

## Successful Treatment of Generalized Granuloma Annulare with Pentoxifylline

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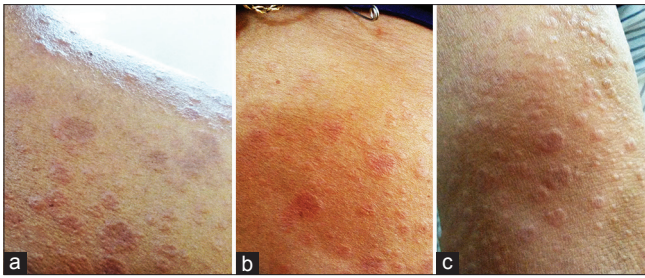
Granuloma annulare is a necrobiotic disorder of unknown etiology. The clinical variants include localized, generalized, perforating and subcutaneous types.<sup>[1]</sup> Generalized granuloma annulare is characterized by skin colored or erythematous papules in an annular configuration, with pruritus being the prominent complaint.

Therapy is usually disappointing. Various forms of therapies reported with variable response are steroids, dapsone, cyclosporine, systemic retinoids, phototherapy and rifampicin, ofloxacin and minocycline (ROM) therapy.<sup>[2]</sup> Here, we are reporting a case of generalized granuloma annulare which was successfully treated with pentoxifylline.

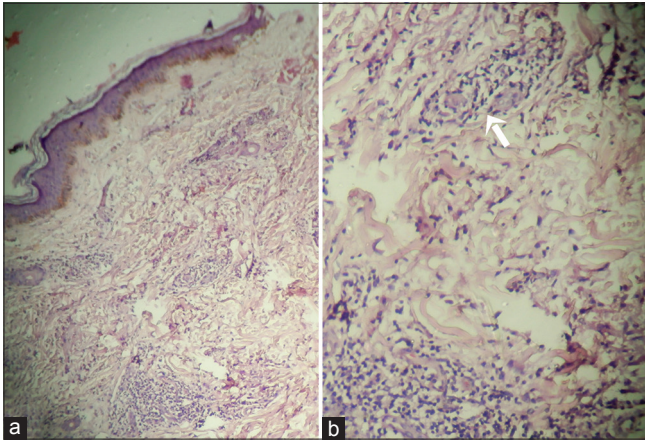
A 60-year-old female presented with multiple reddish itchy lesions on the back and forearms since 2 years. She was a diabetic, with no other comorbidities. The lesions were initially noted on the dorsum of the left hand, which slowly progressed to involve the forearms,

abdomen, back and lower limbs over 3 months. On examination, multiple erythematous annular plaques with beaded borders were present on the upper limbs, lower limbs and trunk sparing the face, oral and genital mucosa [Figure 1]. She had consulted many doctors and was given topical steroids and phototherapy with no improvement.

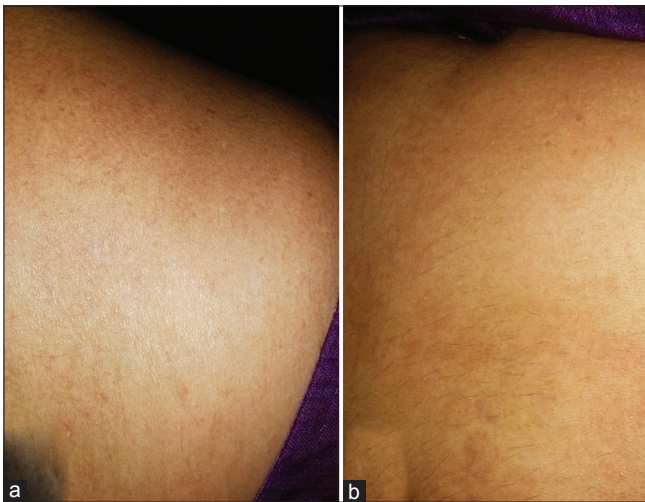
Routine investigations were unremarkable other than those for elevated blood sugars. Skin biopsy showed foci of degenerated collagen in the dermis with histiocytes and lymphocytes arranged in an interstitial pattern, suggestive of interstitial granuloma annulare [Figure 2]. Owing to the lack of response to multiple treatment modalities and the generalized involvement, after reviewing the literature, a trial of pentoxifylline was given in a dose of 400 mg thrice a day, along with emollients. She responded in a month without any adverse effects, and a dramatic improvement was seen in 3 months. No recurrence was seen at 6-month follow up [Figure 3].



**Figure 1:** Annular erythematous plaques on (a) upper back, (b) abdomen, and (c) forearm



**Figure 2:** (a) Dermis showing necrobiotic granulomas (H and E,  $\times 100$ ). (b) High power view showing lymphohistiocytic infiltration in an interstitial pattern (arrow) (H and E,  $\times 400$ )



**Figure 3:** Complete resolution of lesions after 3 months of duration (a and b)

First described by Colcott Fox in 1895 and named by Radcliffe Crocker in 1902, granuloma annulare is a benign, usually self-limited, inflammatory skin disease.<sup>[1]</sup> Trauma, insect bites, viral infections and certain drugs are known triggers. Proposed pathogenetic mechanisms include a delayed type hypersensitivity response and an immunoglobulin mediated vasculitis.<sup>[1]</sup>

Generalized granuloma annulare has a protracted course with only rare spontaneous resolution. It

comprises 8–15% of all the cases.<sup>[3]</sup> Diabetes has been reported in 21% of generalized granuloma annulare.<sup>[4]</sup> Laboratory abnormalities such as hyperlipidemia, hypergammaglobulinemia and presence of circulating antinuclear antibodies have been observed.<sup>[4]</sup> Investigations of our patient did not reveal any of these abnormalities except for high blood sugars. As described earlier, the histopathological changes in our patient were typical of interstitial granuloma annulare, which is the most common pattern reported in generalized granuloma annulare.<sup>[4]</sup>

Generalized granuloma annulare is poorly responsive to therapy. Because our patient had an unsatisfactory response to multiple treatment options, pentoxifylline was given which showed a striking response.

Pentoxifylline is a phosphodiesterase inhibitor which is commonly used in intermittent claudication. Its dermatological uses include Raynauds phenomenon, livedoid vasculopathy, necrobiosis lipoidica and venous ulcers. Even though the drug has been in use since many decades, novel indications are emerging even in recent times.

Pentoxifylline has been successfully used in generalized granuloma annulare by Rubel *et al.*<sup>[5]</sup> and Patrascu *et al.*<sup>[6]</sup>

The exact mechanism of action of pentoxifylline in granuloma annulare is not known. We postulate that, in granuloma annulare, pentoxifylline, probably with its TNF alpha blocking action, inhibits macrophage activation, and hence the granulomatous inflammation. Moreover, with its anti-inflammatory action, it may also reduce the vasculitis occurring in granuloma annulare.

With its favorable toxicity profile and familiarity among dermatologists, pentoxifylline may be a good choice for this difficult to treat and distressing condition. We report this case as resolution of lesions of granuloma annulare with pentoxifylline has rarely been reported.

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### *Conflicts of interest*

There are no conflicts of interest.

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