CASE REPORT

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Crohn's disease with oral presenting signs masquerading as chronic osteomyelitis

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Abstract

Background: A case of Crohn's disease (CD) was diagnosed following recognition of oral and systemic signs and symptoms in a 19-year-old male patient.

Methods: Clinical investigation utilized included blood tests (full blood count, electrolytes, urea, creatinine, liver function tests), computed tomogrphy scans, magnetic resonance imaging scans, oral biopsies, colonoscopy and biopsies of the terminal ileum and colon.

Results: A diagnosis of CD was made which then allowed appropriate medical treatment to be initiated.

Conclusion: The importance of a thorough medical history and full physical examination with appropriate investigations as dictated by clinical findings is demonstrated.

Key words: Crohn's disease, osteomyelitis, clubbing, inflammatory bowel disease.

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CASE REPORT

A 19-year-old male was referred to the Department of Oral and Maxillofacial Surgery at the Royal Brisbane Hospital for investigation of a persistent sinus following the surgical removal of tooth 48. This extraction was performed under local anaesthesia by a general dental practitioner 12 months prior to the current presentation. Two biopsies with curettage of the affected area had been performed by a consultant maxillofacial surgeon prior to referral. The initial histopathology reported non-specific inflammatory and reparative changes. The second biopsy showed a more advanced healing pattern with areas of woven bone associated with fibrous tissue containing a chronic inflammatory cell infiltrate. This contained aggregates of foamy macrophages and occasional multinucleate giant cells (Fig 1) but without evidence of cystic cavitation or an epithelial component. Anaerobic and aerobic cultures of swabs taken from the site were uninformative and did not identify a specific pathogen. Gram and Ziehl-Neelsen stains for acid fast bacteria were unhelpful and specific cultures for Mycobacterial and Actinomyces spp were negative.

Radiographic examination prior to referral included an orthopantomogram (OPG), computed tomography (CT) and magnetic resonance imaging (MRI) scans. The OPG was consistent with a healed extraction site but the CT scan suggested a 'periostitis ossificans' but without any obvious intrabony pathology to stimulate a periosteal reaction (Fig 2). The MRI scan was performed with T1, T2 and STIR windows. The T2 weighted scan revealed a thin rim of high signal along the outer border of the right mandible and an increased signal within the marrow space of the right mandibular angle. This extended to the body of the right mandible and was reported as a possible low grade osteomyelitis.

At the initial consultation a thorough medical history revealed a 50kg weight loss over an 18 month period. The patient reported an intermittent and chronic diarrhoea which he believed corresponded to courses of amoxycillin and clavulanic acid. He denied bloody diarrhoea or melaena. He was a normal vaginal delivery at term without post natal problems and his mother confirmed he achieved normal developmental milestones without an increased susceptibility to respiratory tract infections as a child. His general medical practitioner had investigated the weight loss with a stool culture and excluded diabetes with a glucose tolerance test.

The patient presented as a tall and thin young man in no distress. Marked clubbing of his fingers was noted, together with palmar and conjunctival pallor. There were no splinter haemorrhages or other peripheral stigmata of infective endocarditis. Abdominal examination was unremarkable with an absence of hepatosplenomegaly and no detectable Virchow's node.

Clubbing is an important clinical finding which can be seen in numerous medical conditions. It is defined as a loss of the nail fold angle and when it is present, the tips of the fingers appear bulbous. Clubbing is seen in suppurative lung diseases such as cystic fibrosis, in

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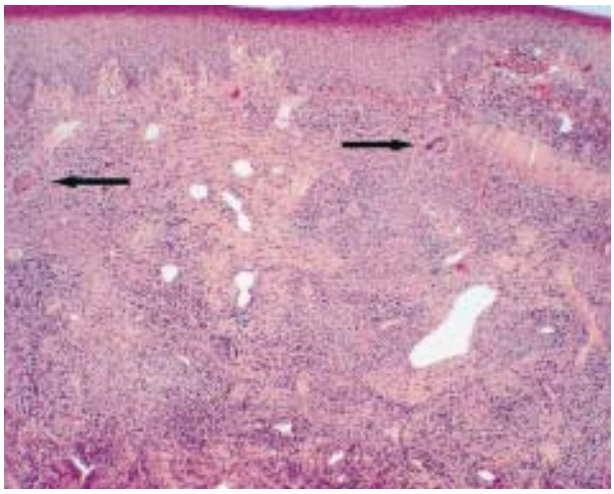

Fig 1. Gingival biopsy showing an oedematous fibrovascular tissue with multifocal plasma cell clusters and occasional giant cells (arrows). Original magnification x 40.

inflammatory bowel disease, in some malignancies of the lung and occasionally in healthy individuals. The presence of clubbing should alert the dental practitioner to the possibility that serious systemic disease may be present in an affected individual.

