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Langerhans' cell histiocytosis of the jaw bones. Report of 11 cases

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Abstract
Eleven cases of Langerhans' cell histiocytosis of the jaw bones are reported. The clinical and radiographical features are described, and the role of the dentist in the diagnosis and management of this disorder is discussed.

Key words: Langerhans' cell histiocytosis, oral involvement, jaw bones.

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Introduction

In the past Langerhans' cell histiocytosis (LCH) has been described by means of a variety of terms such as histiocytosis-X and eosinophilic granuloma. The aetiology of the disease is not known, although there is some evidence that the disorder is a manifestation of an immunological aberration.[1]

It is characterized by the proliferation of bone marrow derived cells, called Langerhans cells, which belong to the mononuclear phagocyte system and (or) dendritic system.[2] The diagnosis of LCH is based on microscopic examination showing dense infiltrates of large cells with eosinophilic cytoplasm and characteristic indented ovoid nuclei: Langerhans' cells. Together with these cells a granuloma consisting of a variable number of eosinophils, lymphocytes, giant cells and histiocytes is present.[3]

Immunohistochemically, Langerhans' cells can be recognized by a positive reaction with monoclonal antibodies (OKT6).[4] Their cytoplasm stains positively with S-100 protein and peanut lectin.[5] A positive staining with the enzymes a-D-mannosidase and ATP-ase can be also of additional help.[6,7] Ultrastructural examination of the proliferative cells shows characteristic intracytoplasmic organelles, known as 'Birbeck granules'.[8]

The clinical manifestations of LCH range from solitary or multiple bone lesions with a chronic course to progressive disseminated visceral, skin and bone lesions.[9] In a review of 1120 patients, Hartman reported oral involvement in LCH in 10 per cent of the cases.[10]

The purpose of this article is to describe the clinical and radiographical features in eleven patients of LCH with oral involvement, and to discuss the role of the dentist in both diagnosis and management.

Materials and methods

In this retrospective study the records of eleven patients with Langerhans' cell histiocytosis with oral involvement were surveyed. Six of the records were obtained from the files of the Oral Pathology Biopsy Service of the Royal Dental Hospital of Melbourne and five of the records from the Department of Oral and Maxillofacial Surgery/Pathology of the Free University Hospital Amsterdam. The data for the patients are summarized in Table 1.

To be included in this study, the patients were required to have one or more histologically proven osseous lesions of LCH affecting the maxilla and/or mandible. In six patients, a total body scan was made, and four of these showed extraoral bony lesions; in two other patients radiograph examination showed extraoral involvement. Lesions were found in the mastoid, ribs, vertebrae, femur and pelvis. Follow-up data were available on eight of the eleven patients. The follow-up period ranged from 6 months to 6.5 years, with a mean of 3.3 years. Three patients were lost for follow-up.

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Table 1. Clinical features of eleven patients with Langerhans' cell histiocytosis and oral osseous involvement

Patient; gender	Age (years)	Distribution of the lesion(s)						Extraoral lesions	Treatment	FU-period (years)	Outcome
		Maxilla	Mandible	Anterior	Posterior	Unifocal	Multifocal				
1; m	3	+	+	-	+	-	+	-	S	-	-
2; f	3	-	+	-	+	+	-	-	S	-	-
3; f	5	-	+	-	+	-	+	+	S	1	Pt died with widespread LCH
4; m	14	-	+	-	+	+	-	-	S	-	-
5; m	16	-	+	+	+	-	+	+	S, C	6.5	Extension of oral and extra-oral lesions
6; m	19	+	+	-	+	-	+	-	C	1.5	Extension of oral lesions, confirmed diabetes insipidus
7; m	23	+	+	+	+	-	+	+	S, R, C	5	New oral lesions, progression extraoral lesions
8; m	27	-	+	-	+	+	-	-	S	0.5	No recurrence of oral lesions
9; m	33	-	+	-	+	-	+	+	S	3	No recurrence of oral lesions, extraoral lesions stable
10; m	39	-	+	+	+	+	-	+	W & S	4	Oral- and extraoral lesions stable
11; m	46	+	+	-	+	-	+	+	S, C	5	New oral lesions

S=surgery; R=radiotherapy; C=chemotherapy; W & S=wait and see.

