Chronic lip swelling as the sole presentation of Crohn's disease: three case reports

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Chronic lip swelling may be a clinical sign of a systemic disease, such as Crohn's. We report two cases of children in Greece where the chronic lip swelling was not only the initial, but the sole clinical symptom of Crohn's, and another case with only granulomatous cheilitis up to now. All lip biopsies revealed granulomatous cheilitis. The ileocolonoscopy revealed granulomatous ileitis, and the video capsule endoscopy aphthous lesions in the jejunum in the first two cases. The diagnosis of Crohn's was then established, and treatment was started. In the third case only granulomatous cheilitis was revealed. He was started on minocycline and corticosteroids and remains under frequent monitoring in case he should develop Crohn's. Clinicians should bear in mind that inflammatory bowel disease may present with atypical symptoms. This could thus be the case for any child with persistent lip swelling, and therefore further examinations should be performed to establish the diagnosis.

Key words: lip swelling, Crohn's disease, orofacial granulomatosis, granulomatous cheilitis.

Lip swelling may present due to allergic reaction, but chronic, persistent, non-tender, non-pruritic swelling may be a clinical sign of a systematic disease, such as Crohn's disease. Orofacial granulomatosis is the persistent swelling of the orofacial area due to an underlying granulomatous inflammatory process in the absence of any recognized systematic disease[1-3], whereas granulomatous cheilitis refers in particular to the lips, with the presence of granulomas in the lip biopsy. Crohn's disease, orofacial granulomatosis (Miescher syndrome or Melkersson-Rosenthal syndrome), sarcoidosis, chronic granulomatous disease, foreign body reaction, tuberculosis, leprosy, atypical mycobacterial disease, fungal infection and allergic reaction should be considered in the differential diagnosis of granulomatous cheilitis[1, 4, 5]. Melkersson-Rosenthal syndrome is defined as a triad of orofacial granulomatosis, fissured tongue, and unilateral palsy of the facial nerve, whereas Miescher syndrome is the monosymptomatic form of the above-mentioned syndrome (orofacial granulomatosis only)[6]. In rare cases, Crohn's disease presents with extraintestinal symptoms, and not with the classical gastrointestinal symptoms[6].

Data about orofacial granulomatosis and oral Crohn's disease in children, and the relationship between these two clinical entities, are scarce. Data regarding orofacial granulomatosis as the initial manifestation of Crohn's disease are also scarce[6-8]. We report two cases of children in Greece, where a chronic, persistent swelling of the lips (granulomatous cheilitis) was not only the initial, but the sole clinical symptom of Crohn's disease, and a third case of persistent lip swelling without development of Crohn's up to now.

Case Reports

We report two cases of Crohn's disease presenting with chronic, painless lip swelling:

an 11-year-old boy with swelling of both lips for 2.5 years (Fig.1), and a 9.5-year-old girl with the same symptom for 2 years. They had no other gastrointestinal symptoms, e.g., diarrhea, abdominal pain, nor other signs, e.g., perianal lesions, and they reported no pain in the lips. They were initially treated with antihistamines for a possible allergic reaction, but showed no response to the treatment.

The lip biopsies revealed granulomatous cheilitis. Further work-ups were ordered, and ileocolonoscopy revealed granulomatous ileitis in both cases. The boy had raised levels of anti-*Saccharomyces cerevisiae* antibodies (ASCA), while the girl did not. Both children had a mildly elevated erythrocyte sedimentation rate (40 mm 1h and 25 mm 1h, respectively). They underwent a video capsule endoscopy, which revealed aphthous lesions in the jejunum (Fig. 2). A diagnosis of Crohn's disease was made in both cases, and they were started on azathioprine and corticosteroids.

The PCDAI (pediatric Crohn's disease activity index) score showed mild disease in both cases. A year later, the boy's disease was inactive, with improvement of the lip swelling after a 4-month course of minocycline, while the girl's disease remained mild, but with a lower score, with limitation of the lip swelling after treatment with corticosteroids.

Regarding the third case, the 16-year-old male patient had swelling of the lips, first of the lower and then of both lips, and painful mouth ulcers for 4 years. The lip biopsy revealed granulomatous cheilitis. No evidence of luminal disease was found in the ileocolonoscopy or the video capsule endoscopy; in addition, the erythrocyte sedimentation rate was within the normal range, and ASCA antibodies were not elevated. He was started on minocycline and corticosteroids with good results, but the symptoms relapsed after the end of treatment. He remains under frequent monitoring in case he develops Crohn's.

In all cases, examinations that might reveal other causes of granulomatous cheilitis, such as tuberculosis, sarcoidosis and chronic granulomatous disease, were performed, and these diagnoses were excluded.

