© Med Sci Monit, 2009; 15(6): CS95-99
PMID: 19478707

www.MedSciMonit.com
Case Study

CS

Received: 2007.09.25
Accepted: 2008.10.28
Published: 2009.06.01

Bifocal manifestation of eosinophilic granuloma in a pediatric patient

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Rosario Guiglia[1ABDEF], Giuseppe Pizzo[1ADEF], Maurizio Aricò[2B], Emiliano Maresi[3B], Domenico Compilato[1BEF], Giuseppina Campisi[1AB]

[1] Department of Oral Sciences, University of Palermo, Palermo, Italy
[2] Department of Pediatric Hematological Oncology and Bone Marrow Transplantation, Azienda Ospedaliero-Universitaria Meyer, Florence, Italy
[3] Department of Human Pathology, University of Palermo, Palermo, Italy

Source of support: Departmental sources

Summary

Background: Eosinophilic granuloma (EG) is a clinical variant of the Langerhans cell histiocytosis (LCH) characterized by unifocal or multifocal bone lesions which predominantly affects children, adolescents, and young adults.

Case Report: A case is reported of a 13-year-old Caucasian boy who presented unifocal EG in the mandible as the first clinic manifestation. Radiographic examination and skeletal scintigraphy revealed a further localization with an osteolytic lesion in the right femur. The therapeutic protocol used for the mandibular lesion included causal periodontal therapy, extraction of the compromised teeth, alveolar curettage, and intralesional injections of corticosteroids, in correspondence with femoral and mandibular bone lesions.

Conclusions: Early diagnosis of LCH is considered an important factor which can improve the patient's prognosis and quality of life and also the cost-effectiveness of therapy. Dentists could play a fundamental role in the diagnosis and management of EG. The aim of the treatment is to eradicate EG lesions and provide adequate oral rehabilitation after the tooth loss. A careful multidisciplinary follow-up program is mandatory to identify any signs of local recurrence or dissemination.

key words: **Langerhans cell histiocytosis • eosinophilic granuloma • alveolar bone loss • periodontitis • oral ulcers**

Full-text PDF: http://www.medscimonit.com/fulltxt.php?ICID=869667
Word count: 2084
Tables: –
Figures: 8
References: 16

Author's address: Giuseppe Pizzo, Department of Oral Sciences, University of Palermo, Via del Vespro 129, 90127 Palermo, Italy, e-mail: giuseppepizzo@unipa.it

BACKGROUND

Histiocytic disorders include a group of diverse proliferative diseases characterized by a pathological increase in the number, infiltration, and accumulation of histiocytes (monocytes/macrophages, dermal/interstitial dendritic cells, and Langerhans cells) and other immune effector cells within various tissues [1]. The classification of histiocytic disorders depends on the cell types involved (dendritic cells, macrophages), the organs involved (single-system disease, multisystem disease), and the risk according to the clinical course and response to treatment (disorders of varied biological behavior, malignant disorders) [1,2]. Among the dendritic cell-related histiocytosis, Langerhans cell histiocytosis (LCH), formerly known as histiocytosis X, is currently classified as a disorder with variable clinical course [3,4]. The responsible cell is considered to be the Langerhans cell histiocyte, an immature dendritic cell that lacks the ability to be a functional antigen-presenting cell.

Since the atypical cellular proliferation of Langerhans cell histiocytes could occur in various organs and tissues (i.e. bone, liver, lungs, lymph nodes, spleen, hematopoietic tissue, and mucocutaneous tissues), clinical manifestations might be extremely different and complex. According to the sites involved, LCH is currently classified as a single-system disease (unifocal or multifocal eosinophilic granuloma [EG]) and a multisystem disease (multiple lesions in more than one organ group) [1,5]. In EG, which is the most common expression of LCH (about 60–70% of cases), the typical lesion is a localized unifocal intraosseus defect principally involving the skull, mandible, spine, ribs, and femur, without visceral involvement. Skin lesions are rarely present. Osteolytic lesions may be asymptomatic or may cause pain because of the expansion of the medullary, also leading to pathologic fractures [5,6].

