

Granulomatous cheilitis and Crohn's disease

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I Ahmad, D Owens. Granulomatous cheilitis and Crohn's disease. Can J Gastroenterol 2001;15(4):273-275. Granulomatous cheilitis is characterized by recurrent swelling of the labial tissues and granulomatous histology. Granulomatous cheilitis has been recognized as an early manifestation of Crohn's disease. It may follow, coincide with or precede the onset of Crohn's disease. The first case presented involved an extraintestinal manifestation of Crohn's disease, and the second case presented is of development of granulomatous cheilitis a year before the onset of symptomatic Crohn's disease. Although chronic granulomatous cheilitis is a very rare disorder, once it is diagnosed, the patient should be followed up carefully. These patients should be investigated for asymptomatic Crohn's disease either when the diagnosis of granulomatous cheilitis is confirmed or when gastrointestinal symptoms develop.

Key Words: *Crohn's disease; Granulomatous cheilitis; Orofacial granulomatosis*

Chéilite granulomateuse et maladie de Crohn

RÉSUMÉ : La chéilite granulomateuse se caractérise par un œdème récidivant des tissus labiaux, et l'examen histologique révèle un aspect granulomateux. Elle est reconnue comme une manifestation précoce de la maladie de Crohn. Son apparition peut coïncider avec celle de la maladie de Crohn, la précéder ou la suivre. Dans le premier cas, il s'agit de manifestations extra-intestinales de la maladie de Crohn, tandis que, dans le deuxième cas, la chéilite granulomateuse a précédé d'un an l'apparition symptomatique de la maladie de Crohn. Même si la chéilite granulomateuse chronique demeure une maladie très rare, elle devrait faire l'objet d'un suivi minutieux une fois qu'elle est diagnostiquée. Les patients devraient être évalués pour une maladie de Crohn asymptomatique lorsque le diagnostic de chéilite granulomateuse est confirmé ou lorsque des symptômes gastro-intestinaux apparaissent.

Two cases of granulomatous cheilitis associated with Crohn's disease are reported. Granulomatous cheilitis is an uncommon disorder, characterized by recurrent swelling of the labial tissues. Histologically, the typical form of granulomatous cheilitis is characterized by the formation of scattered aggregates of noncaseating granulomas. Since the report of a case of chronic granulomatous cheilitis that occurred several years before intestinal lesions appeared (1), granulomatous cheilitis has been recognized to be an early

manifestation of Crohn's disease. Granulomatous oral lesions may follow, coincide with or precede the onset of Crohn's disease. To our knowledge, few cases have been reported where the patient initially presented with granulomatous cheilitis and then developed Crohn's disease (1-6). Other patients who were diagnosed with Crohn's disease later developed granulomatous cheilitis (7-12). There has also been a case report of a patient with chronic granulomatous cheilitis who had intestinal lesions compatible with

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Crohn's disease, although the patient had no gastrointestinal symptoms (13). Two cases of chronic granulomatous cheilitis associated with Crohn's disease are presented; the first case is an extraintestinal manifestation of Crohn's disease and the second case is of chronic granulomatous cheilitis that preceded the onset of symptomatic Crohn's disease. Although chronic granulomatous cheilitis is a very rare disorder, the patient should be followed up carefully after having the disorder diagnosed. These patients should be tested for Crohn's disease either when the diagnosis of granulomatous cheilitis is confirmed or when gastrointestinal symptoms develop.

CASE PRESENTATIONS

Patient 1: In April, 1991 a 15-year-old boy presented to the oral surgery department, Gwynedd Hospital, Bangor with painless swelling of the upper lip of six weeks; he also had a history of recurrent colicky abdominal pain since the age of eight years. He had been admitted twice to the pediatric ward with this abdominal pain. On each occasion, abdominal examination revealed generalized tenderness without any guarding or rigidity. Full blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), urea and electrolytes, and liver function tests were within normal limits. Plain radiographs of the abdomen did not show any specific features. On both occasions nonspecific abdominal pain was diagnosed and he was managed conservatively. At the age of 12 years he had an elective appendectomy. The histology of the appendix showed lymphoid hyperplasia consistent with mesenteric lymphadenitis. Clinical examination at the oral surgery clinic, Gwynedd Hospital revealed a swollen upper lip, and there was a lesion in the buccal mucosa that resembled cobblestone. Systemic examination was unremarkable. The biopsy from the lips confirmed the diagnosis of granulomatous cheilitis, and biopsy of the buccal mucosa showed granulomatous change with giant cells, suggestive of Crohn's granulomata. The patient was referred to the gastroenterology department, Gwynedd Hospital for further investigation and had barium follow-through examination of the small bowel, which showed typical ulceration in the ileocecal region. Flexible sigmoidoscopy showed normal mucosa to the splenic flexure. The biopsies taken from the rectum were normal. Since the diagnosis of his Crohn's disease, it has flared up twice requiring oral steroids. There have been no other extraintestinal manifestations of Crohn's disease.

