

Langerhans Cell Histiocytosis

¹S Jayachandran, ²N Balaji

¹Professor and Head, Department of Oral Medicine and Radiology, Tamilnadu Government Dental College and Hospital, Chennai, Tamil Nadu, India

²Postgraduate Student, Department of Oral Medicine and Radiology, Tamilnadu Government Dental College and Hospital, Chennai, Tamil Nadu, India

Correspondence: S Jayachandran, Professor and Head, Department of Oral Medicine and Radiology, Tamilnadu Government Dental College and Hospital, Chennai, Tamil Nadu, India, Phone: 044-25340441, 9444185662, e-mail: drsjayachandranmds@yahoo.com

ABSTRACT

Langerhans cell histiocytosis (LCH) is rare unique disorder of the reticuloendothelial system characterized by an abnormal proliferation of histiocytes and eosinophilic leukocytes. Lichtenstein gave the term Histiocytosis X in 1953 to include three clinical varieties; Eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease, which shared some common histologic features and clinical findings. In 1973, the term LCH was introduced as an alternative to histiocytosis X. LCH may manifest orally with single or multiple lesions of the alveolar or basal bone, ulcerated mucosal lesions accompanied by adenopathies and/or periodontal lesions, presenting gingival inflammation, bleeding, recession, necrosis, mobility of teeth and premature loss of teeth. Herewith, we report a case of LCH in a 45-year-old male with a characteristic oral and radiological findings. The purpose of this case report is to highlight the unique and rare presentation of oral and multiple skeletal involvement of Langerhans cell histiocytosis.

Keywords: Langerhans cell histiocytosis X, Floating teeth appearance.

INTRODUCTION

Langerhans cell histiocytosis (LCH) (formerly Histiocytosis X) is characterized by intense and abnormal proliferation of bone marrow-derived histiocytes (Langerhans cells), together with a variable number of leukocytes, eosinophils, neutrophils, lymphocytes, plasma cells and giant multi-nucleated cells causing tissue destruction. This tissue destruction is a result of the cellular infiltration that replaces bone and invades skin, mucosa and internal organs.¹

In 1953, Lichtenstein observed cytoplasmic bodies, known as X bodies, within histiocytes from tissues of patients suffering from what were previously considered distinct clinical disorders: Eosinophilic granuloma, Hand-Schüller-Christian disease and Abt-Letterer-Siwe disease. As a result of their common underlying histopathology, Lichtenstein grouped these diseases together under the name of histiocytosis X. With Nezelof's discovery in 1973 that these histiocytes were in fact Langerhans cells, the disorder was renamed Langerhans cell histiocytosis. LCH has also been referred to as Langerhans cell granulomatosis, histiocytosis X, Hashimoto-Pritzker's syndrome, nonlipidic reticuloendotheliosis, type II histiocytosis or self-healing histiocytosis.²

The diagnostic criteria are well defined by the writing group of the Histiocyte Society (1987). The usually recommended convention includes histology and immunohistology for S-100 and CD-1a. For staging and scoring clinical examination radiographs, skeletal scintigraphy and a CT or magnetic resonance imaging are generally used.³

Clinical manifestations may range from single or multifocal bone lesions to disseminated oral disease with multi-organ involvement.

Diagnosis is based on biopsy and clinical prognosis of patients becomes worse with the number of involved organs and organ dysfunctions growing, rapid disease progression and the age of first disease manifestations decreasing. Oral lesions may be the earliest and only manifestations of the disease in majority of the cases. Pain and bony swellings are the most commonly presenting complaints.

Intraoral findings include gingival necrosis, mucosal ulceration, loosening and premature exfoliation of the teeth, precocious eruption of permanent dentition, ectopic eruption of permanent molars and halitosis. Radiographic features in jaw lesions include either a unilocular radiolucent appearance with well-demarcated borders in two-third of the cases or poorly defined borders in the remaining cases.⁴ Affected teeth present with a floating teeth appearance due to the destruction of lamina dura and alveolar bone.⁵ Studies have reported an incidence of 7.9% in the jaws with angle and body of the mandible being the most commonly affected sites.² The relative incidence of LCH is not well known, principally due to the heterogenous clinical expression, but is estimated at approximately 2 to 5 cases per million inhabitants per year, being more frequent between the first and third decades of life, although it may affect any age group. Around 80% of cases occur in Caucasians with a predominance in males.¹

CASE REPORT

A 45-year-old male reported to the Department of Oral Medicine and Radiology, Tamilnadu Government Dental College and Hospital, Chennai, with the chief complaints of painful growth on the left side of lower jaw region for a duration of 3 weeks. Past dental history revealed extraction of a left lower second

premolar 3 weeks back, following the extraction a small growth developed in the extracted site. Past medical history and family history were noncontributory.