The incidence of EG is estimated in one new case per 350,000 to 2 million persons per year, and approximately 75% of all patients are below 20 years of age [5,7]. The most common location of EG is the skull (27–28%), followed by the ribs (8–25%) and pelvis (8–10%) [8]. The oral lesions may be the earliest clinical signs of EG and in many cases the jaw and mandible may be the only sites involved, with extensive destruction of the periodontal tissues [5,9]. Such lesions are commonly found in the gingiva, hard palate, and floor of the mouth. The prognosis of unifocal EG is generally good, but permanent sequelae (i.e. bone deformations, functional or aesthetic disorders, bite anomalies, and tooth loss) may be present due to the destructive nature of the bone lesion. The prognosis of multifocal EG is intermediate, whereas the worst prognosis is found when multiple lesions occur in more than one organ group [4,5]. Because of the great enigma as to whether LCH is a neoplastic or an immunodysregulatory disorder, a standardized therapeutic protocol does not exist, but there are many possible combinations of curettage, intralesional steroid injection surgery, chemotherapy, and radiation [4,5,10].

In this article we report the case of a 13-year-old boy with LCH in a bifocal variety of EG diagnosed thanks to its first oral signs. The clinical presentation of the case is discussed emphasizing the importance of the dental practitioners in the early diagnosis and management.

CASE REPORT

In May 2006 a 13-year-old Caucasian boy was referred by his dentist to the Department of Oral Sciences of the University of Palermo, Italy, with spontaneous and intense pain in the left mandibular region. The patient was in good general health and his past medical and dental history did not reveal any significant events. His parents stated that the gingiva of their son had begun to bleed about three months before presentation to the dentist.

Intraoral examination revealed poor oral hygiene and halitosis. The gingival mucosa surrounding the permanent teeth 3.3 to 3.7 (left mandibular canine, first and second premolars, first and second molars) was erythematous, bled easily, and was covered by areas of ulceration and necrosis. The teeth showed severe mobility. On the lingual side, the lesion caused massive damage to the alveolar ridge of the mandible with gingival recession, root exposure, and furcation involvement (Figure 1).

A panoramic X-ray of the jaws confirmed the defect of the bone structure of the body of the mandible in the region of teeth 3.4 to 3.7 (Figure 2), revealing the presence of a massive radiolucent, circumscribed, and sharp unilocular image on the left sides of the mandible. The radiolucent lesion extended from the distal surface of 3.4 to the mesial surface of 3.7, causing the expansion of the buccal and lingual cortical plates and severe alveolar bone resorption. Panoramic radiography proved the typical radiographic image of "floating teeth".

Urinalysis and laboratory tests, including complete blood cell count, coagulation factors, liver function parameters, C-reactive protein, azotemia, glycemia, sodium, calcium, magnesium, and thyroid hormones (TSH, T3, and T4), were all within normal limits. Infection by human herpes virus 6 (HHV-6) or Epstein-Barr virus were also excluded.

For diagnostic purposes, the patient underwent oral incisional biopsy under local anesthesia and samples of gingival tissue were sent for histopathological and immunohistochemical examination to the Department of Human Pathology of the University of Palermo, Italy. The histopathological examination revealed a copious cellular infiltrate composed of eosinophils, granulocytes, and cells with an eosinophilic cytoplasm and a blistering nucleus, associated with B and T lymphocytes. The immunohistochemical examination (Figure 3A,B) revealed that the cells with the eosinophilic cytoplasm were strongly CD1-a and S-100 surface protein positive [3,5]. As all these findings were compatible with a diagnosis of LCH and in agreement with the contemporary classification of histiocytic disorders, the diagnosis of EG was finally formulated [1,3,5].

In the same period, the patient complained of pain in the right femoral region and in the right shoulder, exacerbated by movement and ambulation. The patient was referred to the Operative Unit of Pediatric Hematological Oncology at the Pediatric Hospital of Palermo, Italy, for further investigations. An isotope bone scan revealed regions of increased uptake of technetium-99m methylene diphosphonate (MDP-Tc-99m) in the body of the mandible and in the diaphysis and pertrochanteric (petrous apex) region of the right femur. There were no lesions in the right shoulder.

