Cheilitis granulomatosa and Crohn's disease : a case report

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Abstract

In this case report we describe the evolution of Cheilitis granulomatosa (GC) in a young patient with Crohn's disease during treatment with anti-TNF-alfa therapy. (Acta gastroenterol. belg., **2019**, 82, **326-328**).

Key words : cheilitis granulomatosa, inflammatory bowel disease, Crohn's disease.

Introduction

Cheilitis granulomatosa (CG) is a rare, persistent, non-tender swelling of one or both lips caused by a non caseating, granulomatous inflammation, first described by Miescher in 1945 (1). CG can be a manifestation of a systemic granulomatous condition such as Crohn's disease or Sarcoidosis, it can be idiopathic or it can be part of the Melkersson-Rosenthal syndrome which is a triad of recurrent orofacial swelling, fissured tongue, and intermittent facial palsy.

Case report

A 13 year-old male patient presented with bloody diarrhea, anal abscess and weight loss. Crohn's disease was diagnosed, affecting the peri-anal region, the rectum and the terminal ileum. The colon was mildly ill with scattered aphtoid lesions. A treatment with budesonide 6mg qd and mesalazine 2g qd was initiated with a favorable response. Two years later a relapse occurred with severe diarrhea, abdominal pain and oral aphtous ulcers. Infliximab monotherapy every eight weeks was initiated. After three induction and two maintenance infusions, interval of infusion was shortened to six weeks because of persisting symptoms. During the sixth infusion the patient developed an allergic reaction. Since then, administration of infliximab was combined with intravenous corticosteroids. At this time, trough levels of infliximab were undetectable and antibodies were positive. Regularly antibiotics were prescribed because of relapsing bloody diarrhea. After seven infusions of infliximab, the interval was again extended to eight weeks despite severe symptoms of IBD. A combination therapy with azathioprine was proposed but rejected by the patient's parents because of possible side effects.

Swelling of the face was mentioned for the first time at the age of 16. The swelling was accompanied by a severe flare of Crohn's disease with bloody stools, aphtous stomatitis and joint pain. For this reason (after ten infusions of infliximab) infusion intervals were again shortened to six weeks. Gastro-intestinal symptoms disappeared but swelling of the lower lip persisted for

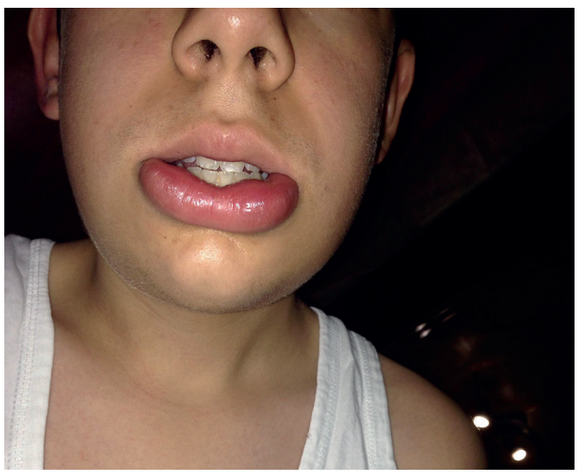

Figure 1. — Acute swelling of the lower lip during infliximab therapy.

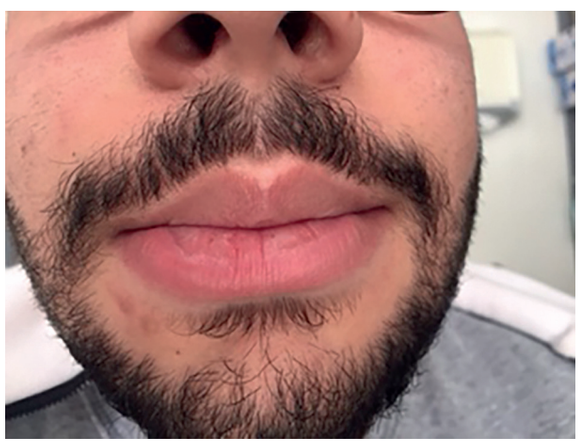

Figure 2. — Nearly complete disappearance of the swelling when in clinical and endoscopical remission.

