et al., 2017; Siessegger et al., 2002; Annibali et al., 2009; Sabrine et al., 2020), should raise clinical suspicion of an underlying systemic condition. Panoramic radiographs often revealed typical features such as ill-defined radiolucencies or the "floating teeth" pattern, as widely documented (Salam et al., 2017; Sabrine et al., 2020).

A definitive diagnosis requires histopathological confirmation with immunohistochemical positivity for CD1a and S-100, findings reported in all reviewed cases (Uckan et al., 1996; Xie et al., 2021; Terada, 2013; Salam et al., 2017; Siessegger et al., 2002; Annibali et al., 2009; Sabrine et al., 2020). The expression of CD1a, S-100, and CD68 in the present case reinforces the proliferative nature of the Langerhans cells involved and is consistent with the findings of Xie et al. (2021) and Terada (2013).

Systemic involvement was documented in nine patients as part of multisystemic LCH, affecting the femur (11.11%), risk organs (16.6%), and multiple skeletal sites (11.11%) (Annibali et al., 2009; Sabrine et al., 2020). In contrast, in 28.57% of cases the disease was confined to the maxillofacial region (Xie et al., 2021; Terada, 2013), while in 42.85% the extent of involvement was not specified (Uckan et al., 1996; Salam et al., 2017; Siessegger et al., 2002).

Therapeutic approaches showed wide variability. Most reports described local surgical treatment through extractions and curettage (Uckan et al., 1996; Sabrine et al., 2020), whereas systemic cases required oncologic protocols with vinblastine, corticosteroids, or combination chemotherapy, as reported by Annibali et al. (2009). Our patient was managed with local extractions and curettage supplemented by systemic chemotherapy with prednisone and mercaptopurine, achieving complete remission and maintaining mandibular bone stability over a four-year follow-up.

Complications were reported in three patients: recurrence of lesions (Terada, 2013; Annibali et al., 2009), one pathologic mandibular fracture (Sabrine et al., 2020), and one case of osteoradionecrosis in a previously irradiated area (Xie et al., 2021). Follow-up ranged from one month (lost to follow-up) (Sabrine et al., 2020) to 18 years (Annibali et al., 2009). Long-term monitoring demonstrated a substantial rate of clinical remission, with follow-up durations ranging from 0.6 to 18 years (Uckan et al., 1996; Xie et al., 2021; Terada, 2013; Siessegger et al., 2002; Annibali et al., 2009). The most frequent complications were recurrence (Terada, 2013; Annibali et al., 2009), mandibular fracture (Sabrine et al., 2020), and osteoradionecrosis (Xie et al., 2021), emphasizing the importance of prolonged clinical and radiographic surveillance. In our case, no maxillofacial complications were observed during follow-up, likely due to early diagnosis and multidisciplinary management.

This study underscores the crucial role of general dentists and maxillofacial surgeons in the early detection of LCH, particularly in adults, where the disease may manifest solely through oral signs. Recognition of atypical radiographic patterns, clinical suspicion in cases of unexplained tooth mobility, and timely referral for biopsy are essential to prevent diagnostic delays.

The current evidence on LCH with maxillofacial involvement in adults remains scarce and is largely limited to case reports and observational studies. This constrains the establishment of standardized therapeutic guidelines, while heterogeneity in treatment approaches, follow-up periods, and diagnostic criteria further complicates comparison across reported cases.

4 CONCLUSION

Langerhans cell histiocytosis in adults can initially manifest through isolated maxillofacial symptoms, often mimicking common odontogenic conditions and leading to diagnostic delays. Given the potential aggressiveness of LCH and the risk of systemic involvement, an interdisciplinary approach and long-term follow-up are recommended. Continued education of the dental team regarding systemic diseases with oral manifestations would greatly aid in early diagnosis and improve patient outcomes.

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