Topical ruxolitinib for the treatment of granuloma faciale

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Key words: eosinophil-associated dermatosis; granuloma faciale; interferon-gamma; interleukin-5; JAK inhibitor; janus kinase; pathogenesis; ruxolitinib; topical ruxolitinib; treatment.

INTRODUCTION

Granuloma faciale (GF) is a rare, chronic, and benign eosinophilic dermatosis that predominantly affects middle aged adults, particularly White men. It typically presents as a solitary, asymptomatic red-brown plaque on the face. Histologically, GF classically demonstrates a grenz zone, a mixed inflammatory infiltrate (neutrophils, plasma cells, eosinophils, lymphocytes, and histiocytes), leukocytoclastic vasculitis and fibrosis. First line treatment is intralesional triamcinolone; however, GF is typically resistant to therapy. Here, we present a case of GF in a 75-year-old woman successfully treated with topical ruxolitinib.

CASE

A 75-year-old White female presented to our clinic with a solitary, asymptomatic, well circumscribed, red-brown plaque on her right forehead that has been present for months (Fig 1, *A*). A thorough physical exam and review of medications was nonrevealing. Other history was also noncontributory. A shave biopsy was performed and histology was consistent with GF (Fig 2). The patient was initially treated with intralesional triamcinolone (5 mg/cc) every 6 weeks and tacrolimus ointment (0.1%) twice daily for 6 months with only modest improvement (Fig 1, *B*). She was then treated with topical ruxolitinib cream (1.5%) twice daily for 3 months while previous therapies were discontinued; she was followed at monthly intervals and demonstrated greater improvement as evidenced by her previous photos (Fig 1, *C*). She did not experience any adverse effects from topical ruxolitinib.

Abbreviations used:

GF: granuloma faciale
JAK: Janus kinase

DISCUSSION

GF is a rare, chronic, and progressive eosinophil-associated dermatosis that affects adults over 50, with a slight predilection for white males.[1] It is regarded as a benign IgG4-related disease limited to the skin.[1,2] GF usually presents as a solitary, asymptomatic, red-brown papule, nodule, or plaque on the face. Lesions may demonstrate follicular accentuation and telangiectasia.[1] Uncommonly, patients present with extrafacial involvement or multiple lesions. The differential diagnosis includes erythema elevatum diutinum, pseudolymphoma, lymphomas, tumid lupus, and granulomatous conditions (eg, sarcoidosis).

Histologically, there is typically a grenz zone with a perivascular and interstitial infiltrate of neutrophils, eosinophils, lymphocytes, histiocytes, and IgG4-bearing plasma cells.[1-3] Features of LCV are most evident early on with chronic lesions having fewer neutrophils, more eosinophils and plasma cells, and lamellar fibrosis.[1-3] Despite the name of the condition, there are no granulomas on histology.[2,3]

Although the exact pathogenesis is unknown, there is evidence of high levels of interleukin 5 and interferon-gamma expression in lesions of GF.[3,4] By

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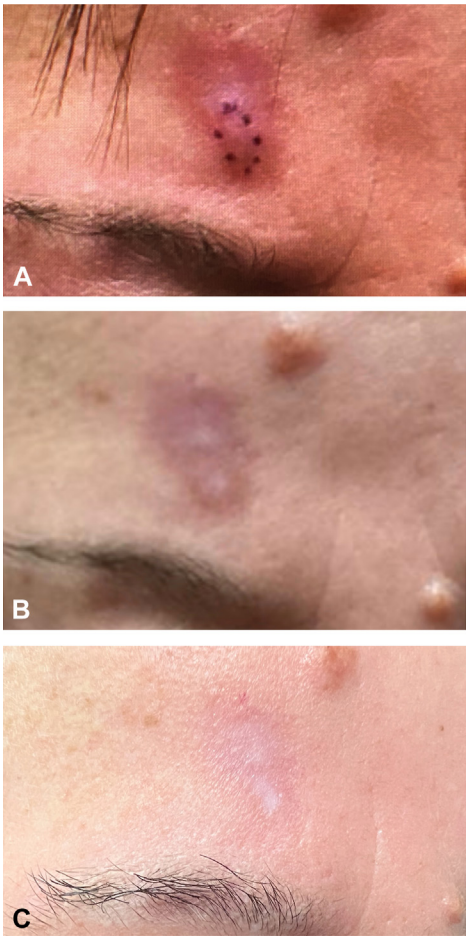

Fig 1. Granuloma faciale. A solitary and well circumscribed *red-brown* plaque above the *right* eyebrow; image taken at the time of biopsy (**A**). Modest improvement after 6 months of treatment with intralesional triamcinolone and topical tacrolimus (**B**). Greater improvement noted with topical ruxolitinib being used 3 months (**C**).

reducing eosinophil recruitment and the adaptive immune response via inhibiting interleukin 5 and interferon-gamma signaling respectively, Janus kinase (JAK) inhibitors such as ruxolitinib have the potential to control the abnormal inflammatory environment. In theory, this is likely the reason our patient improved with topical ruxolitinib therapy.

As GF is usually resistant to current therapies like intralesional triamcinolone and topical tacrolimus, topical ruxolitinib and other JAK inhibitors have the potential to be safe and reliable therapeutic options. Of note, there is a report of refractory GF successfully treated with adjunct topical tofacitinib.[5] The patient failed to adequately respond to oral dapsone, methotrexate and hydroxychloroquine, intralesional triamcinolone, and topical clobetasol; however, once tofacitinib was added to the patient's treatment regimen, she demonstrated significant improvement.[5]

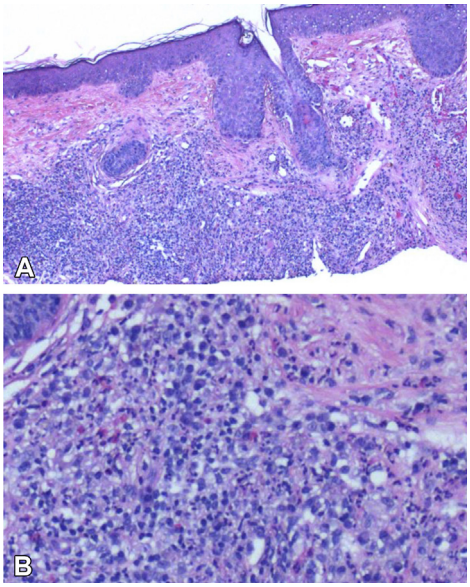

Fig 2. Granuloma faciale histology. There is a dense mixed dermal inflammatory infiltrate with sparing of adnexal structures and a prominent a grenz zone (**A**). The infiltrate is composed of lymphocytes, eosinophils, neutrophils, and plasma cells, and there is leukocytoclasis present (**B**).

No side effects were reported after the addition of topical tofacitinib.[5] We did not find any reports of oral JAK inhibitors being used to treat GF.

In conclusion, topical ruxolitinib represents a promising treatment for GF as inflammatory mediators associated with the development of this disorder (interleukin 5 and interferon-gamma) signal via the JAK pathway. Further randomized control studies are needed to verify its efficacy, safety, and optimal dosage for this condition.

Conflicts of interest

None disclosed.

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