Extraoral examination revealed a diffuse swelling in relation to left side of lower jaw, 6 × 4 cm in size, extending from left commissure, 6 cm posteriorly (Fig. 1).

The swelling was firm and tender. There was a single palpable left submandibular lymphnode, 2 × 1 cm sized, firm, mobile and nontender.

Intraoral examination revealed a growth in relation to extracted 35 region with an unhealed socket. The growth was well defined, smooth-surfaced and firm. Tooth number 34 was lingually displaced with grade III mobility (Fig. 2).

Intraoral periapical (IOPA) radiograph of 34, 35, 36, 37 region revealed an radiolucent lesion with irregular periphery in relation to edentulous alveolus region (Fig. 3).

Mandibular occlusal view revealed a radiolucency in relation to edentulous region with lingually displaced 34 (Fig. 4).

Left lateral oblique view of mandible revealed a radiolucent lesion with irregular borders in relation to left edentulous alveolus. Multiple, round to oval radiolucent lesions were observed in relation to posterior border of ascending ramus, body of mandible (Fig. 5).

To assess both maxillary and mandibular involvement, orthopantomograph was taken.

OPG revealed a radiolucent lesion in relation to left body of mandible and alveolus extending from distal of 31 to mesial of 38 with inferior displacement of mandibular canal with 33, 34 giving a floating teeth appearance with soft tissue shadow (Fig. 6).

PA and Lateral view of skull revealed multiple irregular, radiolucent lesions involving the entire vault of skull (Figs 7 and 8). Complete skeletal survey revealed multiple radiolucent lesions involving the pelvic bones, left humerus, right tibia (Figs 9 and 10).

Axial CT revealed a well-defined, hypodense lesion with soft tissue component in relation to left edentulous alveolus of



Fig. 1: Extraoral view

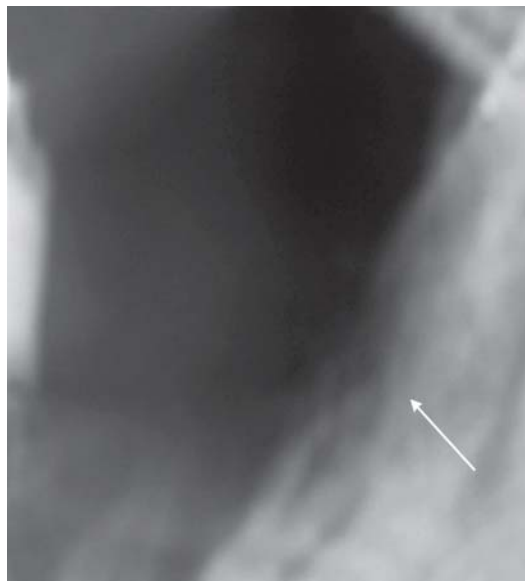


Fig. 3: IOPA shows radiolucency in relation to edentulous alveolus



Fig. 2: Intraoral growth with lingually tilted 34, unhealed socket in 35 region



Fig. 4: Occlusal view shows lingually tilted 34 with soft tissue shadow

mandible in relation to missing 35 to 37 region (Fig. 11) and multiple hypodense lesions in the occipital and sphenoid bones (Fig. 12). Skull and facial bones revealed multiple round and oval hypodense lesions. 3D CT revealed multiple osteolytic lesions in relation to the vault and lateral portions of skull (Fig. 13). Blood investigations including peripheral smear, serum calcium, phosphorus, alkaline phosphatase were done at the Department of Hematology, Government General Hospital, Chennai. Serum chemistry was normal. Differential count was predominated by Eosinophils (72%) (Fig. 14). Eosinophils showed three lobes, multiple nuclei, hypogranularity and vacuoles in cytoplasm. FNAC was performed at the Department of Clinical Pathology, Government General Hospital, Chennai, revealed mature and immature myeloid cells many of which showed monocytoid differentiation.