Discussion

A question that needs to be answered is whether orofacial granulomatosis and oral Crohn's disease are within the spectrum of the same disease, because overlap between the two has been reported[9]. This debate often arises in the literature because patients with orofacial granulomatosis tend to develop Crohn's later on[9]. Studies suggest that patients with orofacial granulomatosis may have subclinical intestinal Crohn's disease[10-13], but this is not always the case. Orofacial granulomatosis can be the first and sometimes the sole symptom of Crohn's[6-8]. Therefore, another question needs to be answered in every case. Is there a systemic versus a non-systemic form of the disease? Is the gastrointestinal tract involved? In instances

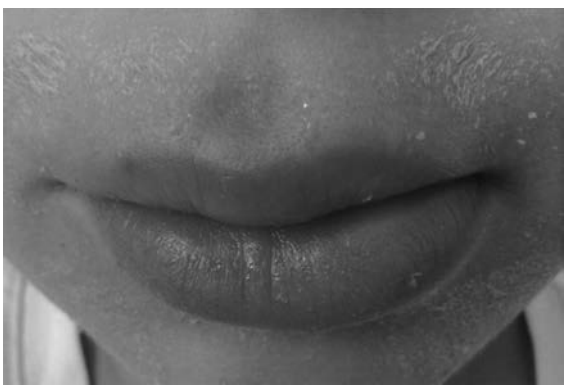

Fig. 1. Boy with chronic lip swelling.

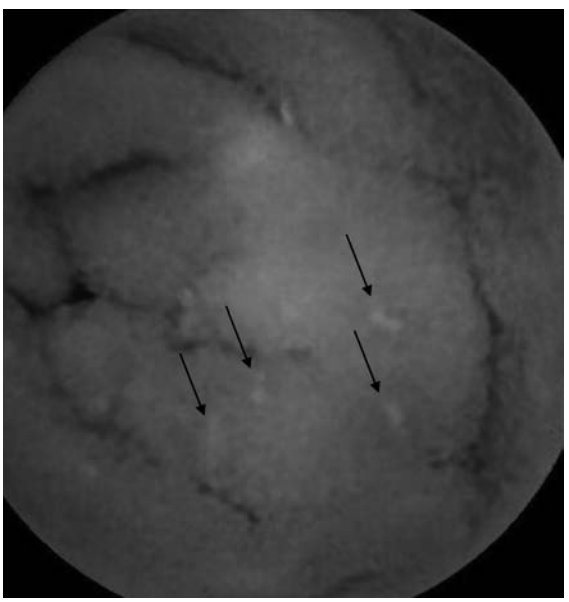

Fig. 2. Aphthous lesions in the jejunum (video capsule endoscopy).

where it is not involved, should orofacial granulomatosis be considered as Crohn's that has not yet developed, or as another clinical entity? In the second case, there would be no need for follow-up endoscopies in the patients.

Sanderson et al.[11] support the idea that orofacial granulomatosis with intestinal involvement is a new inflammatory bowel disease because the exact relationship with Crohn's is not yet known. In this study, 54% of patients with orofacial granulomatosis had detectable intestinal abnormalities without gastrointestinal symptoms, but only 2 of 35 patients had typical Crohn's in biopsies[11]. They also found that only patients with intestinal involvement had elevated ASCA levels[11, 14].

Rowland et al.[13] support the idea that oral lesions at the time of diagnosis of Crohn's disease are a marker of a more severe phenotype, and that oral activity does not match with intestinal activity. Additional follow-up studies would be required to verify the second statement.

Another question is also raised. Should a patient with chronic lip swelling and no gut symptoms, who has a normal initial endoscopy, be under frequent surveillance for subsequent Crohn's development? Some authors believe that this is mandatory, because there is a good possibility of underlying non-symptomatic systemic disease[6]. Data are scarce and there are no guidelines regarding how often such a patient should be reevaluated if there are no gut symptoms, which exam is cost-effective to use in this case, and whether these frequent medical visits influence the quality of life.

Data regarding the hypothesis that orofacial granulomatosis is the monosymptomatic form of Melkersson-Rosenthal syndrome are also controversial[4]. Some authors support the idea that they are different clinical entities because the majority of patients do not develop Melkersson-Rosenthal syndrome[15].

Many treatment options for orofacial granulomatosis/granulomatous cheilitis have been proposed, but none is considered to be the treatment of choice. Use of steroids systemically (prednisolone), intralesionally (triamsinolone injections) or topically has been proposed[1, 4]. Our experience showed that the former has good results and eliminates both oral and intestinal lesions, but the lip swelling usually relapses after the end of treatment. Other options are the use of topical tacrolimus, an exclusion diet and antibiotics[1]. We used tetracycline (minocycline) for several months in all three cases with moderate results. This is compatible with data retrieved from the literature. The third-line treatment would be surgery (cheiloplasty)[4].

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