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Oral Presentation of Lymphoma: Case Report of T-Cell Lymphoma Masquerading as Oral Crohn's Disease, and Review of the Literature

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A 15-year-old male with labial swelling, mouth ulcers and mucosal tags is reported. While the features were clinically consistent with oral Crohn's disease the patient proved to have a fatal T-cell lymphocytic lymphoma.

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INTRODUCTION

ORAL LESIONS in Crohn's disease include diffuse facial or labial swellings of varying severity, mucosal cobblestoning and tags, and oral ulceration [1]. The oral condition is usually benign, though it can be relatively incapacitating. In contrast, oral lesions in lymphomas typically present as discrete, persistent intraoral swellings which may show local ulceration [2]. We report a patient who developed a lethal T-lymphocytic lymphoma, masquerading initially clinically as oral Crohn's disease.

CASE REPORT

The patient was a 15-year-old male caucasian who at presentation complained of persistent swelling of both lips for 2 years together with swelling of his lower eyelids, an acneiform rash, and recurrent oral ulceration. His medical history was clear apart from eczema, and specifically there were no genital or gastrointestinal complaints, and no weight loss.

Examination showed no lymphadenopathy but he had a grossly swollen, oedematous, slightly tender upper lip (Fig. 1) with swellings of his right lower eyelid, aphthous-like ulceration of the buccal and lingual mucosa (Fig. 2), mucosal tags and cobblestoning (Fig. 3). A clinical diagnosis of orofacial granulomatosis or oral Crohn's disease was considered. Oral biopsy, as reported at that time by a general pathologist, showed no specific lesion and was considered consistent with aphthae. However, a conjunctival biopsy and repeat oral biopsy showed sparse granulomas (Fig. 4), with a dense mononuclear cell infiltrate reported initially as consistent with Crohn's disease. A Kveim test was positive but neither serum angiotensin converting enzyme assay, chest radiography nor gallium scan showed evidence of sarcoidosis. Immunological investigations showed a mild T-cell lymphopenia and a reduced CD4:CD8 ratio, but the patient was HIV antibody negative by western blot and enzyme-linked immunosorbent assay (ELISA), and had no anti-neutrophil cytoplasmic antibodies (ANCA) suggestive of Wegener's granulomatosis.

A diagnosis of oral Crohn's disease was therefore made on the basis of the clinical features and the original histopathology report. The labial swellings were treated with intralesional injections of triamcinolone acetonide with some apparent initial benefit. However, periorbital swelling and chemosis increased, failed to respond to systemic sulphasalazine 400 mg twice daily, and he was therefore treated with oral prednisolone 10 mg daily and azathioprine 150 mg daily.

Unfortunately the patient then developed severe ulceration both of his palate (Fig. 5) and right vocal cord, together with

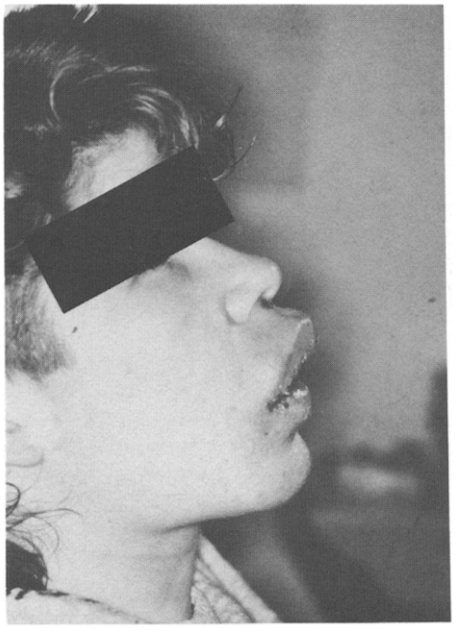

Fig. 1. Labial swelling (1986).