Bone marrow aspiration was performed at the Department of Clinical Pathology, Government General Hospital, Chennai, revealed a hypercellular marrow, more than 50% of myelopoiesis by eosinophils and their precursors. Incisional biopsy was taken

from the intraoral growth and the histopathological examination revealed stratified squamous epithelium, focal hyperplasia, overlying moderate polymorphous infiltrate of lymphocytes, abundant eosinophils, scattered plasma cells, neutrophils, large paler histiocyte-like cells with vesicular nucleus and moderate pale eosinophilic cytoplasm exhibiting occasional nuclear grooving and some showing nucleoli (Fig. 15). The definitive diagnosis of Langerhans cell histiocytosis involving multiple bones was entered by correlating clinical and histopathological findings. The patient was referred to Department of Medical Oncology, Government General Hospital, Chennai, where he was managed by chemotherapeutic agent vincristine 1 mg, once a week for four weeks and prednisolone 25 mg daily orally for six weeks. There was symptomatic reduction in generalized pain. The patient after the first course of chemotherapy was reviewed after one week. The patient was placed under intensive medical care as he was progressively losing weight and his general condition was deteriorating. However, he finally succumbed to the disease.



Fig. 5: Lateral oblique view shows erosion of left alveolus, multiple radiolucent lesions in posterior ramus, body of mandible



Fig. 7: PA view of skull shows multiple irregular radiolucent lesions in vault and lateral skull

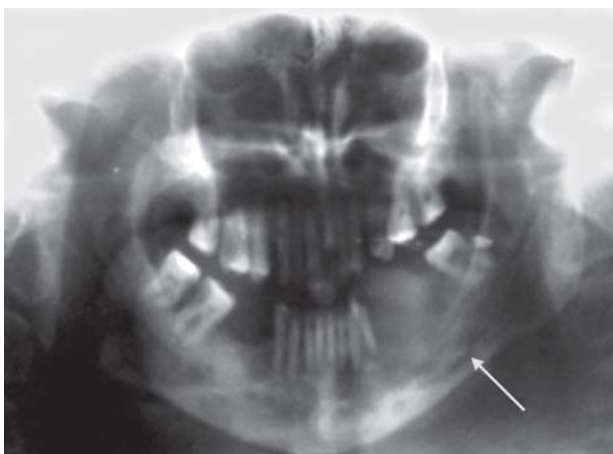


Fig. 6: OPG shows erosion of left alveolus, soft tissue shadow, multiple radiolucent lesions in body of mandible



Fig. 8: Lateral skull shows multiple irregular radiolucent lesions in the lateral skull



Fig. 9: Radiolucent lesions in pelvic bone

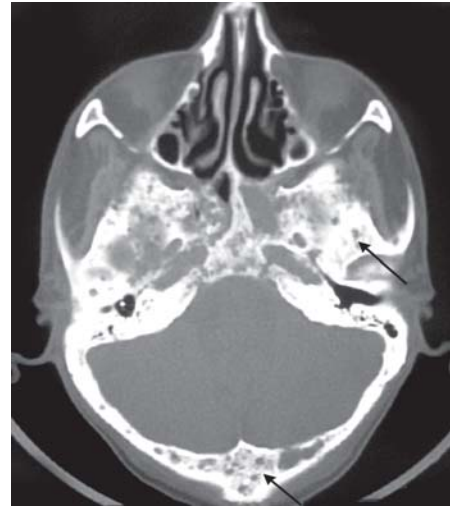


Fig. 12: Multiple round and oval hypodense lesions in sphenoid and occipital bones



Fig. 10: Radiolucent lesions in left humerus

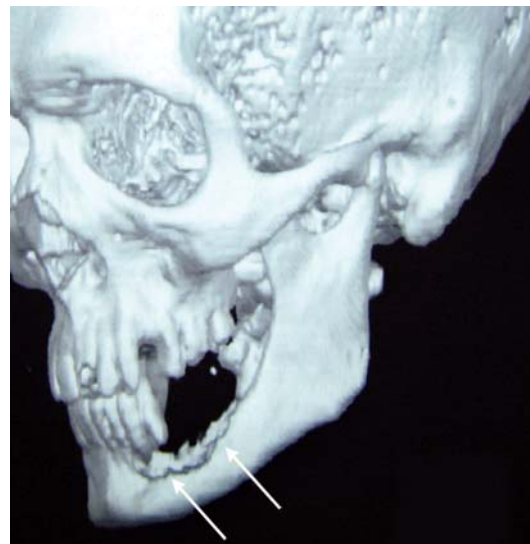


Fig. 13: 3D-CT shows multiple osteolytic lesions in vault and lateral skull, left edentulous alveolus with floating teeth appearance