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months (Figure 2). An allergy to nuts was assumed based on a skin prick test positive for peanut and the impression of the patient who made a link between eating nuts and the swelling. Anti-histamines were introduced daily without beneficial effect and epinephrine was prescribed. A small reduction in swelling when corticosteroids were started was noticed; at temporization of the corticosteroids, the swelling recurred. For the patient, a link with gastro-intestinal symptoms was difficult to withhold although he did have the impression that swelling was more present just before infusion of infliximab and after eating nuts.

In the meantime, infusions with infliximab and intra-venous corticosteroids were continued every five to eight weeks depending on the patient's symptoms. During all this time, levels of CRP were always elevated and an iron deficiency anemia was present. Antibodies to infliximab remained always high and serum levels were always undetectable. Three years after starting infliximab, when reaching the age of 18, adalimumab was started because of continuing symptoms, the presence of antibodies and the allergic reactions to infliximab. A colonoscopy at that time showed a pancolitis with ulcerations of the rectum and diffuse aphtoid lesions scattered throughout the remaining colon. The ileocaecal valve was completely deformed and could not be intubated. After starting adalimumab there was a favorable clinical evolution and normalization of CRP, colonoscopy and fecal calprotectin. Swelling of the lower lip decreased significantly but never disappear completely (figure 2). We observed no more flares of the swelling. Before the start of adalimumab, a biopsy of the lower lip was performed. Histology showed a granuloma suggestive of a Cheilitis Granulomatosa in a Crohn's patient.

We can conclude that the patient's Crohn's disease was poorly controlled with many flares during years. Flaresof gastro-intestinal symptoms seemed to be associated with swelling of the lower lip. Once intestinal disease was controlled, no more swelling of the lower lip wasobserved.

Discussion

Cheilitis granulomatosa (CG) is the histopathological description of a chronic swelling of the lip caused by a granulomatous inflammation. In 1928 Melkersson described a patient with an infiltration of the lip in combination with a facial paralysis and in 1930 Rosenthal described a similar patient who presented also with a fissured tongue. Thereby the combination of a granulomatous inflammation, a facial paralysis and a fissured tongue is called the Melkersson-Rosenthal syndrome. The presence of CG without lingua plicata or facial paralysis is also called Miescher syndrome, which falls under the broader category of orofacial granulomatosis (OFG). OFG encompasses conditions characterized by non-necrotizing granulomatous inflam-mation of the oral and maxillofacial region that present clinically as labial enlargement, perioral and/or mucosal swelling, oral ulcerations and gingivitis. The unifying term "OFG" has been introduced to integrate the spectrum of various disorders which can include CG like the Melkersson-Rosenthal syndrome, Crohn's disease, sarcoidosis and infectious diseases such as tuberculosis

CG is a rare condition of which the etiology is unknown. Many factors, including allergy to foods, genetic predisposition, infection, and atopy have been implicated.

CG may also present as an oral manifestation of chronic inflammatory conditions such as Crohn's disease. It may precede involvement of other areas by several years as shown by Sanderson et al who studied a population of 35 patients with OFG without gastro-intestinal symptoms. (2) They all underwent endoscopic evaluation. Ileal or colonic abnormalities were detected in 54% of patients suggesting that the presence of an OFG should lead to an extensive gastro-intestinal check-up.

The diagnosis can be made after examination of a lip biopsy which shows granulomatous inflammation. Granulomas are noncaseating, small, scattered and contain Langerhals giant cells.

Spontaneous remission is rare and in lack of controlled trials, different therapeutic approaches have been used with regard to the primary etiology of the CG and the personal experience of physicians. When it comes to CG as a manifestation of a systemic disease like Crohn's disease, the underlying disease should be treated (3). When it comes to isolated GC treatment with topical, intralesional en systemic corticosteroids have been reported (4-6). Antibiotics such as minocycline (7), roxythromycin (8), metronidazole (9), clofazimine (10) and dapsone (11) have been used. Publications are also available on treatment with thalidomide (12) and anti-TNF (13-14) agents. Patients with persistent and disfiguring lip swelling, unresponsive to conservative treatment, may benefit from reduction cheiloplasty (15).

In conclusion, CG is a rare extra-intestinal mani-festation of Crohn's disease. It can be present before intestinal symptoms occur and responds well to treat-ment of the underlying disease. The symptoms are typically a chronic swelling of the lip(s) due to chronic inflammation. This can be confirmed on a biopsy, done before treatment.

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