Acta Dermatovener (Stockholm) 52: 75–79, 1972

ORAL MANIFESTATIONS OF HISTIOCYTOSIS X

J. E. Winther, O. Fejerskov and H. P. Philipsen

From the Departments of Oral Surgery and Oral Pathology, Royal Dental College, Aarhus, Denmark

Abstract. A case of histiocytosis X in a 21-year-old female is reported. The manifestations of the disease were primarily found in the oral cavity. The changes were unspecific and mimicked necrotizing gingivitis, aphthous stomatitis and simple periodontitis. However, differences in location and severity between histiocytosis X lesions and periodontal inflammatory changes made a distinction possible. Nodular infiltrations of the lungs were interpreted as constituting possible pulmonary involvement. The oral lesions were treated with combined surgical and radiation therapy. Recurrence was observed 5 months postoperatively. This, along with the possible pulmonary involvement, makes prognosis uncertain.

The term histiocytosis X comprises eosinophilic granuloma, Hand-Schüller-Christian disease and Letterer-Siwe disease. They have been grouped together on the basis of similar pathological findings, and in order to avoid eponyms, Lichtenstein (5) proposed the above-mentioned term, as the histiocyte is the characteristic cellular component, common to all three forms. The letter X was added to denote the unknown etiology of the disease.

Upon analysis of 65 cases, however, Nyholm (8) concludes that eosinophilic granuloma and Hand-Schüller-Christian disease may be regarded as a single entity and termed eosinophilic xanthomatous granulomatosis.

Numerous reports stress the fact that oral manifestations may be among the earliest signs of histiocytosis X (1, 2, 3, 10, 11). The symptoms are usually non-specific, related to sore, swollen gingiva, ulcerative lesions or loose teeth, often resembling periodontal disease in an advanced stage. These changes when seen in adult patients may not arouse immediate suspicion, but their presence in children and adolescents requires consideration of a diagnosis of histiocytosis X. To illustrate this important diagnostic feature and to discuss certain problems of classification and pathogenesis, the following case is presented.

CASE REPORT

The patient, a 21-year-old female, was referred to the Royal Dental College, Aarhus, with gingival ulcerations of 1 ½ years duration, which started while she was hospitalized for salpingitis. She had had no other serious ailments and no drugs were taken routinely. The initial lesion was described as a rather large, painful, soft swelling situated on the labial side of the alveolar process in the upper left canine region. This lesion ulcerated with regular intervals and persisted for 1 year. It was treated topically with several agents including sprays of hydrocortisate, obviously without any effect at all. Finally, however, the ulcer healed, leaving a slight scar. Following this attack multiple ulcerations occurred in the gingival area of the mandibular premolar and molar regions. The lesions were painful and tender especially while chewing. Again, local application of different ointments and sprays failed to produce any effect.

At the initial, clinical examination in December 1969, the following observations were made: Healthy but somewhat pale appearance. Lymph nodes in both submandibular regions were palpable and tender. The dentition was well kept with adequate fillings. The oral mucosa outside the gingival area did not exhibit any pathological conditions except for a small scar in the apical region of the upper left canine. The buccal and lingual gingiva of the mandibular premolar and first molar regions and the lingual gingiva of the incisor region were grossly enlarged, hyperemic and in some places revealed fibrinous ulcerations destroying the marginal and part of the alveolar mucosa (Figs. 1 and 2). Pseudopockets were present, and the tissue was extremely painful on probing. In the lower left canine region the alveolar mucosa on the labial side showed an element different from the other lesions (Fig. 3). An ulcer was surrounded by raised hypertrophic margins with slings of blood vessels concentrically arranged. The premolars revealed increased mobility, especially the second one on the right side.

Roentgenographic examination of the mandible showed

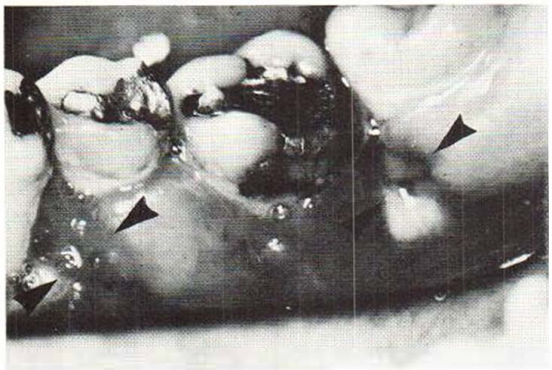

Fig. 1. Lingual aspect of the lower right premolar and molar region. Note the fibrinous ulcerations destroying the marginal and part of the alveolar mucosa.