Patient 2: In 1987, a six-year-old boy presented to the dermatology clinic, Gwynedd Hospital with an eight-month history of a painless, swollen upper lip. The biopsy of the lip showed noncaseating granulomas.

These granulomas were composed of epithelioid cells and multinucleated giant cells, confirming the diagnosis of granulomatous cheilitis. A year later, he presented with diarrhea and abdominal pains but no rectal bleeding. The inflammatory markers ESR and CRP were significantly higher compared with normal values. Barium follow-

through examination of the small bowel was normal. The colonoscopic examination showed typical, patchy Crohn's colitis that was confirmed on biopsy. He had several relapses during the course of his illness.

DISCUSSION

Crohn's disease is an idiopathic inflammatory process that can affect any portion of the alimentary tract from the mouth to the anus. The original description of the disease by Crohn, Ginzberg and Oppenheimer (14) in 1932 localized the disease to segments of the ileum. Oral lesions in Crohn's disease have been found in 6% to 20% of patients (15,16). The oral manifestation of Crohn's disease has been described as being more common in patients with colonic disease compared with disease confined to the small bowel. Clinically, granulomatous cheilitis is characterized by recurrent swelling of the labial tissues, which may be followed by a permanent enlargement. Histologically, the typical form of granulomatous cheilitis is characterized by the formation of scattered aggregates of noncaseating granulomas. All granulomatous conditions restricted to the face and oral cavity are termed 'orofacial granulomatosis'. Orofacial granulomatosis is a clinical entity of either unknown or specific causation. Specific causes include sarcoidosis, chronic infective granulomas and Crohn's disease. The association of granulomatous cheilitis with Crohn's disease is well documented. It may follow, coincide with or precede the onset of Crohn's disease, and about one of three of these cases is said to precede gastrointestinal symptoms. In such cases, the distinction of granulomatous cheilitis from other uncommon oral disorders, such as sarcoidosis, tuberculosis, chronic infective granulomas and Melkersson-Rosenthal syndrome may be difficult. Melkersson-Rosenthal syndrome involves triad recurrent orofacial swelling, relapsing facial paralysis and a fissured tongue. There are no published data on the incidence and prevalence of granulomatous cheilitis. To our knowledge, few cases have been reported that initially presented with granulomatous cheilitis and then developed to Crohn's disease several years later (1-6). Other patients with Crohn's disease later developed granulomatous cheilitis (7-12). There has also been a case report in which patients with granulomatous cheilitis with no gastrointestinal symptoms were investigated and found to have lesions in the small bowel that were compatible with Crohn's disease (13).

Crohn's disease may exist as an entity without intestinal involvement, and in one study, up to 63% of patients presenting with oral Crohn's disease had no overt gut signs or symptoms. However, 37% were subsequently found to have occult intestinal involvement. Scully et al (17) suggested that patients with oral granulomatous lesions should have investigations of their gastrointestinal tract by means of colonoscopy and barium follow-through examination of the small bowel, because one of three of these patients will have asymptomatic intestinal involvement. In a 10-year review of seven patients with orofacial granulomatosis without gut Crohn's disease, five subsequently developed Crohn's dis-

ease (18). Since 1988, systemic antibodies against the yeast *Saccharomyces cerevisiae* have been reported in the sera of patients with Crohn's disease. Although great variation was found both in patients' antibody responses and in relative antigenicity of different strains, these antibodies have been associated with Crohn's disease (19-21). These antibodies to oligomannosidic epitopes of the yeast *S cerevisiae* are serum markers associated with Crohn's disease. Challacombe et al (22) suggested that systemic and mucosal immunological responses to *S cerevisiae* are markedly raised in orofacial granulomatosis and Crohn's disease, but the different patterns of responses are found in those with oral and gut involvement compared with those with orofacial granulomatosis alone. Some patients with orofacial granulomatosis have been intolerant of certain foods, the elimination of which from the diet leads to a resolution of the facial swelling (23). Provoking molecules include cinnamaldehyde, carvone and piperitone, although a wide range of food or flavourings may be implicated. The only reliable way of detecting specific provoking factors is by the use of an elimination diet. Orofacial granulomatosis can be successfully treated by systemic or intralesional infusion of corticosteroids (24). Thalidomide and clofazimine (antileprosy drug) have been used successfully in steroid-resistant cases

(25,26). Usually long term maintenance medical treatment, at a lower dosage, is required to avoid recurrence. If there is no response to medical treatment, surgical excision and reconstruction can be considered (27).

The first case presented shows granulomatous cheilitis as an extraintestinal manifestation of Crohn's disease, as indicated by colicky abdominal pain for several years, which remained undiagnosed for several years because the patient had normal inflammatory markers. Finally, the biopsy of the lip led to the investigations of the small bowel, confirming the diagnosis of Crohn's disease. In the second case, there were no symptoms to suggest Crohn's disease when granulomatous cheilitis was diagnosed, but a year later he developed Crohn's disease. There is a possibility of underlying asymptomatic Crohn's disease. There is no doubt that patients with granulomatous cheilitis should be investigated for Crohn's disease by means of small bowel follow-through examination and colonoscopy if there is a history of abdominal pain, diarrhea or unexplained weight loss. However, it is controversial to investigate all patients with granulomatous cheilitis for Crohn's disease in the absence of symptoms. One can either investigate for the Crohn's disease when the diagnosis of granulomatous cheilitis is confirmed or wait for the development of gastrointestinal symptoms.