Auscultation of his chest revealed vesicular breath sounds with equal air entry bibasally. There was a faint systolic murmur best heard at the apex and which did not radiate.

Apart from the conjunctival and palmar pallor, no other signs indicative of a haematological disorder were noted. There were no ecchymoses or petechial haemorrhages and no lymphadenopathy of the axillary, cervical or epitrochlear nodes evident.

Intra-oral examination showed a well healed 48 extraction site with some mucosal erythema and swelling adjacent to the buccal aspect of the socket. There was evidence of the previous biopsies and curettage present. An extensive examination of the remainder of his oral mucosa, oropharynx and salivary glands did not show any abnormality. Teeth 45-47 were clinically and radiographically sound. Relevant laboratory studies are summarized in Table 1.

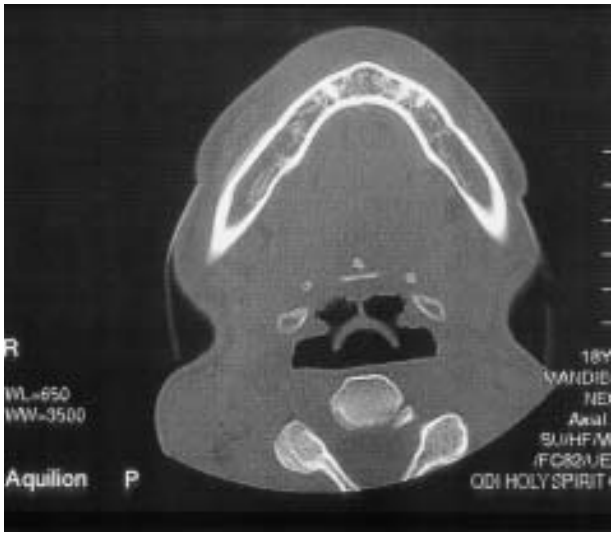

Fig 2. CT scan showing possible periostitis ossificans.

Table 1. Relevant laboratory findings

Parameter	Patient value	Normal range
Haemoglobin	138g/L	135-180g/L
Mean cell volume	79fL	80-98fL
Mean cell haemoglobin	27pg	27-35pg
White cell count	7.8x10⁹/L	4-11x10⁹/L
Total protein	58g/L	60-82g/L
Serum albumin	29g/L	35-50g/L

The significant history of weight loss with diarrhoea and the signs of clubbing and pallor on examination strongly suggested an underlying medical condition, possibly inflammatory bowel disease and this needed to be adequately investigated and managed. Other conditions which may have accounted for his weight loss included ulcerative colitis and coeliac disease. However, these were considered unlikely in light of his history and physical examination. He was referred to a gastroenterologist who obtained biopsies of his colon and terminal ileum. These revealed inflamed ileal mucosa with oedema and villous distortion. The colonic biopsies showed areas of inflammation with early crypt abscesses. Together with his history and physical signs, a diagnosis of Crohn's disease (CD)/regional enteritis was made.

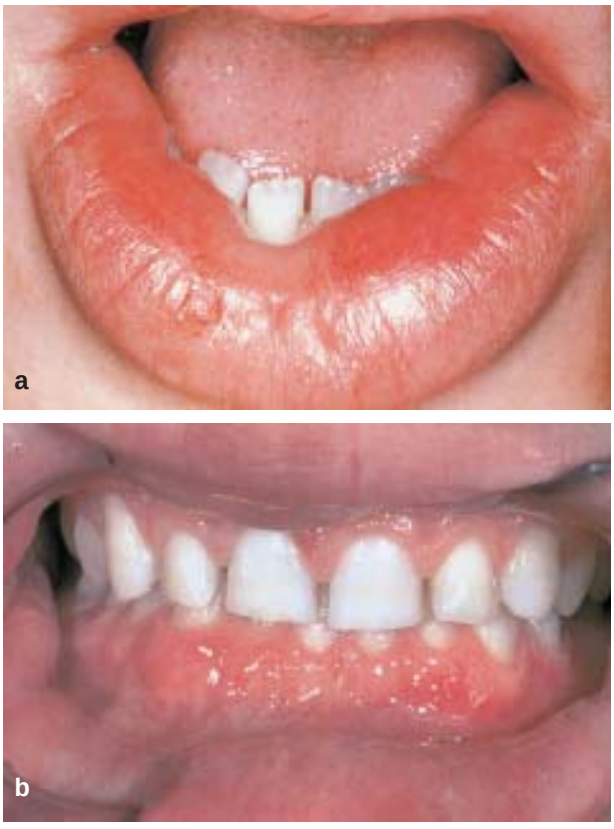

Fig 3a, 3b. The marked lip swelling seen in this patient is typical of the oral presentation of Crohn's disease and is usually seen in association with an erythematous mucogingivitis (3b).