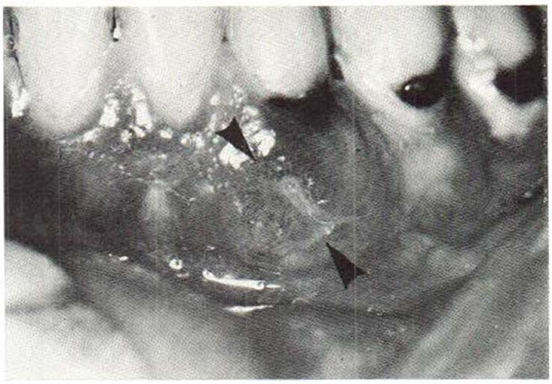

Fig. 3. Histiocytosis X lesion of the labial alveolar mucosa in the lower left canine region.

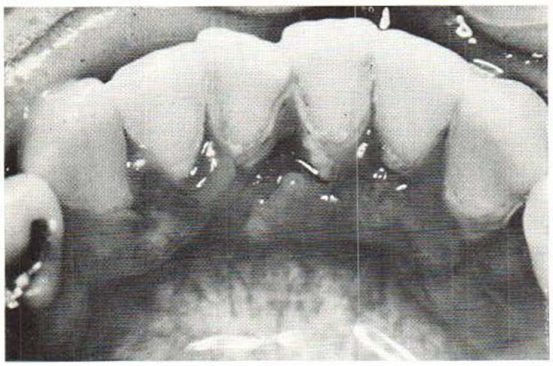

Fig. 2. Lingual aspect of the lower incisor region showing oedematous and hyperemic gingiva ulcerated between the central incisors.

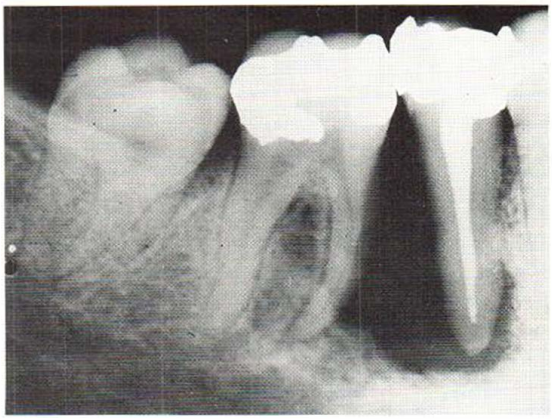

Fig. 4. Roentgenogram showing osseous focus destroying the alveolar bone adjacent to the lower right first molar and second premolar.

large bony pockets between the central incisors, around the premolars, and mesial to the lower right first molar. In the latter location the bone destruction extended below the apex of the second premolar (Fig. 4). In the maxilla a poorly defined radiolucent area was found adjacent to the root of the left canine (Fig. 5). Nowhere could root resorptions be demonstrated. Roentgenograms of the skull and skeleton revealed no pathological foci. Chest roentgenogram showed, however, nodular infiltration of the lungs. Re-evaluation of a roentgenogram taken routinely during hospitalization $1\frac{1}{2}$ years earlier showed similar but less marked infiltrations. Routine laboratory tests showed normal values. A tentative diagnosis of histiocytosis X was made and incisional biopsies were taken from the lower left premolar and canine regions. The biopsy removed from the latter region showed that the changes were confined to the mucous membrane with no involvement of the underlying bone.

Histological examination: The gingival epithelium showed simple hyperplasia and ulcerations (Fig. 6). The underlying connective tissue showed chronic, non-specific inflammation and granulation tissue dominated by numerous histiocytes. Focal accumulations of eosinophilic leucocytes and lymphocytes were found along with a few uncharacteristic multinucleated giant cells. In many areas the histiocytes were in close contact with the squamous epithelium (Fig. 6), and in the areas of ulceration the ulcers were dominated by histiocytes with a few polymorphs only. Small foci of necrosis were found, mainly in the superficial part of the tissue close to the ulcerated surface. The nuclei of the histiocytes were irregular with foldings and often lobulated (Fig. 7), but no abnormal chromatin pattern was found. Normal mitotic figures were present in great numbers. The cytoplasm was granular or in a few cases foamy with ill-defined cell boundaries. The histological diagnosis was: eosinophilic granuloma.

