

Hand-Schüller-Christian Syndrome (Disease) – Multiple Eosinophilic Granulomas in the Maxillary Bones Compromising the Periodontal Tissues: Case Report

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We report a clinical case of a three-and-a-half-year-old girl with multiple radiolucent central lesions within the body and the ascending ramus of the mandible and the alveolar and basal bone of the maxillary sinus.

In both maxillary bones additional destruction of the periodontal tissues was seen from the molar region to the canines. We confirmed a definitive diagnosis by histological analysis of a Langerhans cells histiocytosis (histiocytosis X) in its sub-variant of Hand-Schüller-Christian (H-S-C) syndrome (co-existence of diabetes insipidus and desquamative skin injuries).

This case report illustrates the potentially rapid growth of eosinophilic granulomata, the difficulties and importance of a prompt diagnosis, and secondary periodontal infections with periodontopathogenic micro-organisms.

Key words: histiocytosis X, eosinophilic granuloma, periodontal disease

INTRODUCTION

Histiocytosis-X or Langerhans cell histiocytosis is an immunoregulatory disorder characterised by a proliferation of this sub-population of cells of the immune system. It also frequently infiltrates and destroys the periodontal tissues when it involves the oral cavity. There are three subcategories which have similar histological characteristics but differ in severity and extent:

- Eosinophilic granuloma
- Hand-Schüller-Christian (H-S-C) syndrome
- Letterer-Siwe syndrome (Artzi et al, 1989).

An extension of this classification has been described as follows:

- 1.) A localised and chronic form of the disease, with unique or multifocal lesions, compromising the bone tissue, known as eosinophilic granuloma;
- 2.) A chronic and disseminated form corresponding to the H-S-C syndrome;
- 3.) The acute disseminated form of the disease, Letterer-Siwe syndrome, which represents a malignant neoplastic process, with fatal consequences frequently reported (Bhaskar et al, 1993).

The H-S-C syndrome is also characterised by an additional visceral compromise of the lymphatic nodes, and in most of the cases diabetes insipidus is reported along with skin and retro-orbital lesions

that cause exophthalmus. The cutaneous lesions are desquamative, similar to pseudo-psoriatic lesions, in the three syndromic forms of the disease. Although the aetiology of the disease is still unknown, proliferating cells infiltrate into the cutaneous lesions and also into the visceral lesions that are associated with the disseminated form of the disease (Bhaskar et al, 1993). It has also been associated with an immunological deficiency of the suppressor cells, like the Langerhans cells themselves, T lymphocytes or both (Artzi et al, 1989; Bhaskar et al, 1993; Van Dyke et al, 1982). The presented case illustrates the potential diagnostic difficulties associated with the condition due to its very low prevalence, the coexistence of a periodontopathic infection of the periodontal tissues surrounding the lesion, the presence of a diminished PMNL response, the co-existence of diabetes insipidus (which completed the medical profile), the very premature appearance of the disease and its rapid progression.

CASE REPORT

A three-and-a-half-year-old girl attended the Universidad Católica de Chile, Department of Dentistry and Maxillo Facial Surgery, in June 2000, following referral from the paediatric department, with a presumptive diagnosis of Papillon-Lefèvre syndrome, due to desquamative cutaneous lesions of the lower abdomen and the presence of periodontal inflammation. Her medical and family histories were unremarkable. A clinical examination involving panoramic radiographs was performed.

The clinical examination revealed no extraoral tumoral mass or swelling, but a marked halitosis. The intraoral examination demonstrated a lesion that compromised all maxillary molars, the marginal gingivae in relation to these teeth, the keratinised gingivae beyond the mucogingival line and also the mucosa of the floor of the mouth. This lesion had an inflammatory appearance with a granulomatous component.

These lesions involved the second molar to the canine of the four maxillary and mandibular quadrants. In relation to the gingival margin, large amounts of bacterial plaque and debris were observed, which also adhered to the teeth, both at the clinical crown and root level, exposed by gin-

gival recession secondary to periodontal attachment loss. The periodontal probing depths ranged between 7–8mm, and the gingivae were very painful, with abundant gingival bleeding. The maxillary molars had Class III furcations and grade III tooth mobility.