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pyrexia, raised plasma viscosity and normochromic normocytic anaemia. Although unresponsive to topical, intralesional and systemic corticosteroids, the laryngeal ulcer resolved after a short intravenous course of cyclophosphamide and prednisolone. However, the palatal ulcer gradually extended, eventually involving the underlying bone, resulting in an extensive oro-nasal fistula (Fig. 6) and the patient lost 12 kg in weight over 6 months.

At this time review by an oral pathologist of the earlier lip biopsy material showed perineural invasion and infiltration of muscle (Fig. 7) and a retrospective diagnosis of a well differentiated atypical lymphocytic lymphoma was made. Immunocytochemistry undertaken at this time was, however, inconclusive. Therefore, a short course of radiotherapy was started, involving 2 Gy to the palatal lesion over 2 weeks. There was an initial improvement, but the general condition of the patient then deteriorated rapidly, and he developed ascites, pleural effusions, and hepatosplenomegaly. A liver biopsy confirmed lymphocytic lymphoma and the first course of the "Plymouth Hope Schedule" was given (doxorubicin, vincristine, prednisolone and etoposide) but the patient developed thrombocytopenia (platelets 19 000/d1) and succumbed from massive internal bleeding.

Autopsy examination showed widespread lymphocytic lymphoma involving many tissues including lymph nodes, liver, kidney and heart. Repeat immunocytochemistry on the original lip biopsy specimen confirmed that the diagnosis was indeed, a T-cell lymphoma.

DISCUSSION

Oral lesions are common in patients with proven Crohn's disease of the intestine and include aphthae [1, 3, 4], diffuse swellings of the cheeks or lips [4], chronic inflammatory hyperplasia with fissuring and a cobblestone appearance of the mucosa [5], mucosal tags [4], vertical fissures in the lips [6], and hyperplastic gingivitis [7]. This is regarded as a fairly pathognomonic constellation of clinical features. These lesions may antedate bowel symptoms, and can be the only obvious site of disease [8]. Some patients with oral lesions have silent intestinal disease [9]. The term orofacial granulomatosis was introduced for lesions that resemble those of Crohn's disease clinically and histologically in patients who do not have accompanying gastrointestinal symptoms [9].

The distinction between orofacial granulomatosis and other conditions with non-caseating granulomas such as oral Crohn's disease, may not be easy. Orofacial granulomatosis can be part of a spectrum of disorders that includes Melkersson–Rosenthal syndrome and Miescher's cheilitis granulomatosa. Melkersson–Rosenthal syndrome is primarily a triad of fissured tongue, facial or labial swelling, and facial palsy but there may be other lesions [10], and some patients have manifested sarcoidosis or Crohn's disease [11]. Miescher's granulomatous cheilitis is characterised by isolated labial swelling,

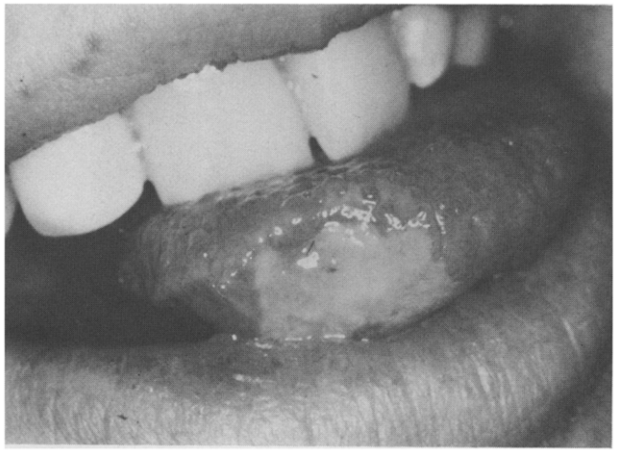

Fig. 2. Oral ulceration (1986).