Fig. 11: Well-defined hypodense lesion with soft tissue component in left body of mandible

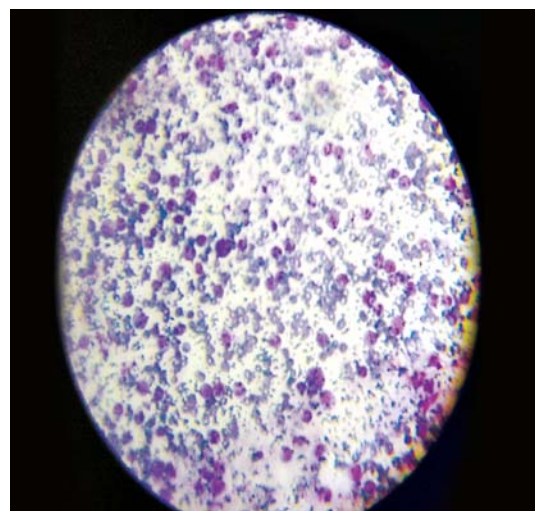


Fig. 14: Peripheral blood smear shows abundant eosinophils with cells and monocytoid differentiation

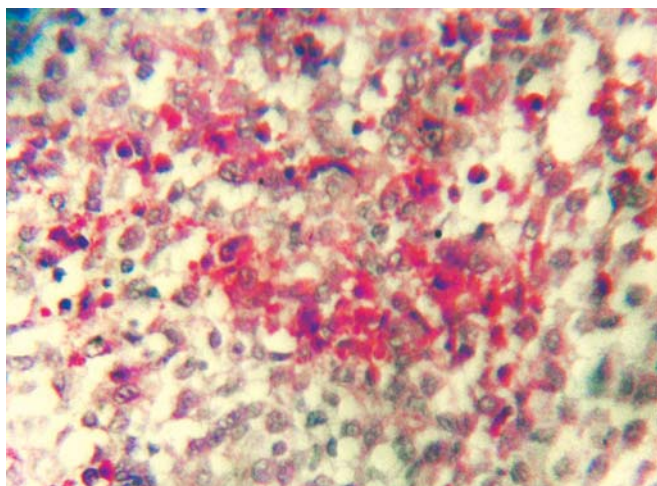


Fig. 15: Histopathological examination shows polymorphous infiltrate with abundant eosinophils, lymphocytes, plasma cells, large paler histiocytes

DISCUSSION

Langerhans cells are bone marrow-derived antigen processing cells and represent the most peripheral extension of the immune system. The pathologic proliferation of these cells is referred to as Langerhans cell histiocytosis.⁶ Langerhans cell tumors are currently classified by World Health Organization (WHO) into Langerhans cell histiocytosis (LCH) and Langerhans cell sarcoma (LCS).⁷

LCH is still a very rare disease in head and neck region, the etiology and pathogenesis of which remain unclear. Varieties of etiological factors have been proposed including immunologic reactions, viruses, bacteria and genetic influences. Possible development of LCH under the influence of colony stimulating factor (GM-CSF), interleukin-3 and tumor necrosis factor-alpha have also been suggested, and recently, cytogenic studies have proposed the role of tumor suppressor genes (p53), oncogenes (c-myc, h-ras), growth factors, cell surface immunologic markers and apoptotic factors in LCH as well.⁴

Manifestation of LCH may take various forms, such as:

1. Acute disseminated form, previously referred to as Letterer-Siwe disease, most likely represents a malignant neoplastic process. It is characterized by a rapidly progressive, clinical course and widespread in organs. Bone and skin involvement by the proliferative process in infants has been the common presentation.
2. Chronic disseminated form, previously referred to as Hand-Schüller-Christian syndrome with the classic triad of lytic bone lesions, exophthalmos and diabetes insipidus.
3. Chronic localized form, with only unifocal or multifocal bone lesions, previously termed eosinophilic granuloma, by Lichtenstein and Jaffe in 1940.⁵