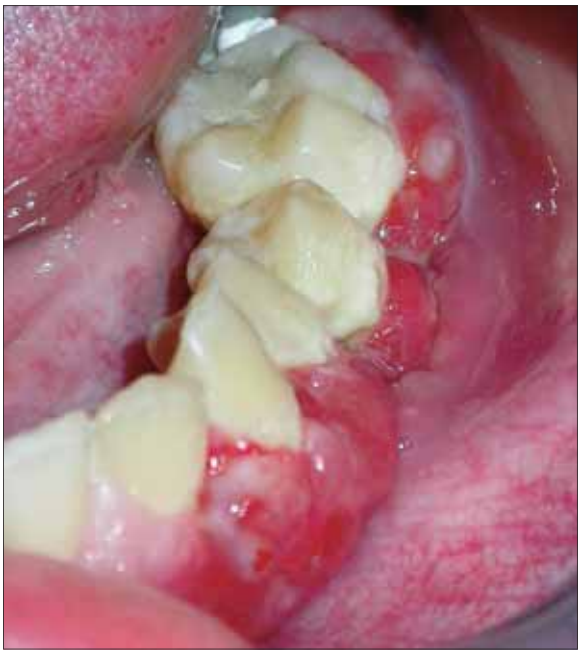

Figure 1. Initial presentation of EG. Hypertrophic/granulomatous oral lesions associated with notable plaque deposits and surrounding teeth 3.3 to 3.7.

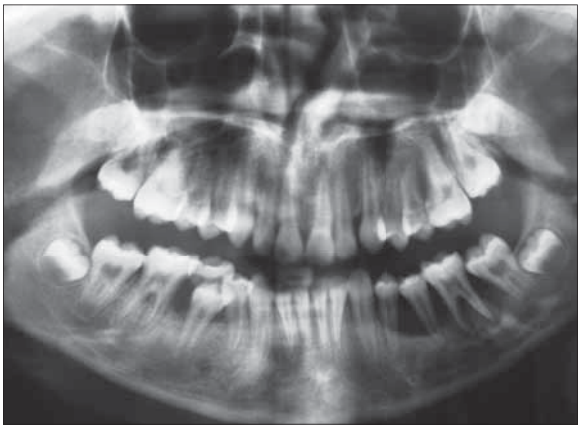

Figure 2. Bone resorption from 3.4 to 3.7. The defect appears as a massive radiolucent, circumscribed, and sharp unilocular image. Note the typical radiographic image of "floating teeth".

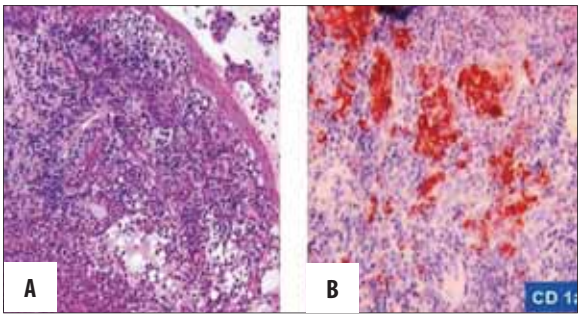

Figure 3. (**A**) Histopathologic examination shows a copious infiltrate of eosinophils, lymphocytes, and cells with eosinophilic cytoplasm. (**B**) Immunohistochemical stains revealed that the cells with eosinophilic cytoplasm were strongly CD1-a positive.

Figure 4. Osteolytic lesion in the right femoral diaphysis.

Radiographic examination of the right femur confirmed the presence of an osteolytic lesion in the diaphysis (Figure 4) and an oval radiolucent lesion in the pertrochanteric femoral area, surrounded by a thick margin of reactive bone (Figure 5). Radiographic examination of the right shoulder did not reveal any abnormalities. Chest X-ray and pulmonary Computed Tomography did not reveal lytic bone lesions or pulmonary parenchyma alterations (i.e. nodules with air-filled cysts and pneumothoraces).

To treat plaque-related gingivitis, the patient underwent supragingival and subgingival scaling. An intensive individual oral hygiene program was also implemented to establish the most appropriate non-traumatic procedures and to obtain the best possible standard of plaque control. The patient was instructed to use an erythrosine dye tablet daily for detection of dental plaque and to use a toothbrush, dental floss, inter-dental brushes, and a 0.2% chlorhexidine mouth rinse. Irrigations with methylprednisolone succinate (Solumedrol® 250 mg, Pfizer, Italy Srl) in a NaCl 0.9% solution by means of an oral douche were recommended twice daily. The importance of meticulous supragingival plaque removal for gingivitis resolution and maintenance of periodontal health following therapy was unequivocal.