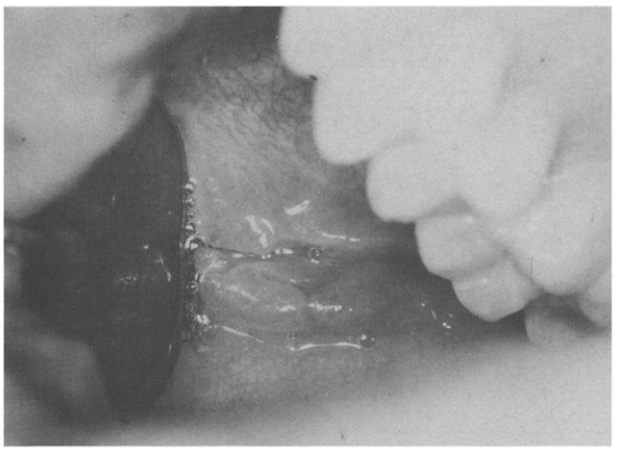

Fig. 3. Cobblestoning of buccal mucosa (1986).

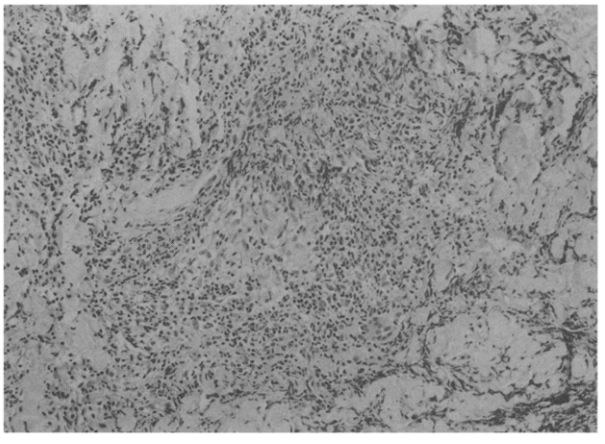

Fig. 4. Small epithelioid granuloma surrounded by dense lymphocytic infiltrate. Haematoxylin and eosin. Original magnification ×150.

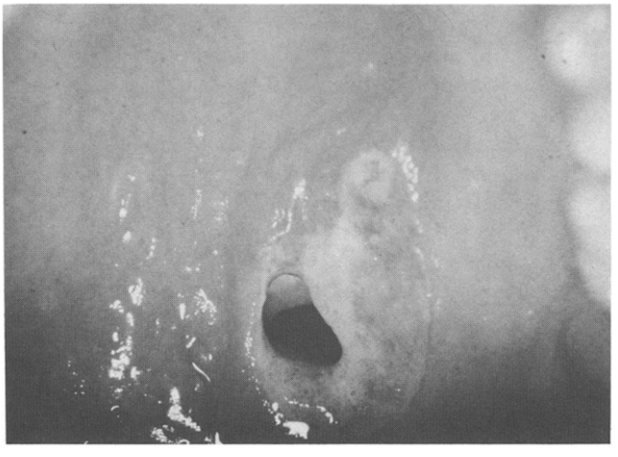

Fig. 5. Palatal ulceration (April 1988).

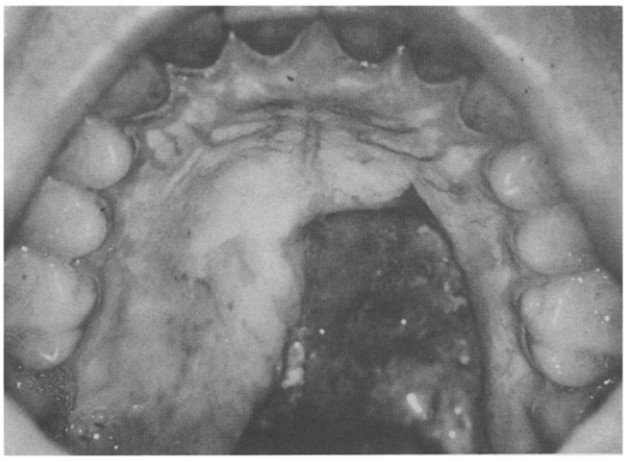

Fig. 6. Palatal ulceration extending (July 1988).