Instrumental Examinations Result and Treatment Plan

We proceeded to take microbiological samples from the periodontal pockets for molecular diagnosis by PCR (polymerase chain reaction) for 12 periodontopathogenic micro-organisms, *Candida albicans* and *Herpes simplex* virus from the molars, canines, tongue and inner buccal mucosa. The presence of *Fusobacterium nucleatum* and *Prevotella nigrescens* was noted at a high level (50.000–500.000 bacteria per sample). *Peptostreptococcus micros*, *Streptococcus intermedius*, *Tannerella forsythensis*, *Treponema denticola*, *Eikenella corrodens* and *Prevotella intermedia* were present at a medium level (5.000–50.000 bacteria per sample) and finally, *Capnocytophaga sp.* and *Porphyromonas gingivalis* were identified at low levels (500–5.000 bacteria per sample). *Actinobacillus actinomycetemcomitans*, *Candida albicans* or *Herpes simplex* virus could not be detected. We also took smears from the palatal mucosa for cytological identification of *Candida albicans* (the lesion of the palatal mucosa had the appearance of erythematous candidosis). However, *Candida albicans* was not isolated from the palatal mucosa.

A full blood count was performed along with blood glucose levels to eliminate underlying systemic disease, alterations of protein or carbohydrate metabolism, such as anaemia, leukaemia or diabetes. Genetic exams (cerotype) were performed to investigate chromosomal disorders such as trisomy and defects of chemotaxis, phagocytosis and adherence of PMNLs. Immuno-adherence analysis for PMNNS showed a diminished immuno-adherence.

With the presumptive diagnosis of Papillon-Lefèvre syndrome, the patient began her treatment with initial periodontal care (oral hygiene instructions, mechanical and chemical plaque control), followed by surgical treatment. At the same time, the patient was examined at the Department of Nephrology because she also presented with polydipsia, polyuria and abrupt weight loss within a two-

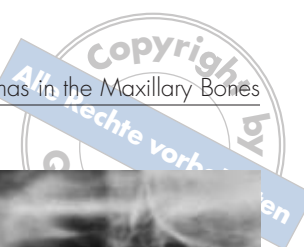
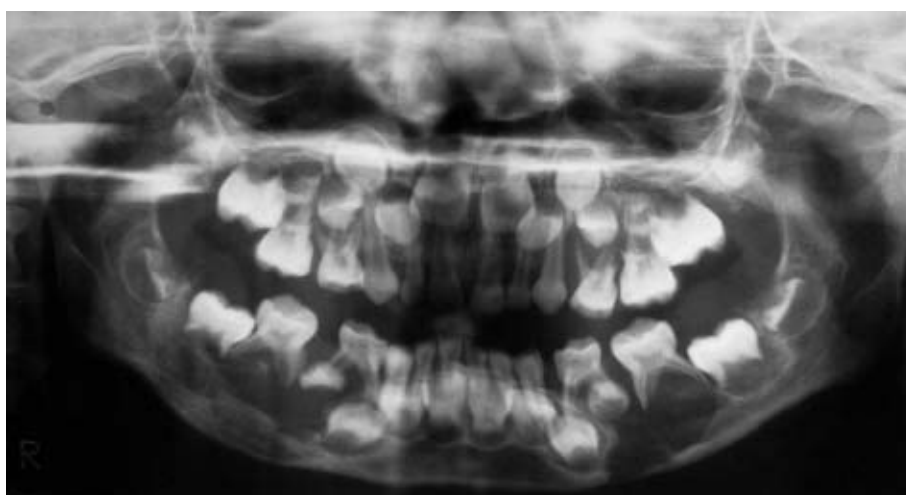


Fig 1 Panoramic radiograph at the time of consulting.



Fig 2 Panoramic radiograph four months later. Note the rapidly progressing lesion, especially in the lower jaw.



month period (> 5kg). The nephrological examination determined the presence of diabetes insipidus, which in combination with the post-surgical histopathology completely changed our presumptive clinical diagnosis.

