

## Localized Perforating Granuloma Annulare

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**ABSTRACT** Perforating granuloma annulare (PGA) is a rare type of granulomatous skin disease. The etiology and pathogenesis of PGA are still unknown. Diagnosis and treatment of PGA is complex and challenging. We present the case of a 31-year-old male patient with a localized form of PGA successfully treated with topical steroids.

**KEY WORDS:** perforating granuloma annulare, localized granuloma annulare, granuloma

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### INTRODUCTION

Granuloma annulare (GA) is a chronic, relatively common, benign inflammatory skin condition of an unknown etiology. The clinical variants of GA include localized, generalized, disseminated, subcutaneous, perforating, and arcuate dermal erythema (1-4). Perforating granuloma annulare (PGA) is a rare subset of GA which usually manifests in children and young adults (5). PGA is divided into two distinct types: localized, where lesions are present mostly in the upper limbs and palms or with predilection for the lower limbs, and generalized, involving the abdominal area, trunk, and both upper and lower limbs (5). Treatment of PGA and GA in general is not always successful, and deciding which treatment option to choose for the patient can be challenging due to the lack of detailed clinical trials that would confirm treatment efficacy.

### CASE REPORT

A 31-year-old male patient was referred to our Department with a one-month history of asymptomatic erythematous and papulopustular lesions on the dorsum of his hands (Figure 1). He was

otherwise healthy and was taking no medications. He had elbow and foot fractures 10 years before referral, which were properly treated. There was no history of recent trauma, insect bites, or excess solar exposure. A physical examination showed multiple indurated erythematous papules and papulopustules, partially with central umbilication and sparse desquamation affecting the dorsal part of his hands and wrists (Figure 1). Laboratory tests which included complete blood cell count, biochemistry, serology for syphilis, HIV, and hepatitis B and C infection together with chest X-rays were all within normal limits, with the exception of elevated liver enzymes (alanine transaminase (52 U/L), aspartate transaminase (362 IU/MI), and gamma-glutamyl transpeptidase (176 U/L). Abdominal ultrasound examination found no abnormalities. Quantiferon test was positive, while a purified protein derivative (PPD) skin test was negative. Mycological swabs taken from the dorsal parts of both hands were negative. A biopsy from the umbilicated papule from the dorsal side of the right hand was compatible with PGA showing dermal necrosis with sparse



**Figure 1.** Localized form of perforating granuloma annulare (PGA). Erythematous and papulopustular lesions on the dorsum of the hands, partially with central umbilication and sparse desquamation.

mucin deposits surrounded by a of palisade histiocytes and multinucleated foreign body giant cells (Figure 2a and Figure 2b). One section showed epidermal perforation and a channel which communicated with necrobiotic granuloma (Figure 2b). PAS staining was negative. To exclude *Mycobacterium spp* or fungal infection as a possible etiology of granuloma found in the skin biopsy specimen, two pieces were sent for mycological culture and PCR detection, which were both negative. The patient was treated with beta-methasone dipropionate cream under occlusion for three weeks followed by neutral creams. Two months after treatment, only residual hyperpigmented macules were present with no further recurrences of lesions on follow-up appointments (Figure 3).

## DISCUSSION

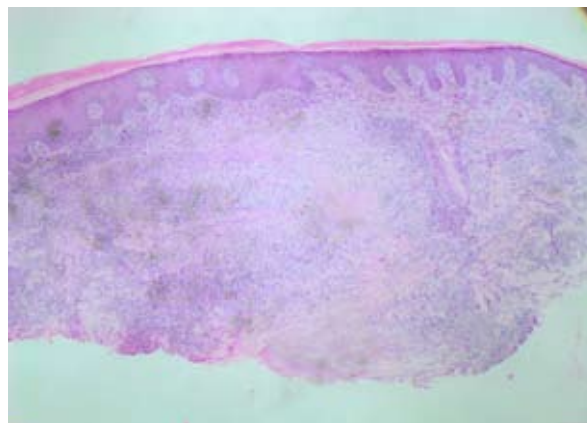
Granuloma annulare is easily clinically diagnosed in its localized form, but less so in its rare forms, when skin biopsy is the golden standard for establishing the correct diagnosis (6). The lesions in PGA are usually present as crusty, scaly, umbilicated, flesh-colored or pustule-like papules of 1-5 mm as well as plaques and scars (5). Although resembling pustules, the lesions are not truly pustular lesions but degenerated collagen extruding through the epidermis, which can be usually confirmed by histological examination (5). Patients with PGA are usually asymptomatic; however, pain and itching may appear in up to 25% of cases (5).

