

Granulomatous Cheilitis: A Stiff Upper Lip

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To the Editor:

A 51-year-old woman presented to her dermatologist with recurrent and progressive upper lip swelling of 2 years' duration. Her condition was previously evaluated by several other physicians without a diagnosis or resolution of the symptoms. The swelling began on the right side of the upper lip and right cheek; however, over the course of 2 years, the swelling had progressed to involve the entire upper lip with complete sparing of the lower lip. She denied pain but reported numbness of the upper lip. The patient visited her dentist who ruled out periodontal infection as the cause of the swelling. Diphenhydramine provided no relief; however, the cheek swelling resolved after a course of antibiotics prescribed by an ear, nose, and throat physician.

She consulted her primary care physician and was subsequently referred to a neurologist and allergist who were unable to provide a definitive diagnosis or complete relief of the symptoms. She denied any history of hypersensitivity reactions, odontogenic infections, gastrointestinal concerns, or any other signs or symptoms of systemic granulomatous disease.

On physical examination, the upper lip was swollen symmetrically without evidence of ulceration, fissuring, or scaling (Figure 1). Palpation of the upper lip was notable for firm, nontender, nonpitting edema without nodularity. The oral mucosa did not appear swollen or erythematous. Examination did not reveal ulceration or a cobblestone appearance.

A full-thickness skin biopsy of the upper lip was performed. Histopathology revealed perivascular

nonnecrotizing granulomas adjacent to ectatic vascular channels with associated lymphoplasmacytic infiltrate (Figure 2). Periodic acid–Schiff stain was negative for fungal hyphae, tissue Gram stain was negative for bacteria, Fite and acid-fast bacillus stains were both negative for acid-fast organisms, and polariscopy was negative for polarizable foreign material. In this clinical context, the morphologic findings were consistent with the diagnosis of granulomatous cheilitis (GC).

Granulomatous cheilitis is a rare disorder of the lips and orofacial mucosa that was first described by Meischer¹ in 1945 as persistent or recurrent orofacial swelling secondary to lymphatic obstruction by granulomatous proliferation. It often has been described as a monosymptomatic form of Melkersson-Rosenthal syndrome (MRS). In its entirety, MRS constitutes a triad of GC, facial nerve palsy, and lingua plicata (also known as fissured tongue).^{2,3} Although many authors agree that GC is associated with MRS, some believe that GC is a distinct entity because the majority of patients who present with GC subsequently do not develop MRS.⁴



Figure 1. Upper lip swelling without ulceration, fissuring, or scaling. The lower lip was completely spared.

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The authors report no conflict of interest.

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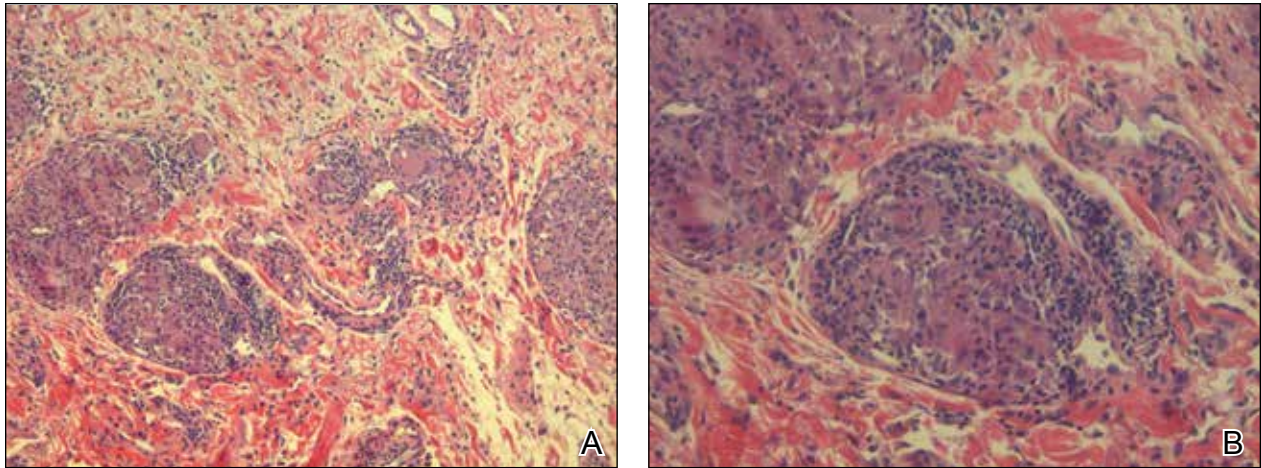


Figure 2. Upper lip biopsy showed dermal edema, vascular ectasia, perivascular nonnecrotizing granulomas, and perivascular lymphocyte predominant inflammatory infiltrate (A)(H&E, original magnification $\times 100$). Higher magnification of granulomas with perivascular lymphoplasmacytic infiltrate (B)(H&E, original magnification $\times 200$).