After stabilising the diabetes we proceeded with the second phase of periodontal-surgical treatment. In this phase of the treatment, the upper and lower molars and the four maxillary canines were extracted and the central tumours were surgically removed. One can observe, especially in the mandible (Fig 3), the aggressive and extensive lesions, compromising the basilar bone and the lingual bone cortex of the mandible, leaving the vascular neural complex without any surrounding bone tissue, which mandated the removal of all bicuspids and first molar tooth germs.

All post-surgical reviews demonstrated that the patient had made satisfactory progress, and no evidence of infection or inflammation was found. The

girl is currently subject to a periodic recall programme and within a rehabilitation phase of her treatment. She is also under an neurological-oncology control programme after another lesion affecting the Sella turcica was discovered.

HISTOLOGY

The histopathology report of the extracted teeth (eight deciduous molars, deciduous canines, tooth germs from the eight bicuspids and tooth germs of the eight first molars) revealed no dental tissue alterations, except variable degrees of radicular resorption of the deciduous teeth. In relation to the soft tissues and central intraosseous tumours, granulation tissue was found, with abundant macrophages, more or less rounded, with a kidney-like nucleus and multiple eosinophils between them, some neutrophils and necrosis with dilated capillary vessels

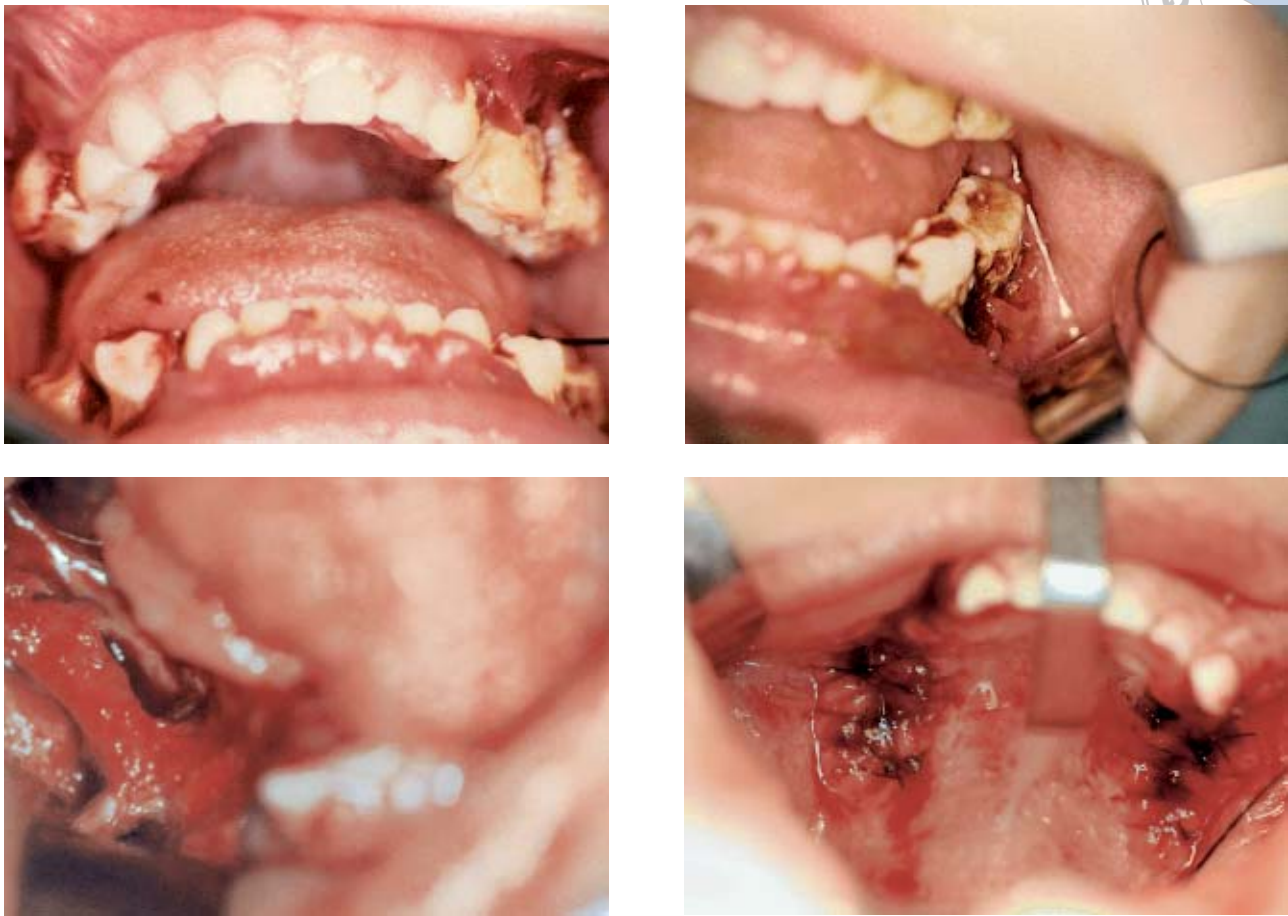


Fig 3a–d Intra-oral approach pre and post surgery. Note the mandibular nerve after the tumour resection in the mandible (Fig 3c) and the collapse of the alveolar bone after the resection of the lesions in the maxillary bone (Fig 3d)

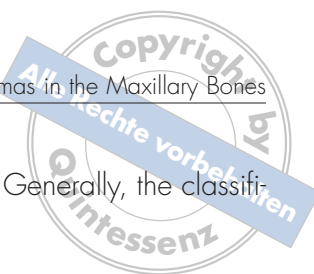


Fig 3e Post-surgical pieces (deciduous molars and canines, germs of the definitive bicuspids and molars).

and lymphocyte foci. This tissue was also observed in the root canals. Consequently, the histological and clinical findings led us to a definitive diagnosis of Langerhans cell histiocytosis with multiple eosinophilic granulomas of the jaws, diabetes insipidus and impaired neutrophil function (Hand-Schüller-Christian syndrome).

DISCUSSION