A generalized form of PGA is usually associated with systemic illness such as diabetes mellitus, HIV, HBV, HCV infection, lymphoma, thyroiditis, etc. (6).

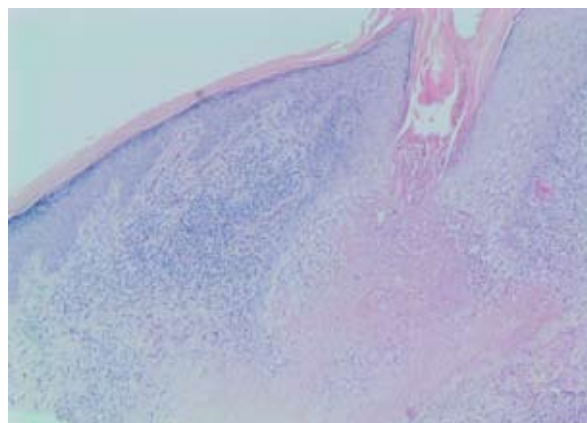
It has been suggested that in the etiopathogenesis of GA the presence of immune system imbalance

results in necrobiotic granulomas and extracellular matrix degeneration and remodeling (7,8). According to some studies, immune reaction includes delayed-type hypersensitivity with vasculitis and tissue changes (9-11). Furthermore, studies have shown that the immune process of delayed hypersensitivity, in which infiltration of helper T-cells with receptor for  $\text{INF-}\gamma$  and macrophage expression of  $\text{TNF-}\alpha$  and matrix metalloproteinases, could lead to tissue damage and formation of granulomas (12,13). There are some indications that it is not only collagen alteration, but also elastic fiber degeneration that can lead to GA (14). The pathogenesis of the perforating process in PGA is still unknown. However, it could be due to the epidermal destruction, an ischemic consequence of vascular destruction and necrobiotic granuloma or a transepithelial elimination process (7).

The etiology of GA is also still unknown. The possible etiologies include infections, diabetes, minor



**Figure 2a.** Dermal necrosis with sparse mucin deposits surrounded by a palisade of histiocytes and multinucleated foreign body giant cells. Hematoxylin and eosin  $\times 2$ .



**Figure 2b.** Epidermal perforation and a channel which communicates with necrobiotic granuloma. Hematoxylin and eosin  $\times 4$ .



**Figure 3.** Residual hyperpigmented macules 2 months after treatment.

trauma, thyroiditis, insect bite reactions, but also co-existence of multiple factors (1,2,15,16).

Treatment options for GA depend on the clinical presentation. Systemic treatment is used for generalized or disseminated forms, along with other options such as topical treatment and psoralen and ultraviolet A (PUVA) therapy or pulsed diode laser (PDL) (17). However, PDL treatment has shown better success in treating localized than generalized forms (18). Systemic treatment includes immunomodulatory and immunosuppressive drugs such as isotretinoin, dapsone, and tacrolimus (7,20). In some case reports, treatment with dapsone was successful in both generalized and localized forms of GA (7,17,19,20). The second line of treatment includes antimalarials, systemic steroids, cyclosporine, pimecrolimus, anti-TNF- $\alpha$  agents such as adalimumab and infliximab, and vitamins (5).

We presented a case with localized PGA successfully treated with topical steroid cream for three weeks under occlusion. There have been few reports of successful treatment of PGA with local steroid cream alone or combined with liquid nitrogen (21-23). Other successful options for localized form are imiquimod cream, PDL, photodynamic therapy, high-dose UVA1, and surgical treatment (5,24,25). However, the majority of localized PGA forms are self-limiting (5,26,27). Rare and generalized cases must be recognized and checked for comorbidities and other physical symptoms (28,29).

## CONCLUSION

The etiology and pathogenesis of PGA are still unknown and diagnosis and treatment are complex and challenging. Local steroid treatment could be successful in localized PGA forms, although there are many other treatment options. Considering the

therapeutic difficulties of PGA cases, it is notable that our patient showed regression of lesions with only 3 weeks of local corticosteroid treatment.

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