Results

Common presenting complaints of the patients were pain and loosening of teeth. Other symptoms were necrotizing and ulcerating defects of the mucosa and jaw swelling (Fig. 1). Mental nerve anaesthesia was present in only one patient. Two patients suffered from a pathological fracture of the mandible. (One has been previously reported.[11])

The radiographic appearance of the lesions showed a radiolucent, destructive, often well defined process, with sometimes irregular margins (Fig. 2). They varied in size, and occasionally the loss of bone was so severe, with perforation of the cortical bone, that the teeth appeared to be 'floating in air'.

Apart from routine histopathological examination (Fig. 3), immunohistochemical staining with S-100 protein was performed in three cases to confirm the diagnosis. Biopsy specimens of two patients showed a positive reaction with OKT6, and in two cases ultrastructural examination confirmed the diagnosis LCH by the demonstration of Birbeck granules (Fig. 4).

Surgery in the form of curettage or excision of the jaw lesions was used for treatment in nine out of eleven patients. Radiotherapy was used in one patient for lesions involving both the upper and lower jaw. Two patients received ratiotherapy for lesions involving the mastoid. Four patients received chemotherapy, three in combination with surgery for the oral lesions. One patient was treated locally by intralesional injection with corticosteroids and in one patient it was decided to follow a 'wait-and-see' policy.

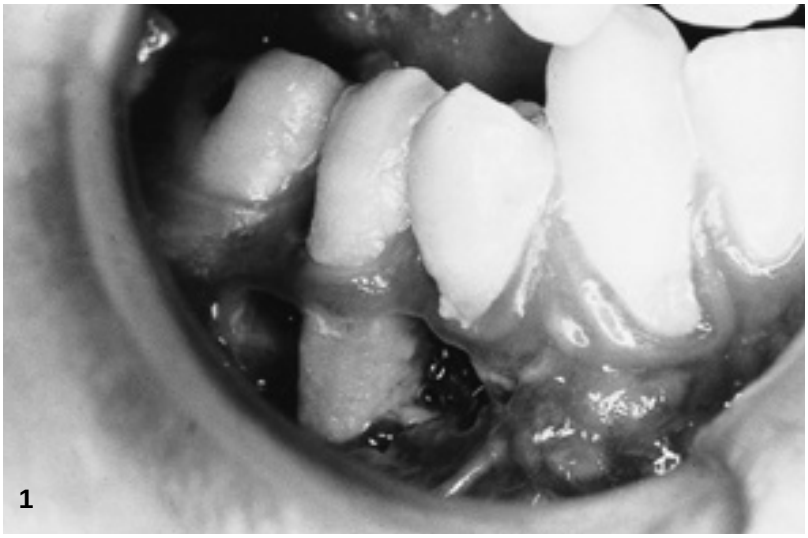
One patient died after one year with widespread LCH. In two patients the oral lesions extended despite therapy and two developed new oral lesions. No recurrences were seen in two patients who received surgical treatment. Intralesional injection with corticosteroids did not appear to have any effect on the lesion in one particular patient who did not respond to surgery, or chemotherapy and radiotherapy. The lesion in the patient who received a 'wait-and-see' policy remained stable.

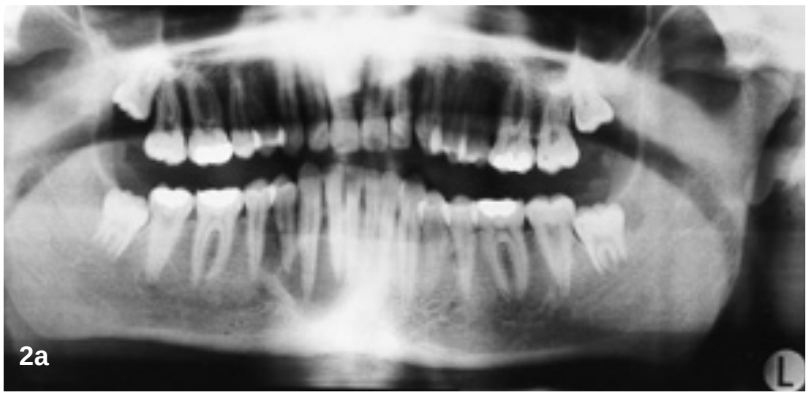
Discussion

The first manifestations of LCH may occur in the mouth.[12] Symptoms that would cause a patient to consult a dentist vary from a 'continuous gingival infection' or a 'dental abscess' to necrotizing, ulcerating defects or a painful jaw swelling. Loosening and early exfoliation of (deciduous) teeth should alert the dentist. Sometimes the lesions are asymptomatic. In a series of 50 patients with LCH, 36 per cent had oral involvement and the dentist was the first to see them in 16 per cent of the cases.[13]