The patient was then referred to the Radium Center, University Hospital, Aarhus, for treatment. Mediastinoscopy and bronchoscopy gave no evidence of Boeck's sarcoid or tuberculosis. A combined oral surgical and radiation therapy was undertaken. Under local anesthesia a mandibular gingivectomy was done with thorough curettage of bony pockets and extraction of the right first

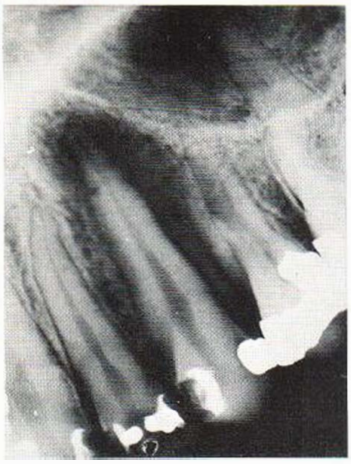

Fig. 5. Ill-defined radiolucent lesion surrounding the apex of the upper left canine.

molar and second premolar, and of the left premolar. A periodontal pack was applied for 14 days. After primary healing, the affected areas of the mandible were radiated (1 600 R), and a 3 month postoperative check up revealed no signs of recurrence (Figs. 8 and 9). However, in the upper left canine region a tumorous outgrowth was noted at the site of the scar tissue. The lesion was curretted, revealing soft, granulomatous material easily separated from the bone, exposing part of the root surface of the canine. Histology showed: eosinophilic granuloma. The wound healed uneventfully, and was covered with normal mucosa except for a small denuded area of the root.

At the 5 month control a recurrence was noted on the gingiva distal to the lower right first premolar. Furthermore, a gingival focus had developed around the upper left first molar. Both lesions were similar to the previously encountered ones, and on histology showed eosinophilic granuloma. After thorough curettage the lesions were subsequently irradiated (1 600 R). The pulmonary lesions were not treated, as control roentgenograms 5 months postoperatively showed a stationary pattern.

DISCUSSION

The present case clearly demonstrates that oral lesions may be the first diagnostic sign in histiocytosis X. Sleeper (11), Blevins et al. (2), and Sedano et al. (10) find that 50 to 77 % of the patients have oral and dental symptoms as chief complaints. The oral manifestations of histiocytosis X represent, however, a picture entirely different from that found in other locations. This is probably due to the unique anatomy of the tooth-supporting structures, and to the bacterial milieu of the mouth which predisposes to secondary infections. Blevins et al. (2) point out that the oral soft tissue lesions of histiocytosis X have been erroneously diagnosed as Vincent's infection, aphthous or herpetic stomatitis and similar conditions. Johnson & Mohnac (3) illustrate the varied oral appearance of Hand-Schüller-Christian disease and eosinophilic granuloma in a review of 7 patients. Among the initial lesions listed are: large infiltrating mass of the mandible with loss of supporting alveolus, necrotizing gingivitis, delayed healing after extractions, swelling of the mandible, ulcerated lesions with bone loss simulating periodontal disease and a small, solitary radiolucent area in the retromolar region.

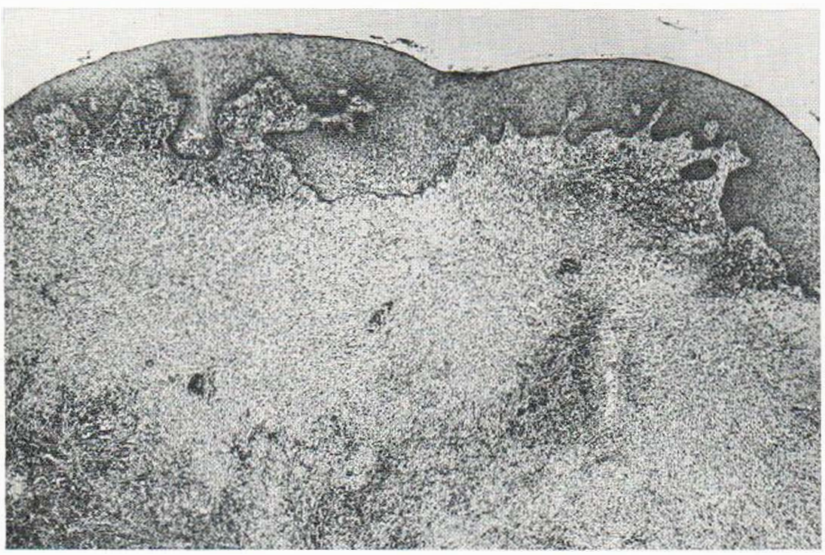

Fig. 6. Incisional biopsy from the lesion shown in Fig. 3. The submucosal connective tissue is replaced by granulomatous foci dominated by histiocytes. Hematoxylin-eosin, × 130.