In the maxillofacial area, skin involvement may appear as a papular rash; scalp involvement has a seborrhea-like presentation. Oral mucosal involvement, although infrequent, is characterized by gingival hypertrophy and ulcers of the buccal

mucosa, hard and soft palates and tongue. Osseous involvement is observed in 78% of patients, the cranium being the bone most commonly affected 49%. Bony lesions of the maxillomandibular area are also frequent, occurring in 30% of adult cases, particularly affecting posterior regions of the mandible. Pain and swelling of the mandible with mobility and loss of teeth may be the presenting symptoms of the disease.² In general, diagnosis of LCH involving the jaw bone is not difficult. The lesions are single or multiple, round and osteolytic with sharp or ill-defined noncorticated borders. When lesions are restricted to the alveolar bone, they can resemble severe periodontal disease.⁸ The lymphatic system may be affected with enlargement of lymphatic ganglions, Waldeyer's ring or the thymus. Other soft tissues have been reported to be affected in the head and neck area, such as the eyelids, parotid and submandibular glands, the external auditory canal, the middle ear, the thyroid and the gastrointestinal tract.²

Surgery, chemotherapy and radiotherapy have been used alone or in combination to treat LCH of the jaws. Surgical curettage is the principal approach, but its efficacy is dependent on the extent of LCH involvement. Local injection of corticosteroid was also found to be effective and beneficial treatment in localized disease.⁹

Low-dose radiation of 6.5 to 15 Gy appears to have beneficial effects, whereas higher doses do not seem to produce more favorable responses. However, a consistent reproducible relationship between dose and effect has not yet been firmly established for LCH.¹⁰ Various chemotherapeutic agents have been used in this disease. Systemic chemotherapy should be used in more diffuse lesions untreatable by surgery, and when local treatment is unsuccessful in localized disease or in multisystemic disease. Recently, the epipodophyllotoxin etoposide (VP16) has emerged as one of the most active and least toxic chemotherapies.¹ The common side effects after chemotherapy including nausea, vomiting, hairloss, increased risk of infection, tiredness and diarrhea are very unusual, as mild treatment is generally recommended for LCH.⁸

REFERENCES

1. Cristina Madrigal-Martínez-Pereda. Langerhans cell histiocytosis: Literature review and descriptive analysis of oral manifestations. *Med Oral Patol Oral Cir Bucal* 2009 May 1;14 (5):E222-28.
2. Jose Antonio Garcia de Marcos. Langerhans cell histiocytosis in the maxillofacial area in adults: Report of three cases. *Med Oral Patol Oral Cir Bucal* 2007;12:E145-50.
3. Arnd Bartnick, Reinhard E Friedrich, Kerstin Roeser, Rainer Schmelzle. Oral Langerhans cell histiocytosis. *Journal of Cranio-Maxillofacial Surgery* 2002;30:91-96.
4. M Gunashekhar, A Ponnudurai. Langerhans cell histiocytosis involving maxilla and mandible. *Journal of Dentistry*, Tehran University of Medical Sciences, Tehran, Iran 2009;6(2).
5. Jayachandran S, Murali Gopikamanoharan GV. Langerhans' cell disease: A case report *JIAOMR* 1999;10(1).

6. Rawal YB. Langerhans cell histiocytosis in a periapical cyst: A wolf in a sheep's clothing? *Journal of the Tennessee Dental Association* 88-84.
7. Tohru takahashi, Mitsuru Yoshimoto, Nobuo Kodoh. Spontaneously regressed langerhans cell histiocytosis of lymphnodes in an elderly patient. *The Japanese Society of Internal Medicine* (DOI:10.2169/internalmedicine.46.0356).
8. Kikuo Takahashi. Diagnostic confirmation of Langerhans cell histiocytosis of the jaws with CD1a immunostaining: A Case Report. *J Oral Maxillofac Surg* 2003;61:118-22.
9. Yoichi Nakagawa, et al. Treatment for localized Langerhans' cell histiocytosis of the maxilla by corticosteroid injection: A case report. *Oral Science International* May 2007;59-62.
10. Pratibha ramani, et al. Langerhans' cell histiocytosis in a six-year-old child. *Indian J Dermatol Venereol Leprol* March-April 2007;73(2).