Twenty-eight cases of histiocytosis X (17 males, 11 females) involving the head and neck region with intra-oral compromise have been reported in a review by Piatelli et al (1995). More than 50% of those patients were under the age of 10, although adult cases are also reported relatively frequently (Scolozzi et al, 2004). According to other authors, the appearance of eosinophilic granuloma is most frequent (85%) during the first three decades of life (Regezi and Sciubba, 1989). In 54% of cases the tumours were located only in the head and neck region; in 87% the lesions were observed in the mandible, with the molar region being the most predominant location. Characteristic signs and symptoms of periodontal disease were present in 22 (79%) of the 28 cases reported by Piatelli et al, including gingival bleeding, periodontal pocketing, alveolar bone destruction and periodontal abscesses. One case presented lesions ex-



tending from the molar region to the palate, and two cases showed a unique palatal compromise. In our case report, in relation to the upper jaw the tumour extended from the molars and also included the palate.

We additionally searched for the presence of herpes simplex virus in the periodontal pocket, and the initial diagnosis was of pre-puberal periodontitis associated with Papillon-Lefèvre syndrome. According to several authors, the presence of certain viruses such as herpes, human Epstein Barr virus and human citomegalovirus is related to pre-puberal periodontitis. Down syndrome associated with periodontitis, periodontitis associated with Papillon-Lefèvre syndrome, acute necrotising ulcerative periodontitis and aggressive periodontitis are related to rapid progression and severity of attachment loss (Slots, 2000; Contreras et al, 2001).

In relation to the blood investigations, the patient presented with diminished immunoadherence of neutrophils. Numerous publications have reported an association between pre-puberal periodontitis and defects of PMNL chemotaxis, adherence and phagocytosis, which increases susceptibility to periodontal infections (Kinane et al, 1989; Sigusch et al, 2001; Van Dyke et al, 1982; Van Dyke et al, 1985). However, a defect in PMNL responsiveness to bacteria is also a symptom of histiocytosis X, which could facilitate the establishment of an infection by periodontopathogenic microorganisms (Artzi et al, 1989; Bhaskar et al, 1993; Finney et al, 1988; Lichtenstein, 1953; Mirra, 1989; Piatelli and Paolantonio, 1995).

