

Case Report

Rare Langerhans cell histiocytosis in children: a case report

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Received: 20 January 2019

Accepted: 08 March 2019

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disease, formally known as histiocytosis X that is characterized by abnormal proliferation of histiocytes derived from bone marrow (Langerhans cells), joined with leucocytes, eosinophils, neutrophils, lymphocytes, plasma cells and giant multi-nucleated cells causing tissue destruction. One of the first signs of LCH is oral manifestation, in some cases, the oral cavity may be the only affected area. With the chance of oral lesion incidence in LCH being 77%. Initial symptoms are generally nonspecific, which can easily cause misdiagnoses. The purpose of reporting this case is to discuss the features of LCH clinically and radiographically and in the role of the dentist when diagnosing such lesions for a proper management.

An 11-year-old boy reported a complaint of swelling in the left side of the lower jaw that is asymptomatic and had been gradually increasing in size for the past 6 months without any improvements. After performing a biopsy and diagnosing the lesion as LCH, the patient was then treated with a dose of vinblastine (6 mg/m² intravenous bolus) for 24 weeks as a total period. Two years follow up; the patient showed no sign of recurrence and is in good general condition. In conclusion, reporting this case serves as documentation of the proper route of clinical assessment and diagnosis of LCH with the best possible treatment as guidance.

Keywords: Eosinophilic granuloma, Histiocytosis, Langerhans cell, Osteolytic lesions, Vinblastine

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare disease, formally known as histiocytosis X that is characterized by abnormal proliferation of histiocytes derived from bone marrow (Langerhans cells), joined with leucocytes, eosinophils, neutrophils, lymphocytes, plasma cells and giant multi-nucleated cells causing tissue destruction. In which, it is a result of cellular penetration that invades skin, mucosa and internal organs and substitutes bone. The occurrence of LCH is not acknowledged very well but it is estimated to be 2-5 cases per million inhabitants per year, approximately.¹⁻³ The disease has been staged clinically according to Greenberg et al, into three disorders based on the clinical presentations.⁴ Even

though the etiology of LCH is unknown, several hypotheses have been proposed about its possible pathogenesis.⁵⁻⁷

One of the first signs of LCH is oral manifestation, in some cases, the oral cavity may be the only affected area.⁸ With the chance of oral lesion incidence in LCH is 77%. Initial symptoms are generally nonspecific, which can easily cause misdiagnoses.⁹

The purpose of reporting this case is to discuss the features of LCH clinically and radiographically and in the role of the dentist when diagnosing such lesions for a proper management. Prognosis of LCH and its

management is based on the early detection of clinical manifestation of the lesion.

CASE REPORT

An 11-year-old boy reported along with his father to the family medicine department at Prince Sultan military hospital. With the complaint of swelling in the left side of the lower jaw, that is asymptomatic and had been gradually increasing in size for the past 6 months without any improvements. The patient was then referred to the oral and maxillofacial department with a differential diagnosis of Berket lymphoma for further assessment.

The patient is medically fit with normal vital signs, medical history showed routine prescription analgesics and antibiotics (Augmentin). However, there was no improvement in the patient's condition. Extra-oral examination showed swelling in the left side of the jaw with focal swelling of the cheek contour, swelling is extending from the posterior body of the mandible to the angle with obliterated inferior border. Firm in texture, ipsilateral submandibular lymph node was firm and non-tender under palpation (largest 2.3 x 2.1 cm).

Intra-oral examination showed severely inflamed retro-mandibular mucosa with vestibular hard swelling; lower dental midline shifted up to 10 mm the left along with a posterior cross-bite was noted. Vitality test was done for the affiliated tooth and was seen vital with no mobility.



Figure 1: Initial orthopantomogram radiograph (OPG) showed bone resorption in the left mandible.