In July 2006 the extraction of teeth 3.5 and 3.6 and alveolar curettage were performed. Corticosteroid methylprednisolone acetate combined with lydocaine chlorohydrate (Depo-Medrol® + Lydocaine 40 mg, Pfizer Italy Srl) was in-

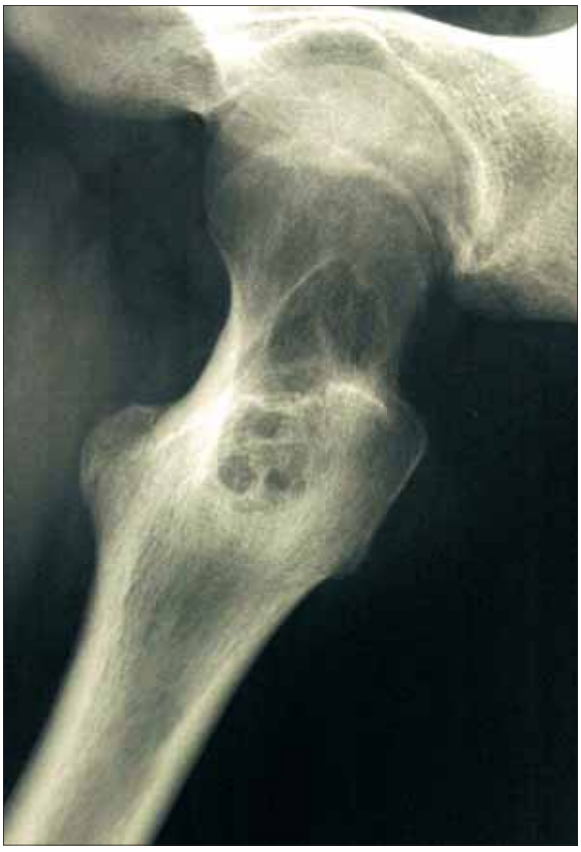

Figure 5. Oval osteolytic areas in the petrochanteric right femoral region.

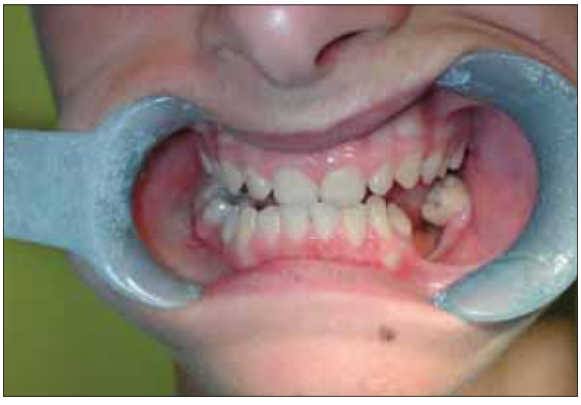

Figure 6. Frontal view taken at follow-up after 12 months.

jected into the lesions of the mandible and femur by a dental practitioner and a pediatric oncologist, respectively [4]. The therapeutic approach for the femur lesion was performed under sonographic guidance. The dose of the steroids employed varied between 40 and 150 mg per injection. After one week a further steroid injection was performed.

Subsequent to the local injections the lesions were monitored by radiographs as well as physical and clinical examination. During the monitoring the patient underwent supra - and subgingival scaling periodically (every two weeks for the first two months and every forty-five days for the following six months). A prosthetic rehabilitation with partial

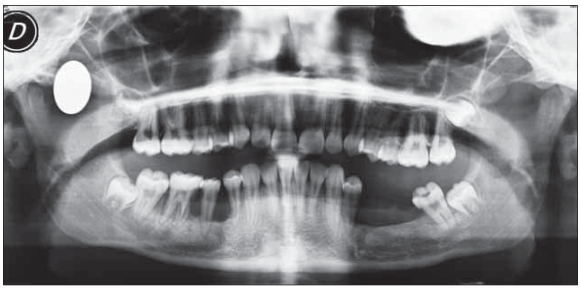

Figure 7. Follow-up panoramic radiograph after 12 months.

