Orofacial granulomatosis successfully treated with mycophenolate mofetil

To the Editor: Orofacial granulomatosis (OFG) is a chronic, relapsing, potentially disfiguring inflammatory disorder of unknown etiology. It is characterized by persistent enlargement of the orofacial tissues and noncaseating granulomatous inflammation on tissue biopsy in the absence of diagnosable Crohn disease or sarcoidosis. It is thought that OFG represents a spectrum of disease ranging from localized granulomatous inflammation of the lips (cheilitis granulomatosa, Miescher cheilitis) to persistent lip or facial swelling with mucosal ulceration, recurrent facial paralysis, and lingual fissuring (Melkersson-Rosenthal syndrome). Due to its unknown etiology and unpredictable clinical course, no definitive pharmacologic therapy is yet available. We present a case of OFG successfully treated with mycophenolate mofetil (MMF), suggesting this treatment may be of benefit in these patients.

A 59-year-old Caucasian woman with a history of systemic lupus erythematosus, hepatitis C, and recurrent herpes labialis presented with a 4-month history of rash and swelling of her upper lip. The lesion started as a “cold sore” with occasional burning and mild pruritus. The lesion started as a “cold sore” with occasional burning and mild pruritus. She was treated with oral steroids and amoxicillin by her primary care physician with temporary relief and was referred for further evaluation by a dermatologist. Her condition was persistent with erythema, mild scaling, and diffuse swelling of the upper lip extending to the right oral commissure and lower lip. No other oral mucosal or lingual lesions were noted and she...
denied any constitutional, respiratory, or gastrointestinal symptoms.

A biopsy of her upper lip revealed chronic dermal inflammation with focal noncaseating granuloma formation (Fig 1). Gram, Fite, and periodic acid–Schiff stains were negative. Complete blood count, serum angiotensin-converting enzyme, C-reactive protein, tuberculin skin test, chest radiographs, funduscopic examination, and prior colonoscopy were all unremarkable. Based on these findings, OFG was diagnosed.

High-potency topical steroids, valacyclovir, and doxycycline yielded no improvement. Systemic steroids were discussed as a treatment option but were contraindicated due to history of avascular necrosis of the hip, and she refused intralesional steroid injections. She was started on MMF 500 mg twice daily with significant improvement after 1 month and near complete return to baseline orofacial structural anatomy after 6 months of therapy (Fig 2). At 1 year of MMF monotherapy, she continues to be disease-free with no clinical or laboratory adverse effects of treatment.

MMF is a potent immunosuppressant widely described in the dermatology literature for its attractive safety profile and effectiveness in a variety of inflammatory skin conditions. Two patients with OFG treated with MMF in combination with topical therapy (corticosteroids and/or tacrolimus) have been reported, although with unclear protocols and outcomes. A search of PubMed and Google Scholar using the terms “mycophenolate mofetil” and “orofacial granulomatosis,” “cheilitis granulomatosa,” “Miescher cheilitis,” or “Melkersson Rosenthal syndrome” showed no previous reports of MMF used as a single-therapy agent in the successful treatment of OFG. MMF may be a beneficial treatment option for these patients, particularly in those who cannot tolerate systemic or intralesional corticosteroid therapy.

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Reversible aquagenic pruritus associated with testosterone-induced erythrocytosis

To the Editor: A 59-year-old healthy man presented for evaluation of new-onset aquagenic pruritus. He started testosterone replacement therapy (200 mg daily) 7 months before presentation for low testosterone level of unknown cause; testicular biopsy at that time revealed normal findings. Four months after beginning testosterone replacement, he noticed generalized intense burning and pruritus, specifically during and after showering, without evidence of rash. Empiric use of emollients and antifungal cream did not alleviate the pruritus. He could not tolerate antihistamines because of drowsiness. On evaluation, his full-body skin examination revealed normal findings. This history and examination are consistent with aquagenic pruritus, which typically presents without cutaneous signs.1 Because aquagenic pruritus is most often associated with polycythemia vera (PCV),2 hematologic studies were performed, revealing an elevated hematocrit of 51.2%, notably higher than his normal baseline of 46.5%. The remainder of his complete blood cell count and differential, renal and liver function tests, antinuclear antibody, and thyroid studies were normal.

Because the aquagenic pruritus tightly coincided with the initiation of his testosterone replacement therapy, the patient’s testosterone dose was tapered to 50%, which resulted in significant improvement in his symptoms; his hematocrit also normalized to baseline levels (Fig 1). Given that his erythrocytosis and his symptoms were improving, the patient was recommended to continue routine monitoring of his hematocrit levels and did not undergo further diagnostic evaluation for hematologic malignancy.

Although most patients with aquagenic pruritus do not have underlying disease, when associated with systemic conditions, PCV is diagnosed in approximately 30% of cases of aquagenic pruritus.3,4 Aquagenic pruritus is reported by approximately 5% to 69% of patients with PCV and may precede the diagnosis of PCV by many years.3,4 Aquagenic pruritus may also occur in the setting of myelofibrosis, malignancy, medications (bupropion, antimalarials), and lactose intolerance.1 However, little is known about the mechanism or pathophysiology of aquagenic pruritus. One study looking at skin biopsy specimens taken from patients with PCV and aquagenic pruritus demonstrated increased skin mast cells, mononuclear cells, and eosinophils.3

Fig 1. Aquagenic pruritus associated with testosterone-induced erythrocytosis: clinical course, hematocrit level, and testosterone dosage.