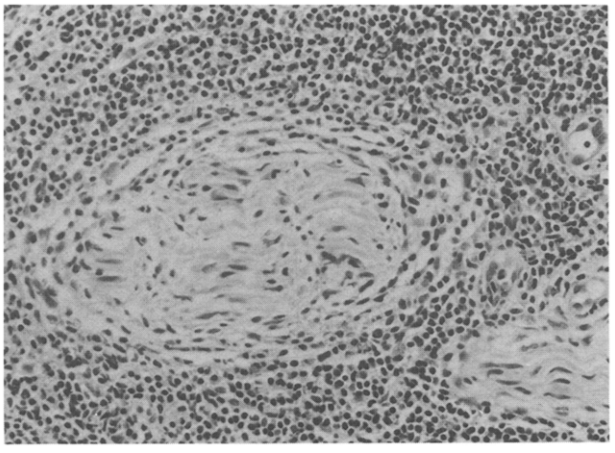

Fig. 7. Heavy infiltrate of small lymphocytes in a perineural distribution. Haematoxylin and eosin. Original magnification ×300.

and is probably an oligosymptomatic form of Melkersson–Rosenthal syndrome [10]. Some patients with orofacial granulomatosis or its variants progress to Crohn's disease, but most do not.

There are only rare reported cases where oral Crohn's disease or its variants have been associated with a lymphoma [12]. However, there are increasing numbers of reports of lymphomas, typically in the small intestine and colon, in patients with gastrointestinal Crohn's disease [13–25]. Furthermore, there is experimental evidence that extracts of Crohn's disease tissue can produce lymphomas in athymic mice [26–29].

Nevertheless, the present case appears to have been a lymphoma *ab initio*, though the clinical features were suggestive of oral Crohn's disease. The indolent course of the disease and the eventual midfacial destructive syndrome with late systemic dissemination are typical features of orofacial T-cell lymphoma, which this lesion ultimately proved to be.

Most oral lymphomas, however, are of B-cell origin and are typically seen in systemic lymphomas. The most common presenting features of oral lymphoma are as a lump, or with pain, sensory changes or ulceration.

Oral lesions are rare in Hodgkin's disease, but have been seen in the oral mucosa of the lips and cheeks [30–32], gingiva [33], buccal sulcus [34], retromolar regions [35] and soft palate [36]. Lesions have also been reported both in the mandible and the maxilla [37, 38].

Oral lesions of non-Hodgkin lymphoma (NHL) are also uncommon, though they now are being seen increasingly in HIV disease. Most are seen in the area of Waldeyer's ring, but in oral sites, the gingiva and the hard palate are most often affected [39]. They may present as a rapidly increasing swelling which may be prone to ulceration. In the early stages, however, much less serious conditions may be simulated, such as pyogenic granuloma, non-specific gingivitis or acute ulcerative gingivitis (Vincent's disease) [40–46]. Palatal lesions appear as swellings that may locate to one or other side of the midline, in the midline, or they may be bilateral [47]. They may be firm, but are frequently soft and spongy and even fluctuant [48]. Tongue lesions are the least common oral lesion. It has been noted that they do not tend to invade deeply and involve muscle so that, even in advanced cases, the tongue may remain mobile [36, 49].

NHL is the second most common malignancy in HIV infection, the incidence is rapidly increasing [50] and most are of B-cell origin [51]. In AIDS patients, extranodal NHL occurs more frequently in the oral cavity than in Waldeyer's ring. Intraorally, NHL presents most often as masses involving the gingiva and palate [52–54].

Oral involvement in mycosis fungoides, a T-lymphocyte malignancy, may include the tongue, palate or buccal mucosa [55–66] with erythematous lesions that may become indurated or ulcerate.

Malignant lymphomas may occasionally *originate* in the oral or perioral region particularly in the palate, sinuses, or nasal cavity. They are often difficult to diagnose and have received a range of descriptions from reticulum cell sarcoma and lymphocytic leukaemia to polymorphic reticulosis [67–69] but up to two thirds are now known to be T-cell lymphomas [70–75] and late dissemination is not uncommon [76], as in the present case.

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