Table 2. Oral lesions seen in Crohn's disease

Lip swelling with or without fissures
Angular cheilitis
Generalized gingival erythema and swelling
'Cobblestoning' of the labial and buccal mucosa
Linear ulceration in the reflection of the buccal sulci
Palatal swelling and erythema
Tussue tags
Submandibular lymphadenopathy

DISCUSSION

Crohn's disease is a chronic granulomatous inflammatory disease that can involve any part of the gastrointestinal tract from the mouth to the anus.[1-3] The small bowel alone is affected in 30 to 40 per cent of patients, small bowel and large bowel together in 40 to 55 per cent and the colon is singly affected in 15 to 20 per cent of patients.[1] The incidence of oral lesions cited in the literature varies from 0.5 per cent to as high as 48 per cent in a prospective study in children in which a paediatric dentist specifically screened known CD patients.[2]

The aetiology of CD is unknown. However, it is theorized that a genetically vulnerable host mounts an inappropriate response to what should be an unremarkable environmental stimulus.[3,4]

Oral lesions in CD are well described and reflect the mucosal lesions seen in the rest of the gut. They include mucosal tags, 'cobblestoning' of the buccal mucosa, lip swelling with or without fissures (Fig 3a), linear ulcers, an erythematous mucogingivitis (Fig 3b) and apthous ulceration.[2] These are a direct result of the presence of local oedema and non-caseating epitheloid granulomata. Table 2 summarizes the oral lesions seen in CD. Patients presenting with oral lesions in the absence of other gastrointestinal manifestations are diagnosed as having orofacial granulomatosis.[2]

A subsequent review of the histopathological features of the initial oral biopsies showed a picture entirely consistent with CD. The gross presentation (Fig 1) was a fibrovascular tissue containing multifocal inflammatory cell accumulations, predominantly plasmacytic, that were consistent with a plaque driven inflammatory process. The tissues were oedematous and closer examination of isolated giant cells (Fig 4a) showed them to be surrounded by epitheloid histiocytes and lymphocytes without evidence of caseous necrosis (Fig 4b) which excludes tuberculosis. A diagnosis of oral CD was retrospectively made.

Treatment of CD is largely medical in nature. However, surgical intervention is often required to deal with complications such as bowel obstruction, stenosis and perforation.[1,3,5] The goals of treatment are to control acute exacerbations, induce and maintain remission and manage any complications arising from the disease process.[3,4]

Currently medical management relies on anti-inflammatory drugs, immunosuppressants and immunomodulators.[3,5] Medications utilized are shown in Table 3. A detailed discussion of the medical

