Langerhans cell histiocytosis: recurrent lesions affecting mandible in a 10-year-old patient

S.V.L. Loducca / A. Mantesso / N.S. Araújo / M.H.C.G. Magalhães

Hand-Schuller-Christian disease is a multifocal variant of eosinophilic granuloma, characterised by the classical triad of bony lesions, exophtamos and diabetes insipidus. This case relates recurrent Langerhan's cell histiocytisis lesions presented as destruction of periodontal support associated with diabetis in a 10-year–old patient. Medical history suggests that the case represents a case of Hand-Schuller Christian disease.
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INTRODUCTION

Langerhans cells histiocytosis is a global term for a spectrum of diseases which include eosinophilic granuloma, Hand-Schuller-Christian disease and Letterer-Siwe disease.[1,2] Eosinophilic granuloma of bone usually presents as a solitary lytic lesion and responds well to conservative treatment. Hand-Schuller-Chistian disease is the multifocal chronic variant of eosinophilic granuloma characterised by bony lesions, exophthalmos and diabetes insipidus. Lettere-Siwe disease is the more severe form of the disease, with involvement of multiple organs, usually running to a fulminant course.[2] In the past these conditions were termed as Histiocytosis X. Histopatholgical characteristics of the lesions comprise proliferation of Langerhans cells, which can be immunhistochemically identified by the presence of the antigens S100 and CD1a.[3]

A case of LCH is presented affecting mandible and producing destruction similar to periodontal disease.

Case Report

A 10-year-old patient was referred to the Special Care Dentistry Centre of the Dental School of the University of São Paulo for routine dental treatment. The patient presented a medical history of previous Langerhans cell histiocytosis, with skull lesions satisfactory treated 5 years earlier by chemotherapy (Figures A and B). He also related to suffer from diabetes insipidus, which was diagnosed when he was 7 years old.

Clinical exam revealed several teeth compromised with decay. The right first mandibular molar (element 36) was virtually devoid of alveolar bone with radicular exposition and tooth mobility. Gingival tissue showed mild inflammation with granulomatous aspect (Figure C). Radiographic exams confirmed the bone destruction with involvement of bifurcation of this tooth (Figure D).

Dental treatment was performed including periodontal procedures on the element 36. However control radiographs and clinical examination during the subsequent 4 months revealed progression of the bone loss around this tooth. This first molar was then extracted and material of curettage was sent to histopathological examination at the Department of Oral Pathology of The Dental School of the University of São Paulo.

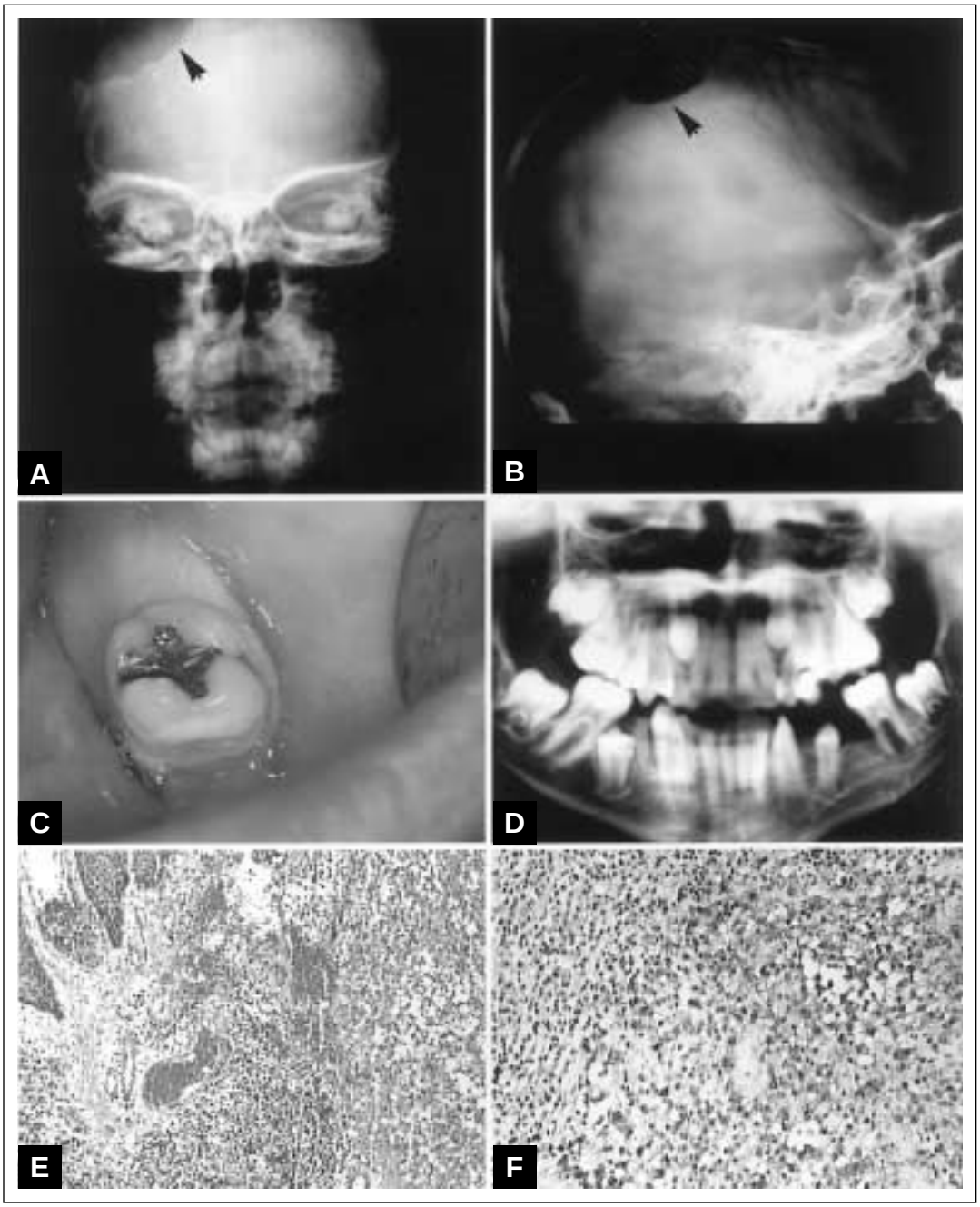
Histopathological characteristics of the biopsied specimen comprised histiocyte-like cells. In some fields these cells presented multilobated nuclei and prominent nucleoli. This predominant cell population was admixed with variable numbers of eosinophils and neutrophils. Focal areas of chronic inflammatory infiltrate and haemoragic exudate were seen. The microscopic differential diagnosis included hematopoietic or lymphoid malignancy and LCH (Figure E). The biopsy specimen was submitted to immunohistochemical stains and the main cell population was positive for S-100 and CD1a, supporting the diagnosis of Langerhans cell histiocytosis (Figure F).