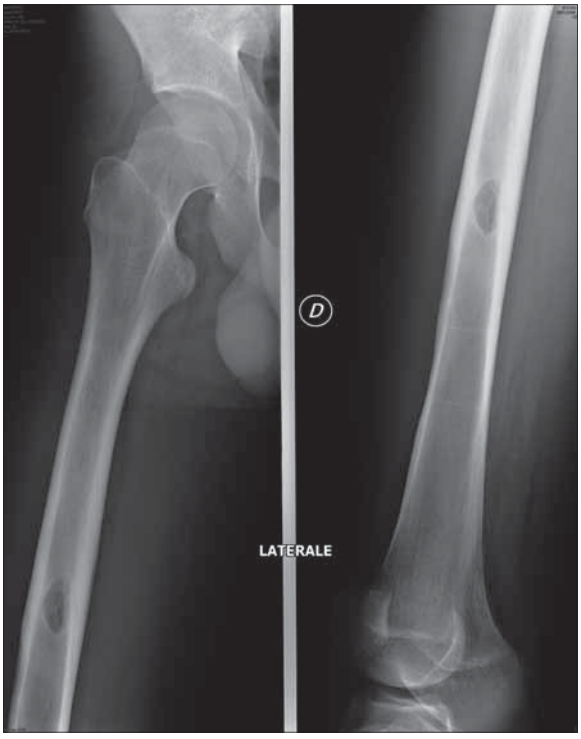

Figure 8. The persistent osteolytic bone lesions of the femur (lateral view) after 12 months.

removable mandibular prostheses was also provided. The prostheses were made with wired acrylic and the subject was instructed to present once a week for a period of one month for inspection as well as possible corrections and adjustments. The boy was very cooperative and compliant. After a one-year period of follow-up, remission of oral lesions was obtained, whereas there was no sign of resolution of the femoral lesion (Figures 6–8).

Discussion

LCH is a group of diseases in which cells from the mononuclear phagocytic system, previously known as the reticulo-endothelial system, are found in the affected tissues. Little is known about etiology and its clinical spectrum is very broad, ranging from a single localization in the bone (e.g. skull, mandible, spine, ribs, and long bones) to severe multivisceral involvement (skin, bone marrow, lungs, liver, pituitary gland, skull, gastrointestinal tract, spleen, lymph nodes, urinary tract, eye, and numerous other sites), leading to dysfunction of vital organs. LCH is rare, and because it may manifests itself

with multiple presentations, often mimicking other diseases, could remain undiagnosed for a long time [11].

Oral lesions may be the earliest manifestation of the condition, and in many cases the mouth may be the only site involved. EG is characterized by single or multiple lytic bone lesions and it is considered the mildest form of LCH [8,12]. In a review of 1120 cases of documented histiocytosis X, Hartman reported that 114 (10%) cases had oral involvement, with the mandible, usually its posterior region, as the primarily affected site, and 78% of the oral lesions were diagnosed as EG [13]. EG can affect different bone segments, but commonly involves the mandible in children, adolescents, and young adults. Clinically, it presents as an intraoral mass with ulcers with local pain, and radiographically with the typical image of "floating teeth", especially in the molar area [12]. If the periodontal tissue is affected, clinical features can resemble and mimic the characteristic signs and symptoms of severe localized periodontitis, characterized by gingival bleeding, gingival recession, deep periodontal pockets, marked destruction of alveolar bone, and tooth mobility [14]. When these lesions occur in children and young adults they may be mistaken for aggressive periodontitis or necrotizing ulcerative periodontitis, so a diagnosis to distinguish between EG and these forms of periodontal disease must be established [11,12]. Further differential diagnosis might include dental or periodontal abscess, primary herpetic gingivostomatitis, recurrent aphthous ulcerations, combined periodontic-endodontic lesions, traumatic ulcerative granuloma, granulomatous diseases (sarcoidosis, tuberculosis, etc), benign and malignant disorders of the oral cavity (fibrous dysplasia, Ewing's sarcoma, osteogenic sarcoma, giant cell granuloma, lymphoma, ameloblastoma), as well as oral manifestations of malignant blood diseases (leukemia, multiple myeloma) [7,11].

The management of patients with LCH continues to be a therapeutic dilemma and usually requires a multidisciplinary approach. The standard treatment pathway is not yet clear and depends upon the severity and progression of the clinical signs and symptoms. It includes observation for spontaneous regression, surgical curettage, radiation, topical injection of steroid, and systemic steroidal therapy. In recent years, pharmaceutical treatment of cases of LCH has become increasingly widespread and concentrated on immunosuppressant agents, immune modulators, or cytostatic drugs [5,10].