The aetiology of histiocytosis X remains unknown, and for many authors it is still a lesion of medullar origin, where it has an intra-osseous location and is believed to be more characteristic of an immunological disorder than a true neoplasia (Bhaskar et al, 1993). In this case the periodontal tissues were affected by extensive attachment loss and additional infection with periodontopathogenic microorganisms. However, the aetiology of the periodontal destruction was the eosinophilic granuloma, which compromised the periodontal structures in a secondary manner. The microbiological profile of the patient may be due to her family environment (Asikainen and Chen, 1999) or may have arisen secondary to the severe tissue damage/necrosis caused by the eosinophilic granulomata.

The patient's medical prognosis will depend upon the extension of the granuloma and the nature of

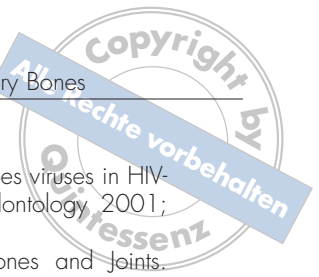
the compromised structures. Generally, the classification is as follows:

1. Unique osseous lesion;
 2. Multiple osseous lesions;
 3. Visceral lesions;
 4. Combination of visceral and osseous lesions.
- (Artzi et al, 1989; Bhaskar et al, 1993; Fechner and Mills, 1993; Finney et al, 1988; Lichtenstein, 1953; Mirra, 1989; Piatelli and Paolantonio, 1995; Regezi and Sciubba, 1989).

In our case, the presence of multiple osseous lesions, associated diabetes insipidus, desquamative cutaneous lesions, deficits in the cellular immune responses and the histopathology all pointed to a definitive diagnosis of Hand-Schüller-Christian syndrome. The prognosis of this and other patients depends on the correct assignment of a diagnosis, complete enucleation of the lesions, ruling out the presence of other lesions during initial therapy and follow-up periods. This is particularly important in our case because of the patient's young age at initial diagnosis.

Presenting symptoms frequently involve pain when chewing or induced by minimal pressure stimuli. In some cases, there are extra-oral swellings. Most of the reported cases only have unique osseous lesions (Finney et al, 1988). These appear like solitary central radiolucent shadows. Multiple lesions may affect the maxillary bones bilaterally or, as in our patient, bilaterally in both the maxilla and mandible. The mandibular condyle is rarely involved (Bhaskar et al, 1993). Other reported bone sites include the skull, mastoid area, clavicle, ribs, pelvis and femur (Mirra, 1989). According to Mirra, the flat bones are affected in about 70% of cases. The size of lesions may vary from 1-1.5cm. Rarely do lesions affect the mucosa alone (Finney et al, 1988), and gingival lesions generally have large subjacent zones of osteolysis.

Early signs and symptoms, which can guide us to the diagnosis, include premature dental avulsions and/or alterations in alveolar healing post tooth loss. The marginal gingivae in our case presented with severe recession, but other cases reported in the literature presented with hyperplastic gingival enlargement at the gingival margin (Piatelli and Paolantonio, 1995). If the neoplastic process continues it can embrace soft-tissue structures near to the primary lesion. It is therefore of vital importance to determine the exact anatomical location of the lesion and its relation to vital structures (large



vessels, nerves, air tract) by means of imaging (panoramic radiographs, maxillofacial CT-scan) to plan the surgical phase of therapy and prevent damage of vital structures.

In our patient we observed an osteolytic process compromising the medullary bone but occasionally compromising the lower mandibular bone cortex also, without central or peripheral bone reformation. The radiographic appearance depends on the state of the lesions, varying from a unique central well-delineated lesion to a multilocular lesion, sometimes with little sclerotic reaction due periosteal compromise. If the lesion perforates one cortical plate, it will extend to the adjacent soft tissues and will appear as a tumoral mass. The occurrence of pathological fractures of the mandible is reported with large lesions.

Differential diagnosis of histiocytosis X affecting the maxillofacial tissues includes cysts, neoplastic processes and chronic inflammatory processes (Bhaskar et al, 1993). If the eosinophilic granuloma involves the periodontal tissues, it rarely causes root resorption. In the reported case, we could see different degrees of resorption of the extracted teeth at the histological analysis. Eosinophilic granulomas could mimic apical inflammatory chronic lesions (for example, caused by septic pulpal necrosis) or periodontal cysts. In addition we have to consider other osteolytic lesions such as osteomyelitis, Ewing's sarcoma, osteosarcoma and non-Hodgkin lymphoma.

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