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Successful treatment of refractory generalized granuloma annulare with abrocitinib

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Dear Editor,

Granuloma annulare is a chronic inflammatory skin disorder characterized by annular dermal papules and plaques.[1] While localized forms often resolve spontaneously, generalized granuloma annulare tends to persist and frequently proves resistant to conventional therapies.[2] The pathogenesis of the disease remains unclear, but increasing evidence suggests a dysregulated immune response involving T cells, macrophages, and cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin (IL)-6, and interferon-gamma (IFN-γ).[3] Given the chronic nature of generalized granuloma annulare and the limitations of standard treatment options, novel targeted therapies are needed. Janus kinase (JAK) inhibitors, which modulate multiple inflammatory pathways, have emerged as promising agents in dermatologic and autoimmune diseases.[4,5] Their role in granuloma annulare, however, has yet to be established.

In this report, we present the successful treatment of refractory generalized granuloma annulare with abrocitinib, a JAK1-selective inhibitor, highlighting its potential as an alternative therapeutic option. A 72-year-old woman with a 10-year history of type 2 diabetes mellitus presented with widespread erythematous annular plaques affecting the right temple, neck, dorsal trunk, and upper extremities. The lesions had been persistent for more than three years and were associated with significant pruritus and discomfort, severely impacting her quality of life. Histopathologic examination confirmed the diagnosis of granuloma annulare, showing palisading histiocytes surrounding degenerated collagen with dermal mucin deposition. The patient had previously undergone treatment with hydroxychloroquine at a dose of 400 mg per day for six months, cyclosporine at 3 mg/kg per day for four months, and dapsone at 100 mg per day for five months. All these therapies failed to achieve meaningful clinical improvement. Given the refractory nature of her condition, treatment with abrocitinib 100 mg daily was initiated.

Within the first month of treatment, the patient exhibited marked improvement, with a significant reduction in erythema and flattening of the lesions (Figure 1). By the sixth month, complete clearance of the skin lesions was observed, with only mild post-inflammatory hyperpigmentation persisting. Importantly, the patient experienced total relief from pruritus and discomfort, dramatically improving her quality of life. No adverse effects were reported, and her metabolic parameters, including glycemic control, remained stable throughout the treatment course. At the nine-month follow-up, the patient remained lesion-free, with no signs of recurrence.

Generalized granuloma annulare presents a significant therapeutic challenge due to its chronic, relapsing nature and frequent resistance to conventional treatments.[1] The lack of an established,

universally effective therapy highlights the need for innovative approaches that target the underlying immunologic mechanisms.

Emerging evidence suggests that granuloma annulare is driven by a dysregulated inflammatory response, with IFN-γ, TNF-α, and IL-6 playing a key role in its pathogenesis.[1,6] JAK inhibitors effectively suppress these pro-inflammatory mediators, making them a rational therapeutic choice for granuloma annulare.[3,7] Abrocitinib, a JAK1-selective inhibitor, has demonstrated efficacy in atopic dermatitis, a condition with overlapping inflammatory pathways.[8]

This case illustrates that JAK inhibition not only induces rapid clinical remission but also alleviates pruritus, a primary symptom of granuloma annulare, reinforcing its potential as a targeted therapy for refractory cases.

A common critique regarding the treatment of granuloma annulare is the possibility of spontaneous resolution. While localized forms may remit without intervention, generalized granuloma annulare that persists for over three years and proves resistant to multiple systemic treatments is unlikely to resolve spontaneously.[1] Another concern involves the long-term safety of JAK inhibitors, particularly in elderly patients with comorbidities. Although long-term monitoring is essential, this patient tolerated the treatment well, with no adverse effects and stable metabolic parameters. Furthermore, given the cytokine-driven pathogenesis of granuloma annulare, the use of JAK inhibitors represents a mechanism-based approach rather than an empirical therapeutic attempt.[7]

Additional studies are needed to confirm their efficacy and define their role in long-term disease management. This case highlights the potential of JAK inhibition as an effective treatment for refractory generalized granuloma annulare. Abrocitinib induced complete clinical resolution, rapidly alleviated symptoms, and was well tolerated. Given the failure of conventional therapies in chronic granuloma annulare, JAK inhibitors should be considered in selected cases with persistent disease. Future controlled studies are warranted to establish their long-term efficacy and safety profile in this setting.

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Figure 1. Clinical presentation of disseminated granuloma annulare before and after one month of treatment with abrocitinib (100 mg daily). **a**, **b**) Baseline: erythematous annular plaques on the neck, dorsal trunk, and right temporal region. **c**, **d**) After one month of therapy: marked reduction in erythema and lesion flattening, with significant clinical improvement.