

Lip swelling with lymphangiectasia



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INTRODUCTION

Orofacial granulomatosis (OFG) presents with orofacial swelling, secondary to intra- and perilymphatic granuloma formation. Multiple etiologic associations have been proposed, but the pathogenesis remains unclear. One frequent association is Crohn's disease (CD) in pediatric patients. In this report, we present a case of an adult presenting with recurrent lip swelling, diagnosed with OFG, and later found to have severe CD in the absence of significant gastrointestinal symptoms.

CASE REPORT

A 30-year old woman presented with intermittent swelling of the lower portion of her lip for 8 months. The swelling was painless and occasionally accompanied by clear fluid drainage. The upper portion of her lip later became involved. She reported symptomatic improvement with courses of oral corticosteroids. She had not applied any topical therapies and denied a history of seasonal allergies and cinnamon-flavored candy consumption. She denied associated stridor, shortness of breath, or any other mucosal changes. Review of systems revealed recent episodes of diarrhea and stiffness of her knees and wrists. Physical examination revealed rubbery edema of both lips with tiny vesicles (Fig 1). There was no appreciable facial paralysis or tongue changes, although a tongue piercing was in place. A biopsy was performed during her initial encounter, noting "proliferation of ectatic lymphatic channels in the lamina propria" (Fig 2). She found no improvement with doxycycline, azithromycin, topical corticosteroids, or intralesional triamcinolone. Patch testing revealed allergy to hydrocortisone. Laboratory studies, including complete blood count, antinuclear antibody, extractable nuclear antibodies, C1-esterase inhibitor, complements C1q and C4;

Abbreviations used:

CD: Crohn's disease
OFG: orofacial granulomatosis

chest x-ray, and rheumatoid factor were unremarkable. Her complete metabolic panel was significant for an albumin level of 2.5 g/dL.

A second biopsy 4 months later observed "non-necrotic granulomata in the lamina propria and edema and ectatic lymphatic vessels with intraluminal granuloma," consistent with OFG with lymphangiectasia (Figs 3 and 4). A diagnosis of OFG was rendered. During dermatologic work-up, she presented to the emergency room for diarrhea. A computed tomography scan of the abdomen suggested colitis of inflammatory etiology. She was referred to gastroenterology, and endoscopy revealed ulcers of the entire esophagus, the ileum, the transverse, descending, and sigmoid colons; and anal canal, leading to a diagnosis of CD.

DISCUSSION

Orofacial granulomatosis (OFG) most commonly presents with swelling of 1 or both lips,¹ and has been observed uncommonly to present with lymphangiectasia.² Oral mucosa and perioral skin may be involved, and some patients develop permanent swelling and disfigurement. Various pathologic factors have been proposed, including delayed hypersensitivity to dental materials or cinnamon, infections, oral dysbiosis³ and allergy.⁴ There is a strong association between allergy and OFG, regardless of the presence of CD; however, it is not yet clear whether or not allergy is an etiopathologic factor in the development of OFG.⁴ Dilated lymphatic channels and peri- or intralymphatic granuloma are seen on histopathology,⁵ as were observed in our second

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Fig 1. Swollen lips with pinpoint vesicles seen on initial presentation.

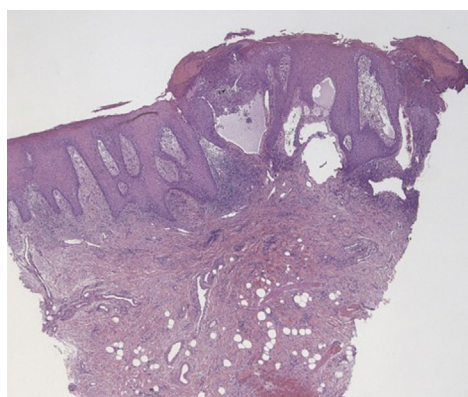


Fig 2. The first biopsy specimen, revealing ectatic lymphatic channels in the lamina propria. (Hematoxylin-eosin stain.)