Generally, with adequate treatment the prognosis of single EG is good [15], but in very rare instances a solitary LCH may recur rapidly within a short period and lead to a fatal outcome [16]. The case reported in this article was a bifocal variety of EG characterized by osteolytic lesions in the mandibular and femoral areas that showed no signs of resolution in the femoral lesion, which remained unchanged, making a careful follow-up program mandatory.

Conclusions

Histiocytic disorders are rare and unexpected diseases that could begin with various clinical signs and symptoms. Diagnosis and treatment is complex and requires a multidisciplinary mutual approach involving a pediatric or medical oncologist, a pathologist, a radiologist, and one or more of the following specialists: orthopedic surgeon, endocrinologist, dermatologist, pneumonologist, and dentist. Since oral lesions may be the first manifestations of LCH, and as the dentist is often the first specialist consulted, the clinical case described is of particular interest. In our young patient the stomatological treatment had numerous objectives: to eradicate and cure the disorder, provide a pleasant aesthetic aspect to prevent psychological problems, recover the lost vertical dimension of occlusion caused by tooth loss, and avoid interference with the eventual eruption of the remaining permanent teeth. The establishment of preventive measures to improve the oral hygiene of these individuals is quite useful. It is mandatory that all cases are subjected to an accurate interdisciplinary diagnosis and a careful follow-up program to identify any signs of local recurrence or dissemination.

References:

1. Satter EK, High WA: Langerhans cell histiocytosis: a review of the current recommendations of the Histiocyte Society. Pediatr Dermatol, 2008; 25: 291–95
2. Weitzman S, Jaffe R: Uncommon histiocytic disorders: the non-Langerhans cell histiocytoses. Pediatr Blood Cancer, 2005; 45: 256–64
3. Favara BE, Feller AC, Pauli M et al: Contemporary classification of histiocytic disorders. The WHO Committee On Histiocytic/Reticulum Cell Proliferations. Reclassification Working Group of the Histiocyte Society. Med Pediatr Oncol, 1997; 29: 157–66
4. Henter JI, Tondini C, Pritchard J: Histiocyte disorders. Crit Rev Oncol Hematol, 2004; 50: 157–74
5. Hicks J, Flaitz CM: Langerhans cell histiocytosis: current insights in a molecular age with emphasis on clinical oral and maxillofacial pathology practice. Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2005; 100: S42–66
6. 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
7. Li Z, Li ZB, Zhang W et al: Eosinophilic granuloma of the jaws: an analysis of clinical and radiographic presentation. Oral Oncol, 2006; 42: 574–80
8. Islinger RB, Kuklo TR, Owens BD et al: Langerhans' cell histiocytosis in patients older than 21 years. Clin Orthop Relat Res, 2000; 231–35
9. Bartnick A, Friedrich RE, Roeser K, Schmelzle R: Oral Langerhans cell histiocytosis. J Craniomaxillofac Surg, 2002; 30: 91–96
10. Weitzman S, Egeler RM: Langerhans cell histiocytosis: update for the pediatrician. Curr Opin Pediatr, 2008; 20: 23–29
11. Alajbeg I, Vucicevic Boras V, Femenic R et al: Unrecognized oral manifestations of Langerhans cell histiocytosis which progressed to systemic disease. Oral Oncology Extra, 2006; 42: 10–13
12. Rapp GE, Motta AC: Periodontal disease associated with Langerhans' cell histiocytosis: case report. Braz Dent J, 2000; 11: 59–66
13. Hartman KS: Histiocytosis X: a review of 114 cases with oral involvement. Oral Surg Oral Med Oral Pathol, 1980; 49: 38–54
14. Torrungruang K, Sittisomwong S, Rojanasomsith K et al: Langerhans' cell histiocytosis in a 5-year-old girl: evidence of periodontal pathogens. J Periodontol, 2006; 77: 728–33
15. Bodner G, Kreczy A, Rachbauer F et al: Eosinophilic granuloma of the bone: Ultrasonographic imaging. Australasian Radiology, 2002; 46: 418–21
16. Ramani P, Chandrasekar T, Baig MF et al: Langerhans cell histiocytosis of the mandible in a six-year-old child. Indian J Dermatol Venereol Leprol, 2007; 73: 114–16