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Case Report

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Patch-Type Granuloma Annulare: A Therapeutic and Diagnostic Challenge

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ABSTRACT

Granuloma annulare (GA) is a common, benign, chronic inflammatory disorder, which is characterized by grouped papules in an annular shape. It has been described in several clinical subtypes, including localized, generalized, subcutaneous, perforating, and erythematous. Herein, we report a 65-year-old woman with pruritic erythematous patches, mimicking mycosis fungoides, which occurred on the abdomen and thights and showed typical clinical and histopatologic findings of erythematous GA.

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Case report

A 65-year-old white woman was referred to our clinic with a 2-year history of asymptomatic erythematous patches increasing in diameter on her abdomen and thighs.

Examination of the abdomen and thighs revealed large erythematous, non-scaly, oval patches, with no induration or atrophy (Figures 1 & 2). Skin sensitivity tests were normal. Physical examination was otherwise unremarkable.

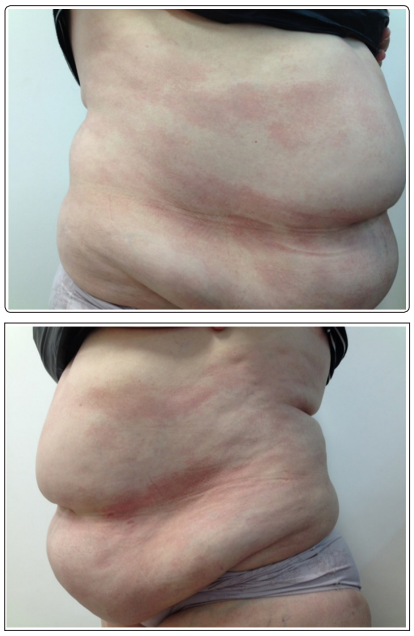

Figure 1 & 2: Erythematous oval patches, non-scaly, with no induration or atrophy on the abdomen

Histopathological examination revealed a moderate superficial and mid-dermal interstitial infiltrate of lymphocytes and histiocytes, and mucin between collagen fibers (Figure 3). These findings are consistent with the interstitial variant of granuloma annulare [1].

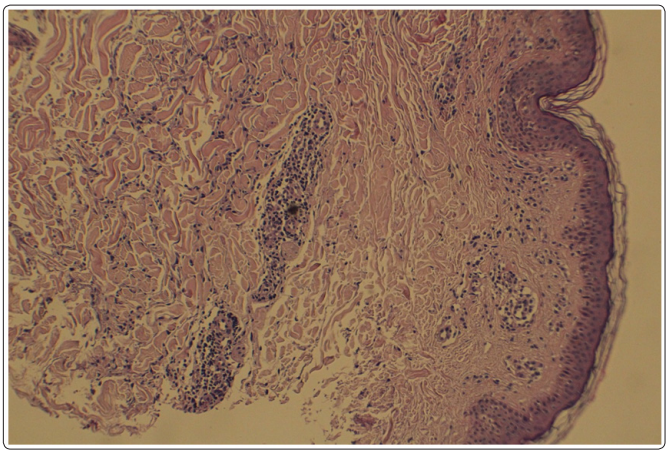

Figure 3: Moderate superficial and mid-dermal interstitial infiltrate of lymphocytes and histiocytes, and mucin between collagen fibers

The diagnosis of patch-type granuloma annulare was made, and the patient was treated with tacrolimus ointment twice daily for 8 weeks with no improvement. Then, tacrolimus was withdraw and hydroxychloroquine was started at a dose of 200mg/day. After 8 weeks, lesions on the abdomen partially improved, while lesions on the thighs disappeared completely (Table).

Discussion

Granuloma annulare (GA) is an idiopathic benign, granulomatous skin disease characterized by skin-coloured or erythematous annular dermal papules and plaques with female predominance [2]. The condition is generally asymptomatic, although there may be some pruritus or even pain [2].

Flat patches of granuloma annulare are rare and may be challenging to distinguish between other conditions, such as mycosis fungoides, interstitial drug reaction, erythema anulare centrifugal, reticular erythema mucinosis, and lupus erythematosus profundus [3].

Table 1: Histopatological differential diagnosis of granuloma annulare

Granuloma annulare	Palisading variant - central zone of altered homogenized collagen with mucin, surrounded by palisaded histiocytes and varying numbers of lymphocytes and neutrophils; interstitial variant – aggregates of histiocytes intercalating between and around collagen bundles with interstitial mucin
Mycosis fungoides	Diffuse lymphocytic infiltrate within the papillary dermis, often associated with coarse fibrosis. Care must be taken to identify foci of epidermotropism or folliculotropism. These foci may consist of a lentiginous pattern (linear accumulation associated with the basement membrane zone), or a pagetoid pattern (with either single cell-infiltration or clustered exocytosis of atypical lymphocytes, also known as Pautrier microabscesses).
Interstitial drug reaction	Vacuolar alteration of the basilar epidermis, necrotic keratinocytes, variable infiltration of the upper dermis by lymphocytes and histiocytes, variable exocytosis, and melanophages. Eosinophils and some lichenoid changes at the dermal-epidermal interface are present.
Erythema anulare centrifugal	In the superficial variant, superficial, perivascular, tightly cuffed lymphohistiocytic infiltrate with endothelial cell swelling and focal extravasation of erythrocytes in the papillary dermis. There are focal epidermal spongiosis and parakeratosis. In the classic deep form or indurated type, a superficial and deep perivascular lymphocytic infiltrate characterized by a tightly cuffed "coat-sleeve-like" pattern is present in the mid and deep dermis.
Reticular erythema mucinosis	Small amounts of dermal mucin and a mild mononuclear infiltrate situated predominantly around blood vessels and hair follicles.
Lupus erythematosus profundus	Lobular lymphohistiocytic infiltrade often with plasma cells, occasionally forming germinal centers. Vascular changes include thrombosis, calcification, or perivascular fibrosis. Fat necrosis with fibrin deposition often eventuates. Mucin deposition may be prominent in well-established lesions.

Source: Elder DE. Lever's Histopathology of the Skin. Philadelphia: Lippincott Williams and Wilkins, 2005

It is reported that patch granuloma annulare will respond to the same therapy as other types of granuloma annulare [2]. The size and localization of granulomatous lesions and the related diseases definitely influence the choice of treatment [2].

In several case reports, topical tacrolimus and pimecrolimus showed positive outcomes [2]. The exact mechanism of action of pimecrolimus and tacrolimus in GA is not clearly established [2]. The incidence of side-effects is low [2].

When available and acceptable to the patient due to time requirements, phototherapy may be tried [2]. Long-term use may lead to actinic damage localized to treatment areas and an increased risk of cutaneous malignancy [2].

If treatment with topical corticosteroids or phototherapy is impractical or ineffective, we suggest systemic treatment with hydroxychloroquine, isotretinoin or dapsone as first choice. Fumaric Acid Esters are mentioned as a second-line treatment option in GGA [2]. Adverse effects include usually mild flushing and gastrointestinal symptoms [2]. Relative lymphopenia is the most frequent laboratory finding in long-term treatment [2]. Resolution of patch-type granuloma annulare after biopsy has been reported [4].

Long-term maintenance therapy has been necessary for prolonged clearance of disease [2]. The described systemic therapies are all immunosuppressive with potential side-effects [2]. Effective therapies with minimal side effects are needed [2].

In conclusion, we present a rare variant of granuloma annulare characterized by patches of erythema on the trunk and thights that mimick micosis fungoides but display the classic histopathological findings of interstitial granuloma annulare and that showed good response to hydroxychloroquine.

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