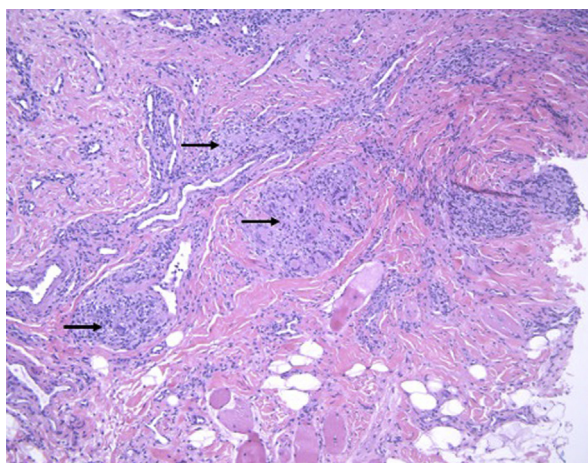


Fig 3. The second biopsy specimen, revealing granulomata (*arrows*) adjacent to dilated lymphatic channels. (Hematoxylin-eosin stain.)

biopsy. It is worth noting that the pinpoint vesicles observed initially reflected early lymphangiectatic changes and were the presenting sign of early intra- and perilymphatic granuloma aggregation. Serial

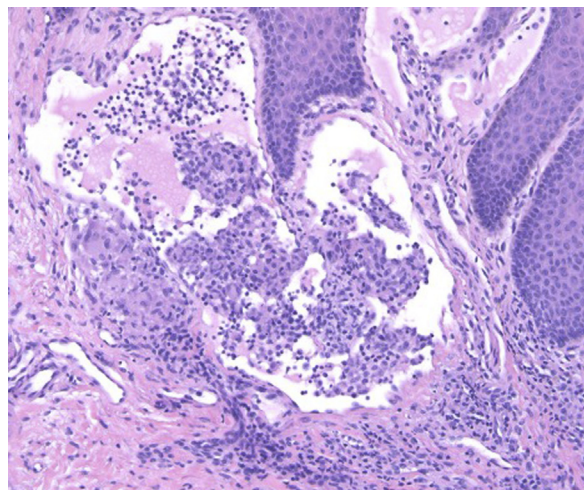


Fig 4. The second biopsy specimen, with focus on granulomata within lymphatic channels. (Hematoxylin-eosin stain.)

biopsy allowed for temporal observation of the progressive lymphatic changes that would occur in OFG.

There is a strong association between OFG and CD in pediatric patients; approximately 50% of those diagnosed with OFG will develop CD, at a mean lag time of 13 months,¹ and pediatric CD-OFG patients are more likely to have pan-enteric disease with extensive intestinal granuloma formation.⁶ The association between OFG and CD in adult patients is not well defined, and OFG does not necessarily precede the onset of CD,^{1,7} with only 20% eventually developing CD. Although judicious surveillance of pediatric OFG patients for systemic symptoms is essential, this case report serves to highlight that the OFG-CD association may also be observed in adults.

Treatment of OFG is difficult, attributed to inadequate appreciation of the etiopathogenesis.⁸ There are reports of successful treatment with topical, intralesional, and systemic corticosteroid use, although no individual treatment has eventuated as superior. Surgical management via cheiloplasty is a last resort.⁸ Recent reports have demonstrated efficacy of tumor necrosis factor- α antagonist use.⁹ Successful tandem treatment of OFG and CD with infliximab has been reported in case series, likely owing to the shared pathogenesis in these patients.⁹ The present patient started treatment with methotrexate and infliximab *per* gastroenterology and noted rapid improvement in her OFG, as well as increased energy levels and resolution of diarrhea and arthralgia. At follow-up, there was significant improvement in lip swelling, induration, and rubbery texture. No further vesicles have been observed.

It is important to include OFG in the differential diagnosis of patients with lip swelling and to screen for inflammatory bowel disease, as OFG may hallmark severe CD in the absence of significant gastrointestinal symptoms in adults as well as children.

Conflicts of interest

None declared.

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