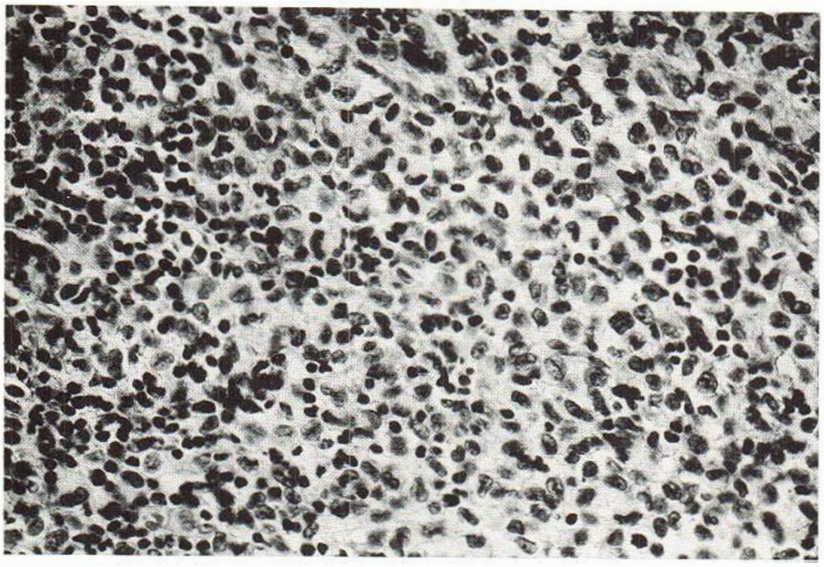

Fig. 7. Higher magnification of histiocytic accumulation shown in Fig. 6. Note ill-defined cell boundaries and lobulated, pale-staining nuclei of the histiocytes. Hematoxylin-eosin, × 350.

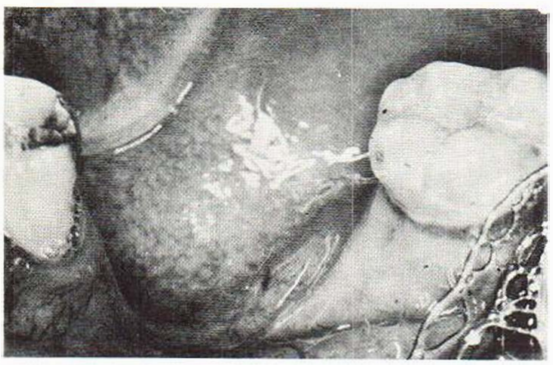

Fig. 8. Lingual view of the area shown in Fig. 1, three months postoperatively. The large defect in the alveolar process is covered with normal mucosa showing no signs of recurrence.

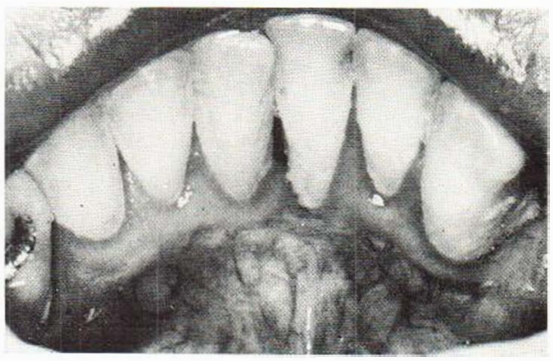

Fig. 9. Lingual view of the gingival area shown in Fig. 2, three months postoperatively. Lesions are eliminated, but some oedema and hyperemia due to imperfect oral hygiene still persists.