REFERENCES

- Carr D. Granulomatous cheilitis in Crohn's disease. *Br Med J* 1974;4:636.
- Tyldesley WR. Oral Crohn's disease and related conditions. *Br J Oral Surg* 1979;17:1-9.
- Brook IM, King DJ, Miller ID. Chronic granulomatous cheilitis and its relationship to Crohn's disease. *Oral Surg Oral Med Oral Pathol* 1983;56:405-8.
- Gomez RS, Ozen Y, Peters KP, et al. Morbus Crohn Erstmanifestation im oralen and anogenitalen Bereich. *Hautarzt* 1989;40:451-5.
- Bunker CB, Gilkes JJH. Granulomatous cheilitis and Crohn's disease. *Br J Dermatol Suppl* 1991;125:75-6.
- Jenss H, Plauth M, Hoffmann R, et al. Granulomatous cheilitis as first sign of Crohn's disease. *Dtsch Med Wschr* 1989;114:1524-7.
- Schiller KFR, Golding PL, Peebles RA, Whitehead R. Crohn's disease of mouth and lips. *Gut* 1971;12:864.
- Ellis JP, Truelove SC. Crohn's disease with mouth involvement. *Proc R Soc Med* 1982;65:1080.
- Croft CB, Wilkinson AR. Ulceration of mouth, pharynx, and larynx in Crohn's disease of the intestine. *Br J Surg* 1972;59:249-52.
- Kint A, Brauwere DD, Weert JD, Hendrickx R. Cheilitis Granulomatosa and Crohnsche Krankheit. *Hautarzt* 1977;28:319-21.
- Scott O. Crohn's disease of the upper lip. *Br J Dermatol* 1983;109:87-8.
- Tantall FM, Dodd HJ, Sarkany I. Crohn's disease with metastatic cutaneous involvement and granulomatous cheilitis. *Proc R Soc Med* 1987;80:49-51.
- Kano Y, Shiohara T, Yagita A, Nagashima M. Granulomatous cheilitis and Crohn's disease. *Br J Dermatol* 1990;123:409-12.
- Crohn BB, Ginzburg L, Oppenheimer GD. Regional ileitis: A pathologic and clinical entity. *JAMA* 1932;99:1323.
- Basu MK, Asquith P. Oral manifestations of inflammatory bowel disease. *Clin Gastroenterol* 1980;9:307-21.
- Williams AJK, Wray D, Ferguson A. The clinical entity of oro-facial Crohn's disease. *Q J Med* 1991;79:451-8.
- Scully C, Cochran KM, Russel RI, et al. Crohn's disease of the mouth: an indicator of intestinal involvement. *Gut* 1982;23:198-201.
- Field EA, Tyldesley WR. Oral Crohn's disease revisited - a ten-year review. *Br J Oral Surg* 1989;27:114-23.
- Main J, McKenzie H, Yeoman GR, et al. Antibody to *Saccharomyces cerevisiae* (baker's yeast) in Crohn's disease. *BMJ* 1988;297:1105-6.
- Barnes RMR, Allan S, Taylor-Robinson CH, et al. Serum antibodies reactive with *Saccharomyces cerevisiae* in inflammatory bowel disease. Is IgA antibody a marker for Crohn's disease? *Int Arch Allergy Appl Immunol* 1990;92:9-15.
- Giaffer MH, Clark A, Holdsworth CD. Antibodies to *Saccharomyces cerevisiae* in patients with Crohn's disease and their possible pathogenic importance. *Gut* 1992;33:1071-5.
- Challacombe SJ, Savage NW, Barnard K, et al. A comparison of systemic and mucosal antibody responses in oro-facial granulomatosis and Crohn's disease. *J Dent Res* 1997;76:142. (Abst)
- Patton DW, Ferguson MM, Forsyth A, James J. Oro-facial granulomatosis: a possible allergic basis. *Br J Oral Maxillofac Surg* 1985;23:235-42.
- Kolokotronis A, Antoniadis D, Papanagioutou P. Granulomatous cheilitis: a study of six cases. *Oral Dis* 1997;3:188-92.
- Safa G, Joly P, Boullie MC, et al. Melkersson-Rosenthal syndrome treated by thalidomide. *Ann Dermatol Venereol* 1995;122:609-11.
- Tausch I, Sonnichsen N. Experiences with clofazimine therapy of Melkersson-Rosenthal syndrome. *Hautarzt* 1992;43:194-8.
- Glickman LT, Gruss JS, Brit BD, et al. The surgical management of Melkersson-Rosenthal syndrome. *Plast Reconstr Surg* 1992;89:815-21.



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