Despite its relationship to MRS, the true incidence of GC largely is unknown. The onset of disease usually occurs in early adulthood but can present in middle-aged or older individuals.

The typical course of GC is relapsing and remitting, nontender and nonpitting swelling of the lips that eventually becomes permanent, leading to possible facial distortion and disability. Involvement of the upper lip is the most common, followed by (in order of decreasing frequency) the lower lip and cheeks.⁵ The swelling may be unilateral or bilateral and generally is not associated with ulceration, fissuring, or scaling; however, these complications have been reported in the terminal stages of the disease in which the macrocheilia has become permanent.

Despite the controversy over the etiology, pathophysiology, and classification of GC, it largely is accepted that when a patient presents clinically with a history of recurrent or persistent lip swelling, a full-thickness skin biopsy of the involved oral mucosa should be taken. Conditions that are considered in the differential diagnosis of orofacial granulomatosis are systemic granulomatous diseases that are known to have oral manifestations including Crohn disease, sarcoidosis, and mycobacterial infections. Given the many causes of orofacial and labial swelling, GC is a diagnosis of exclusion based on a thorough history and physical examination as well as appropriate diagnostic studies, with the cornerstone of the diagnosis resting on the histologic appearance of the lesion. Histologically, the diagnosis lies in the demonstration of granuloma formation, consisting of collections of epithelioid histiocytes and Langerhans giant

cells. Once granuloma formation is documented, special stains are used to rule out other granulomatous diseases.

Intralesional steroids have been reported to provide the greatest improvement; however, in the majority of patients, multiple treatments are required.^{6,7} Allen et al⁸ suggested that the efficacy of intralesional therapy increases when preceded by local anesthesia of the lip, thus allowing larger doses of triamcinolone to be tolerated by the patient. Systemic corticosteroids also have been used with moderate success, but the side effects of long-term systemic corticosteroid therapy make this treatment option less appealing.⁹ Other agents with known anti-inflammatory properties also have been used that may offer better side-effect profiles when used for long-term suppressive therapy, including clofazimine, dapsone, sulfapyridine, danazol, hydroxychloroquine, and antibiotics such as doxycycline and metronidazole.¹⁰

In severe or recalcitrant cases, surgical intervention by way of a reduction cheiloplasty is considered by some to be an appropriate next step in therapy but is rarely needed. Postoperative intralesional steroid injections are necessary due to reported cases of worsening disease when injections are discontinued after cheiloplasty.^{11,12}

Our patient was treated with 5 mg of intralesional triamcinolone acetonide with 10 separate injections of 0.5 cc each along the affected portions of the upper lip. She also was given doxycycline 100 mg once daily for 30 days. The patient reported complete resolution of the upper lip swelling 7 days after the

initiation of therapy. At 1-month follow-up, she reported that the swelling had completely resolved. However, 1 day prior to the scheduled visit, shortly after finishing the course of doxycycline, she noted recurrent swelling. Due to the concomitant initial administration of both the steroid injections and doxycycline, it was unclear which treatment had provided relief. To avoid, or at least delay, the need for chronic intralesional steroid injections, another course of 40 mg doxycycline daily was prescribed. After 2 weeks, the patient reported that the swelling had markedly improved. The patient has maintained remission of the symptoms for approximately 6 months on daily suppressive therapy with 40 mg of doxycycline.

The recurrence of lip swelling after therapy, as in our patient, is typical of GC, and most cases require multiple follow-up visits and frequent alterations in therapy, which is often frustrating for both the patient and physician. However, awareness of this disease entity, its natural course, and the therapeutic options will allow physicians to more appropriately counsel and educate patients of this uncommon disease process.

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