Orthopantomogram radiograph and CT scan were planned for the patient, OPG (Figure 1) and 3 dimensional CT (Figure 2) showed 3-4 cm radiolucent interosseous lesion that is localized in the body and angle of the mandible with tooth displacement of the 2nd molar. CT (Figure 3) showed lingual cortex erosion with bucco-lingual cortical bone expansion, disruption of the overlying cortical margin along with associated extraosseous soft tissue is seen causing the focal swelling of the cheek contour and mild periosteal reaction was also suspected. The associated large submandibular lymph node was indeed

shown to be of 2.3 x 2.1 cm in maximum diameter. The enlarged lymph nodes form soft tissue lesions at their anatomical sites with no evidence of breaking down or matrix calcification.



Figure 2: Three-dimensional computed tomography (3D CT) revealed osteolytic lesion related to the angle of the left mandible.

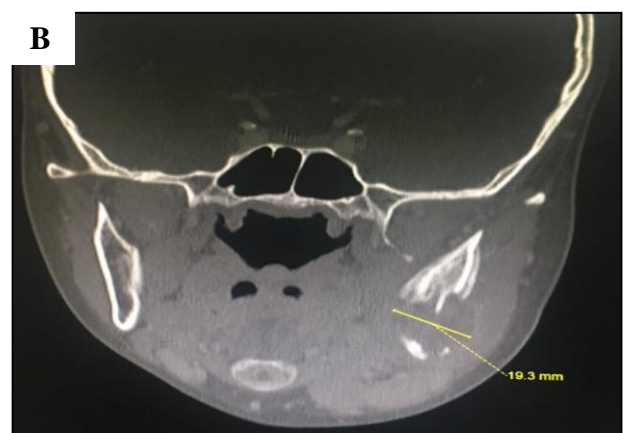


Figure 3: Axial and coronal computed tomography (CT) revealed. (A): bucco-lingual cortical bone expansion, (B): disruption of the overlying cortical margin along with associated extraosseous soft tissue.

Small right submandibular and upper deep cervical lymph nodal enlargement was also seen. The laryngeal cartilaginous skeleton was seen intact sections passed through the brain show no parenchymal lesions of abnormal attenuation values.

Lymphoma, central giant cell granuloma was considered, alongside keratocystic odontogenic tumor and ameloblastoma as a differential diagnosis. Blood investigations showed no abnormality.

An incisional biopsy was performed under General anesthesia for histopathological evaluation. Lower unerupted 3rd molar was shown completely mobile. Biopsy showed granulation type inflammatory tissue fragments with numerous eosinophils, reactive lamellar and woven bone. The inflamed tissue also demonstrated large Langerhans cells having cleaved and vesicular nuclei admixed with osteoclast-like giant cells. Staining was then performed; S100 and CD1a marker reported a strong positive. The histopathological findings along with the immunohistochemical results are diagnostic for LCH.

Surgical curettage was done under GA and patient was referred to the oncology department and received a dose of vinblastine (6 mg/m² intravenous bolus) for 24 weeks as a total period. Two years after diagnosis, the patient showed no sign of recurrence and is in good general condition.

DISCUSSION

The term LCH was introduced as a collective designation for a spectrum of clinicopathologic disorders characterized by proliferation of histiocytes such as cells accompanied by eosinophils, lymphocytes, plasma cells, and multinucleated giant cells.⁹ Langerhans cells are normally found in mucosa, epidermis, lymph nodes and bone marrow as dendritic mononuclear cells. They present and process antigen to t-lymphocytes, LCH literature review showed proliferation of Langerhans cells leading to hard and soft tissue destruction.

The pathogenesis and etiology of LCH is uncertain. However, there are two hypotheses that are widely accepted after reviewing literature, one hypothesis being the disorder is due to neoplastic proliferation and the other is due to immune regulation. However, recent literature has shown monoclonal proliferation of lesional cells, which is suggestive of neoplastic lesion.¹⁰⁻¹³

The predilection of LCH in males is twice that it is in females with LCH affecting children between the age 1 and 15 with the peak between 2-4 years old¹⁴ yearly incidence of children aging <10 years old is thought to be 1 in 200,000 the reported case is in an 11-year-old male child.¹⁴

In the majority of cases, LCH most common clinical signs are bone lesions that are either solitary or multiple

involving ribs, vertebrae, skull and jaw. Particularly in the posterior mandible of the jaw, distal to the canine.^{14,15} In this case, the posterior mandible had been affected.