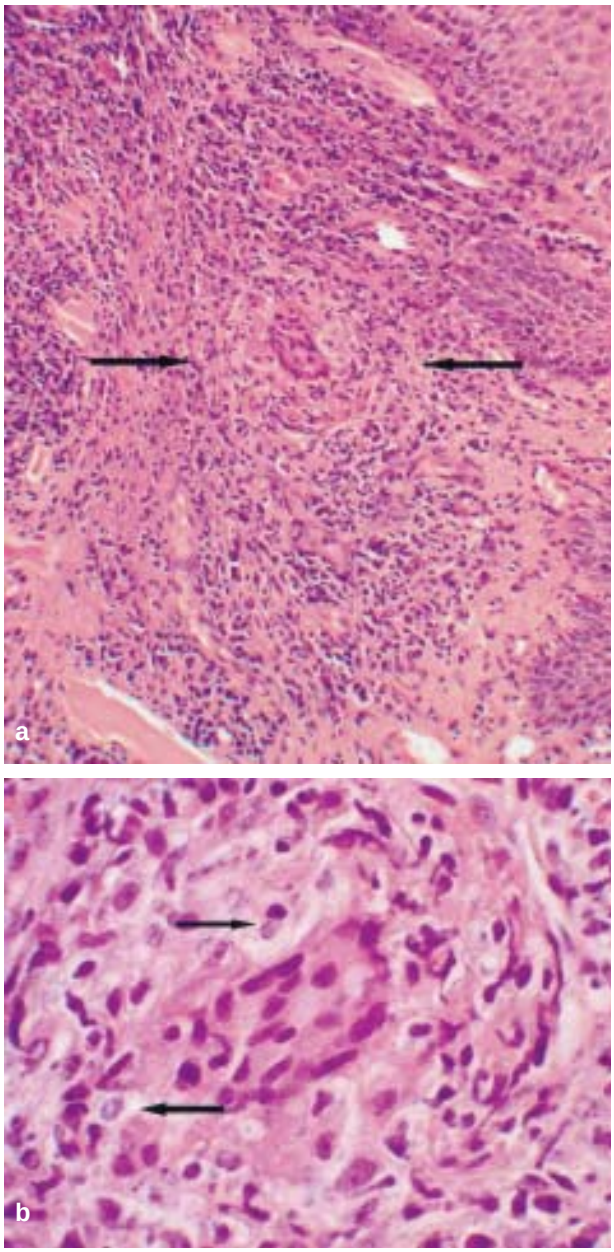

Fig 4a, 4b. Review of the tissues in Fig 1 show the non-caseating granulomas (arrows). Fig 4a. Containing giant cells and epitheloid histiocytes (arrows) Fig 4b. Consistent with an oral CD. Original magnification x 250.

management of CD is beyond the scope of this paper and interested readers are directed to the references for a fuller discussion. However, it should be noted that many of the drugs used may have adverse effects on the oral cavity that dental practitioners may be called upon to manage. For example, long term corticosteroid use may predispose to oral candidiasis, xerostomia and mucosal atrophy and sulfasalazine may induce a severe lichenoid drug reaction which is usually erosive. Azathioprine and 6-Mercaptopurine may suppress bone marrow function resulting in neutropenia and thrombocytopenia. In affected patients the inability to mount a normal inflammatory response may predispose to aggressive oral infections and platelet

Table 3. Medications used in Crohn's disease

Drug	Comment
Anti-inflammatories	
Corticosteroids	Corticosteroids are used to treat acute exacerbations of CD. They may be given IVI, OP or topically as an enema.
Hydrocortisone	
Budesonide	Budesonide has less systemic effects due to a high first pass metabloism in the liver.[4]
Prenisolone	
5-Aminosalicylates	Broken down in gut to release the active 5-Aminosalicylic acid. Specific areas of the bowel can be targeted by manipulating the rate of breakdown.[4]
Mesalamine	
Sulfasalazine	
Immunomodulators	
Azothioprine	Used as a steroid sparing agent and to maintain remission. Need to watch for bone marrow suppression. Azothioprine is a pro-drug of 6-MP. Both are metabolized to the active agent 6-Thioguanine.[4]
6-mercaptopurine	
Methotrexate	
Cyclosporine	Decreases T-cell proliferation and activation by inhibiting production of interleukin-1.[4]
Biological agents	
Infliximab	Infliximab is a TNF-alpha antagonist.
Thalidomide	Thalidomide is a potent downregulator of IL-6 activity.
Antibiotics	
Metronidazole	Microorganisms may have a role in the aetiology of CD. Antibiotics are used for their antibacterial effect and for a postulated inherent immunomodulatory effect.[4]
Ciprofloxacin	
Proton pump inhibitors	
Omperazole	Used for symptomatic treatment in gastroduodenal CD.
Pantoprezole	

counts below 20 may result in post-operative bleeding problems. Cyclosporin is a well known iatrogenic cause of gingival hyperplasia.

In addition to adverse medication reactions the oral presentations of CD can provide the patient with considerable cause for concern and the clinician with a management problem particularly in young patients. They may present with significant lip swelling and a refractory bilateral angular cheilitis with crusting as well as the discomfort from linear sulcular ulcerations. The oral presentations have been described briefly in this communication and the reader is referred to previously cited papers for management options.[2,6]

CONCLUSION

This case demonstrates the need to take a detailed and accurate medical history followed by a full physical examination in any patient who presents with persistent oral signs and symptoms which do not respond to initial local treatment.

An adequate physical examination, as detailed above, is beyond the scope of the general dental practitioner. However, the benefits of referral for a general medical assessment are clear. This case also highlights the need to provide the pathologist with as much clinical information as possible as this can impact on the manner in which tissues are examined and particularly in the formulation of a summary diagnosis consistent with the clinical presentation.

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