The radiographic features are non-specific and may resemble, amongst others, odontogenic cysts, periapical lesions, periodontal disease, osteomyelitis or even malignant neoplasms. Tissue for histologic examination should be obtained of an oral lesion suggestive of LCH. If it is possible, some unfixed tissue should be sent rapidly to the pathologist. Such a procedure allows the appropriate processing of the tissue for ultrastructural examination, and the use of immunohistochemistry with monoclonal antibodies such as OKT6 and S-100 protein.

The treatment of jaw lesions consists mainly of curettage. A recurrence rate of 16 per cent has been reported[10] and recurrences have been observed up to 11 years after first treatment.[14] Radiotherapy and/or chemotherapy should be reserved for lesions which are inaccessible to surgery and for disseminated





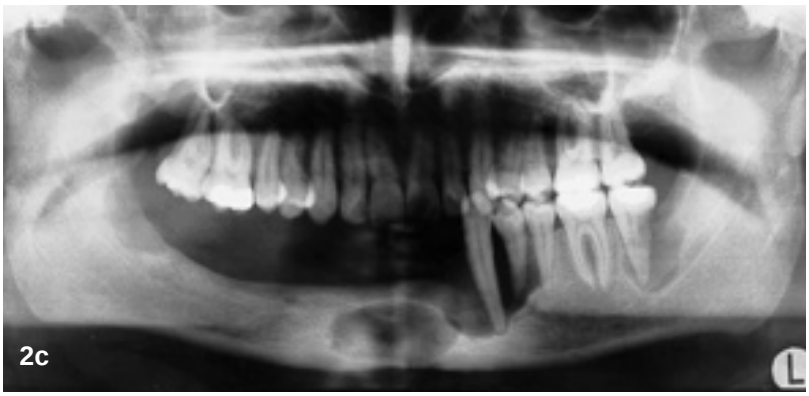


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Fig. 1.–Clinical picture of a 16 year old patient suffering from multifocal Langerhans' cell histiocytosis, showing necrotizing and ulcerating defects of the mucosa in the right canine region of the mandible.

Fig. 2.–a) Panoramic view of the same patient as in Figure 1. The lesions in the right canine region and distally of the 38 showed the presence of Langerhans' cells. This patient also had lesions in the right mastoid and in one of the ribs. b) The lesion between 34 and 35. c) Panoramic view of the same patient 4 years later. The oral and extraoral lesions did not respond to surgery, radiotherapy and chemotherapy. There was still progression of the oral lesions.

visceral involvement. The latter may run an unpredictable course for which treatment is not always effective.[15] The criteria whether or not to follow a 'wait-and-see' policy in one of the patients were partly based on the findings of previous radiographs and the possibility of spontaneous remission, as reported in the literature.[16]

Although unifocal (solitary) lesions of LCH successfully respond to curettage, the possibility of recurrences or new lesions still remains which makes a long-term follow-up necessary.

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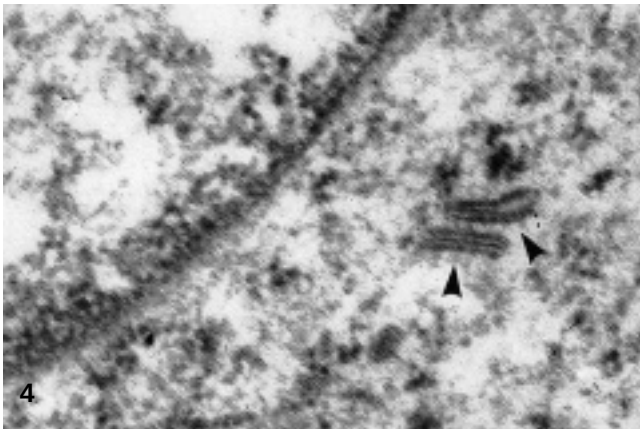

Fig. 3.–High-power view of a biopsy showing large cells with faintly eosinophilic cytoplasm and characteristic indented ovoid nuclei: Langerhans' cells. (H&E. ×250).

Fig. 4.–Ultrastructural picture showing the presence of Birbeck granules in the cytoplasm of the Langerhans' cells. (×36 000).

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