Macrocheilia as a Manifestation of Crohn's Disease: A Case Series

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Introduction

- **Macrocheilia**- painless chronic inflammation of the labial mucosa
  - Etiologies include hypersensitivity reactions, angioedema, infectious and inflammatory disorders including **granulomatous cheilitis (GC)**, and idiopathic processes
  - Granulomatous cheilitis is a lumpy swelling of the lip that is part of the spectrum of **orofacial granulomatosis**
- **Crohn's Disease (CD)–** relapsing inflammatory disease known for GI manifestations
  - Can have skip lesions involving any area of the GI tract
  - Extraintestinal (including orocutaneous) manifestations can precede intestinal manifestations
  - **Oral manifestations of CD** include:
    - Deep linear mucosal ulcers with hyperplastic margins
    - Labial, buccal, or gingival swelling/induration
    - Cobblestone or hyperplastic appearance of the buccal mucosa
- **10% of patients with macrochelia have underlying diagnosis of CD**
  - **Lip biopsy positive for GC strongly supports the diagnosis**
  - Prevalence of OFG in Crohn's disease is unknown but increasingly seen in pediatric patients with CD

This case series serves to increase awareness among otolaryngologists of lip swelling as a manifestation of CD. In such cases, biopsy of the lip demonstrating GC strongly supports the diagnosis of CD and suggests strategies for management. Herein, we describe 3 children with macrocheilia as a manifestation of CD.

Case 1

Biopsy of the lower lip was requested for a 13-year-old male with recurrent non-pruritic lower lip swelling (Fig. 1A). The lip had previously been treated unsuccessfully with diphenhydramine. Following evaluation by Allergy and Immunology 6 months after onset of symptoms, he was started on cetirizine, budesonide/formoterol, and triamcinolone nasal spray but symptoms persisted.

A diagnosis of hereditary angioedema was made despite normal C1 esterase inhibitor testing. Patient reported no GI symptoms. Sarcoidosis was ruled out with CXR.

Biopsy was performed and pathology revealed granulomatous cheilitis. The child was referred to GI and subsequent biopsies from upper GI endoscopy and colonoscopy showed mild active ileitis with rare granuloma consistent with Crohn's ileitis. The patient started on adalimumab (Humira) and prednisone with improvement of lip symptoms documented at four month follow up (Fig. 1B).

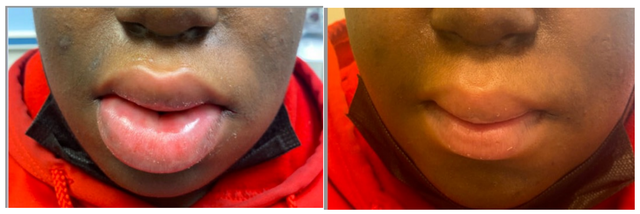

Figure 1. Image left (A): Presenting lip swelling prior to biopsy
Image right (B): Response to treatment with adalimumab (Humira)

Case 2

A 15-year-old male with 6-month history of non-pruritic lip swelling affecting mostly the lower lip was referred for possible lip biopsy (Fig. 2A & B). No triggers were identified. Patient had minimal symptomatic improvement on cetirizine and clotrimazole and continued to have intermittent lip swelling. Hereditary angioedema ruled out as C1 esterase inhibitor and C4 levels were normal.

Dermatology evaluation suggested allergic contact dermatitis. True test patches were negative and negative allergic workup.

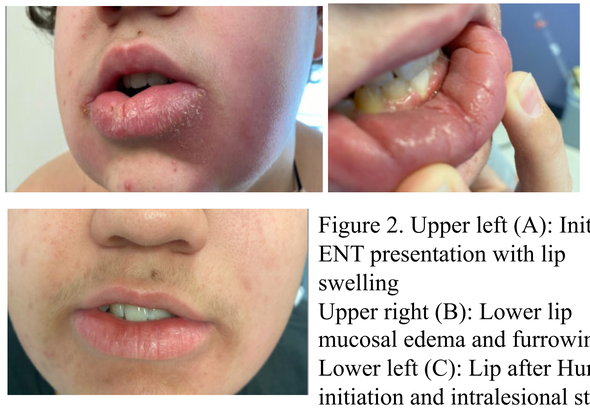

Figure 2. Upper left (A): Initial ENT presentation with lip swelling
Upper right (B): Lower lip mucosal edema and furrowing
Lower left (C): Lip after Humira initiation and intralesional steroid injection

Lip biopsy was consistent with granulomatous cheilitis. Biopsies of the GI mucosa were performed endoscopically revealing histology consistent with clinical impression of Crohn's disease. Patient started on Humira and given intralesional oral steroid injection with a 50% improvement in lip swelling at 3 month follow up (Fig. 2C)

Case 3

A 12-year-old female with known Crohn's disease on infliximab and azathioprine was referred to our pediatric ENT clinic with swelling and a weeping lesion within the lower lip vermillion. The lesion has been refractory to topical steroids. Our service felt the swelling was an oral manifestation of her Crohn's disease. Intraoral mucosal ulceration and striation was also noted. Excisional biopsy of the weepy lesion revealed chronic inflammation and focal granuloma. Patient returned one year later with swelling and fissuring of the upper and lower lips felt again to be related to her Crohn's disease. Patient underwent triamcinolone injection and continued topical triamcinolone with improvement of oral symptoms.

Given the recurrent lip swelling GI transitioned patient from infliximab (Remicade) to ustekinumab (Stelara) which successfully treated the granulomatous cheilitis. At patient's 6-month follow up her oral ulceration and fissure showed moderate improvement though she continued to have mild lower lip swelling, chronic inflammation and focal granuloma.

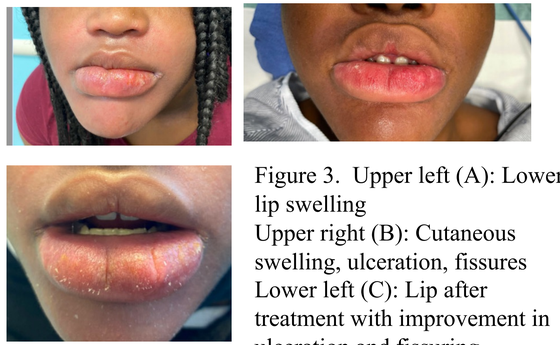

Figure 3. Upper left (A): Lower lip swelling
Upper right (B): Cutaneous swelling, ulceration, fissures
Lower left (C): Lip after treatment with improvement in ulceration and fissuring

Discussion

Herein, we describe three children with macrocheilia as a manifestation of CD, two of whom had swelling of the lip that preceded GI manifestations of the disease. A third child had a diagnosis of CD and subsequently developed macrocheilia. In all cases, lip biopsy revealed granulomatous cheilitis that suggested the diagnosis of CD. Macrocheilia responded to treatment with intralesional steroids in one case, to treatment with adalimumab in a second, and a third responded to a combination of intralesional steroids and a change of biologic to ustekinumab. Although CD is largely a gastrointestinal disorder, the otolaryngologist may be the first to see a CD patient presenting with lip enlargement. It is therefore incumbent on ENT providers to familiarize themselves with the described disorders and their management.

References may be found here:

Disclosure Statement: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.