In the present case $1\,^1/_2$ years elapsed before a definite diagnosis was made and proper therapy instituted. The patient had been treated under various diagnoses such as aphthous stomatitis, necrotic gingivitis, and periodontitis. As the biopsy specimen from the lower left canine region shows, the initial soft tissue lesions may arise in the alveolar mucosa free of the gingival margin in contrast to simple periodontal disease, which originates in the marginal gingiva. The extensive, localized bone destruction in the mandibular premolar regions was of a most pernicious character and in sharp contrast to the almost normal bone septae in the adjacent regions. When combining these clinical and roentgenological findings it is evident that diagnoses other than simple periodontitis must be considered.

The occurrence of mucosal lesions without bone involvement as reported in the present case indicates that at least some oral lesions of histiocytosis X may originate as soft tissue foci. This finding is in opposition to the conclusions drawn by Nyholm (8). However, the close proximity between the lesions and the underlying bone probably leads to early osseous destruction, thus masking the primary focus.

The histological findings in this material clearly confirm the diagnosis of histiocytosis X, but can be of no help in distinguishing between the localized and the chronic disseminated form.

The present case was primarily classified as localized histiocytosis X according to the definition of Lichtenstein (5). If, however, the pulmonary nodular infiltrations are considered as foci of eosinophilic granulomas the present case may in fact be classified as the chronic disseminated form of histiocytosis X (1, 4, 6, 9). The present classification problem could be solved by adopting the term eosinophilic xanthomatous granulomatosis as proposed by Nyholm (8).

Local curettage with or without radiation therapy seems to be the treatment of choice when dealing with oral lesions of histiocytosis X (1, 7). Based on earlier reports, nothing can be said on the recurrence rate of oral lesions. In the present case recurrence of mucosal lesions occurred 5 months after combined surgical and radiation therapy had been instituted.

It is generally accepted that the prognosis for localized histiocytosis X is good while it is more dubious for the chronic disseminated form (1, 3, 5, 8, 9). The findings presented in our case may suggest that the disease at present is in a progressive phase, and possibly in a transitional stage between the localized and the disseminated form of histiocytosis X. A prognostic evaluation is therefore subject to great uncertainty until a definite turn of the disease occurs.

REFERENCES

1. Avery, M. E., McAfee, J. G. & Guild, H. G.: The course and prognosis of reticuloendotheliosis (eosinophilic granuloma, Schüller-Christian disease and Letterer-Siwe disease: A study of 40 cases. J Med *22:* 636, 1957.
2. Blevins, C., Dahlin, D. C., Lovestedt, S. A. & Kennedy, R. L. J.: Oral and dental manifestations of histiocytosis X. Oral Surg *12:* 473, 1959.
3. Johnson, R. P. & Mohnac, A. M.: Histiocytosis X: Report of 7 cases. J Oral Surg *25:* 7, 1967.
4. Jones, J. C., Lilly, G. E. & Marlette, R. H.: Histiocytosis X. J Oral Surg *28:* 461, 1970.
5. Lichtenstein, L.: Histiocytosis. Integration of eosinophilic granuloma of bone, Letterer-Siwe's disease and Schüller-Christian's disease as related manifestations of a single nosologic entity. Arch Path *56:* 84, 1953.
6. — Histiocytosis X (eosinophilic granuloma of bone, Letterer-Siwe disease, and Schüller-Christian disease). J Bone Jt Surg *46 A:* 76, 1964.
7. Mellor, W. C. & Stockdale, C. R.: Eosinophilic granuloma of bone. Oral Surg *11:* 1196, 1958.
8. Nyholm, K.: Eosinophilic xanthomatous granulomatosis and Letterer-Siwe's disease. Acta Path. Microbiol. Scand., *suppl. 216,* 1971.
9. Oberman, H. A.: Idiopathic histiocytosis. A clinicopathologic study of 40 cases and review of the literature on eosinophilic granuloma of bone, Hand-Schüller-Christian disease and Letterer-Siwe disease. Pediatrics *28:* 307, 1961.
10. Sedano, H. O., Cernea, P., Hosxe, G. & Gorlin, R. J.: Histiocytosis X. Clinical, radiologic, and histologic findings with special attention to oral manifestations. Oral Surg *27:* 760, 1969.
11. Sleeper, E. L.: Eosinophilic granuloma of bone, its relationship to Hand-Schüller-Christian and Letterer-Siwe's diseases with emphasis upon oral symptoms and findings. Oral Surg *4:* 896, 1951.

Received May 26, 1971

J. E. Winther
Department of Oral Surgery
Royal Dental College
8000 Aarhus C
Denmark