LCH has been categorized into three variants based on clinical presentation and the age. They include; (1) Acute disseminated form with multiple system involvement often seen in infants (Letterer-Siwe disease); (2) Chronic disseminated form with osseous lesions which are frequently multiple and with extra skeletal lesions (Hand-Schuller-Christian disease); (3) Chronic localized form with solitary or multiple skeletal lesions and occasionally extra skeletal involvement mainly seen in adults (Eosinophilic granuloma). Hashimoto Pritzker syndrome is a congenital form of LCH presenting with deep subcutaneous skin lesions.^{16,17}

In the present case, the patient displayed a solitary skeletal lesion with no extra skeletal involvement there for it was considered as eosinophilic granuloma variant.

The clinical course of LCH depends upon the age of the patient and pathological infiltration of Langerhans cells in various systems such as bone, skin, lymph nodes, bone marrow, liver, spleen, lung, endocrine system, ear, and brain.

Adults and older children present single system disease commonly affecting bone; however, young babies demonstrate multisystem involvement with initial general clinical presentation includes skin rash, otitis media, fever, organomegaly, anemia, pain and pathological fracture of the involved bone, and diabetes insipidus.¹⁸

Intraoral involvement can be the only manifestation seen in LCH, which can lead the patient to visit the dentist. Sore mouth, halitosis, gingivitis, gingival hypertrophy and unpleasant taste, mobility of teeth with alveolar expansion, jaw pain, facial swelling, mental nerve anesthesia and failure of extracted tooth sockets to heal. Loss of supporting alveolar bone mimicking advanced periodontal disease is the main oral signs associated with LCH.¹⁹ In this case, the swelling was present in his posterior mandible along the angle of the mandible with tooth displacement of the 2nd molar.

The diagnosis of LCH is based on the histopathological examination, infiltration of pale staining mononuclear cells that looks like histiocytes with diffused cytoplasmic borders and indented or round vesicular nuclei, eosinophil's number varies and are usually scattered among the histiocytes along with the existence of multinucleated giant cells, lymphocytes and plasma cells.

In all three types of LCH the histopathology is similar. Except in acute disseminated form, as they show acute form of lymphomas.²⁰ In this case, similar histopathology has been present.

Different diagnosis was included based on the clinical and radiographic finding for the presented case. Lymphoma, central giant cell granuloma was considered, alongside keratocystic odontogenic tumor and ameloblastoma as differential diagnosis.

The treatment of LCH depends on the pathogenesis of the disease, the age of the patient and dissemination of the lesion. Surgical curettage and excision can be done when the oral lesion is localized and accessible in maxilla and mandible. As for less accessible lesions, low doses of radiation may be used. However, in younger patients the chance of malignancy secondary to this treatment is a concern.

Multi-system disease and nonresponsive uni-system disease requires a more extensive treatment with systemic chemotherapy. In certain patients with localized lesions, Intra-lesional corticosteroid agents may be effective (e.g., prednisolone 20-30 mg/day for 2-4 weeks and then followed by tapering of the dose). In multi-system and non-responsive uni-system LCH, the most common agents used in different combination regimens and several cycles are corticosteroids, vinblastine, etoposide, cytarabine, 6-mercaptopurine, methotrexate, 2-chlorodeoxyadenosine, cyclosporine, thalidomide, and others. A combination of vincristine and prednisone seems to lower the chance of recurrence.^{20,21}

Prognosis of LCH depends on the following criteria; (1) Age - children aging more than 2 years of age generally have a good prognosis; (2) Number of involved sites - uni-system disease has good prognosis then multisystem disease; (3) Organ dysfunction when absent gives a good prognosis.

CONCLUSION

The aim of reporting this case is to document the proper route of clinical assessment and diagnosis of LCH with the best possible treatment as guidance.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Alfadil L, Almajid E. Rare Langerhans cell histiocytosis in children: a case report. *Int J Res Med Sci* 2019;7:1367-71.