Haematological investigations and urinalysis were within normal limits.

Due to disease reactivation, the patient was re-submitted to chemotherapy.

Send all correspondence to Dr. M.H.C.G. Magalhães, Disciplina de Patologia Bucal, Faculdade de Odontologia da Universidade de São Paulo, Av. Prof. Lineu Prestes, 2227; CEP: 05508-900 São Paulo; SP-Brazil.

Tel/Fax: (11) 818 7902
Email: mhcgmaga@fo.usp.br



A and B: Lesions before the first chemotherapy cycle: Calvarial destructive lesions involving full thickness of skull, being sharply circumscribed (arrows).
C: Periodontal involvement and bone loss around 1st molar.
D: Panoramic radiograph showing radiolucency involving bifurcation of 1st molar (arrow).
E: Low-power photomicrograph showing infiltrate of eosinophilic and clear cells. Hematoxylin and Eosin.
F: Langerhans cells showing positive staining for CD1A. Streptavidin-biotin peroxidase

DISCUSSION

Langerhans cell histiocytosis (LHC), formerly known as histiocytosis X, is a pathological accumulation of mononuclear cells showing the ultrastructural and phenotypic features of Langerhans cells, despite the three different types of clinical manifestations: eosinophilic granuloma, Hand-Schuller-Christian syndrome and Letterer-Siwe disease.[3,4]

The clinical manifestations presented herein (lesions affecting more than one bone and diabetis insipidus) classify the patient in the Hand-Schuller-Christian syndrome subtype. The syndrome is characterised by widespread bone lesions, exophthalmos and diabetes, usually as a result of lesional involvement of hypothalamus or pituitary gland.[3] Oral involvement may mimic severe periodontal disease with premature exfoliation of the

dentition and "teeth-floating in space" radiographic appearance as seen in the present case. Other intraoral symptoms include oral ulceration and leukoplakia.[2,5] The oral lesion present in the patient compromised the integrity of the 1st molar and represented the first detectable clinical manifestation of the LCH recurrence. Tooth extraction was inevitable for the sake of the lesions treatment.

The epidemiological and clinical aspects of mandibular granulomatous lesion presented by our patient are in accordance to most cases reported in the literature.[6] Hartman, 1980, found that just over 10% of cases involve oral tissues, with over 80% affecting males. Hard and soft tissue lesions are common, although intra-osseous defects are predominant; being mandible more affected, usually posteriorly. The gingiva is the most common mucosal site to be affected. In view of these facts both clinicians and pathologist should be suspicious of recurrent granulomatous lesion in the oral cavity with no obvious etiological factor.

Immunological aspects of the disease are not pathognomonic and some may mimic odontogenic cyst, osteomyelitis, giant cell granuloma or malignant bone tumours such as Ewing's sarcoma.[6-8] In the present case, differential diagnosis included periodontal disease, however, considering patient's medical history and unfavorable response to periodontal treatment, dental extraction followed by biopsy was performed. As LCH can be a multifocal bone disease, radiographic skeletal surveys to be a reasonable procedure for a complete evaluation of the bone condition. Additionally, extra skeletal involvement is more likely in patients with multiple bony lesions.[5]

The microscopical aspects of the lesion presented showed typical features of LCH, and immunohistochemical positivity to S-100 and CD1a confirmed this diagnosis. Immunohistochemistry and transmission electron microscopy have been employed as ancillary tools for confirmation of LCH, as positivity to CD1a and presence of Birbeck granules in proliferating cells help to distinguish the latter from other histiocytic lesions.[9] They are especially useful for diagnosis of mature lesions, in which fibrosis and foamy macrophages replace the histiocytic and eosinophilic components.[5]

Treatment modalities for LCH are variable according to location, extension and number of lesions. Surgical curettage, local irradiation and chemotherapy have all been used, alone or in combination, with favourable results.[6,10] Recurrence rates depend on the treatment method and location of the lesion and are reported to range from 1.6 to 25% and patients should be closely followed up for a long period.[6,7] The patient referred in this report presented recurrent lesions in the mandible and the treatment elected involved surgical curettage, which included the dental extraction due to the extension of the area involved. Therapy with Prednisona, Somatotrophin and Desmopressin was also employed. The patient has been reviewed in frequent clinical follow-ups and after 2 years is currently well and free of disease.

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