FEATURE ARTICLE

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A Ringed Enigma

The Clinical Spectrum of Granuloma Annulare

Zisansha Zahirsha and Eden Lake

ABSTRACT: Granuloma annulare is a poorly understood disease typically presenting as localized, nonscaly, annular plaques on the dorsal extremities. Clinical variants, such as generalized, patch, perforating, and subcutaneous types, exist. Therefore, granuloma annulare has a broad range of clinical morphologies and presentations. Knowledge of the clinical features, prognosis, and treatment options of the disease is critical for providers to appropriately diagnose and manage the condition.

Key words: Granuloma Annulare, Clinical Presentation, Clinical Spectrum, Diagnosis, Treatment

Granuloma annulare is a benign, idiopathic disease with a broad clinical presentation. The aim of this evidence-based review is to bring awareness to the entity of granuloma annulare and highlight its clinical spectrum.

EPIDEMIOLOGY

Granuloma annulare is relatively rare with a prevalence and incidence of approximately 0.1%–0.4% (Schmieder & Schmieder, 2019). Greater than two thirds of patients are aged 30 years or younger, and granuloma annulare has a higher incidence among female patients (Rubin & Rosenbach, 2019; Schmieder & Schmieder, 2019).

PATHOGENESIS

The pathogenesis of granuloma annulare is unknown. Hypotheses, including an immune-mediated type III hypersensitivity reaction causing a chronic vasculitis, elastic fiber degeneration, or a Th1 cell-mediated process, have all been speculated as the cause of granuloma annulare (Hanna, Moreno-Merlo, & Andrighetti, 1999; Mempel et al., 2002; Piette & Rosenbach, 2016). In addition, granuloma annulare, especially the generalized variant, has reported associations with systemic diseases such as diabetes mellitus, HIV, and rheumatoid arthritis (Maschio et al., 2013; Studer, Calza, & Saurat, 1996; Toro, Chu, & Yen, 1999).

CLINICAL FEATURES

The presentation of granuloma annulare can vary drastically. In approximately 75% of cases, it presents as a localized variant with asymptomatic, nonscaly, annular papules or plaques with a rope-like border symmetrically distributed on the dorsal distal extremities (Figure 1A–C), wrists, or ankles (Hsu, Lehner, & Chang, 1999; Muhlbauer, 1980; Schmeider & Schmeider, 2019). Up to 15% of cases involve widespread erythematous annular plaques or micropapules scattered throughout the trunk and extremities, known as generalized granuloma annulare (Dabski & Winkelmann, 1989; Schmieder & Schmieder, 2019; Wolff, Johnson, Saavedra, & Roh, 2017). However, granuloma annulare can present as patches, cutaneous cords, or even subcutaneous nodules without epidermal changes on the lower legs, head, and buttocks (Mutasim & Bridges, 2000; Requena & Fernandez-Figueras, 2007; Verneuil, Dompmartin, Comoz, Pasquier, & Leroy, 2001). A perforating granuloma annulare variant has been reported primarily in children, presenting as erythematous papules progressing to yellow umbilicated papules with

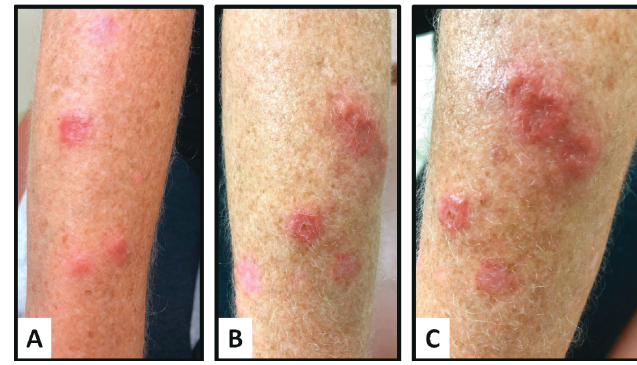

FIGURE 1. (A–C) Granuloma annulare presenting as erythematous, annular, nonscaly pink papules with a rope-like border on the bilateral dorsal forearms.

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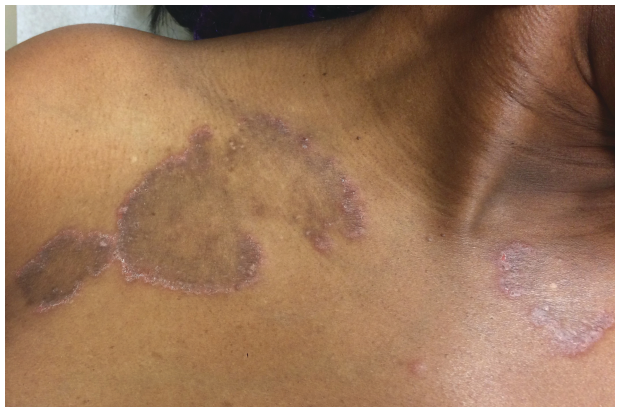

FIGURE 2. Granuloma annulare presenting as erythematous annular plaques with a pink scaly border and hyperpigmented central clearing on the upper chest.

discharge, crusting, and ulceration (Samlaska, Sandberg, Maggio, & Sakas, 1992). The distribution of granuloma annulare is usually the trunk (Figure 2) or extremities, but it can affect most areas of the body, including the genitals.

DERMATOPATHOLOGY

Diagnosis of granuloma annulare is made clinically or histologically. Histopathology shows a granulomatous inflammatory pattern in the superficial and mid-dermis with necrobiosis of connective tissue (Chatterjee, Kaur, Punia, Bhalla, & Handa, 2018; Wolff et al., 2017). In the areas of collagen degeneration, mucin is typically present, which can be best visualized with Alcian blue or colloidal iron stains (Tronnier & Mitteldorf, 2015).

DIFFERENTIAL DIAGNOSIS

The broad clinical presentation of granuloma annulare leads to a wide-ranging differential diagnosis depending on the variant visualized. In the presentation of a classic annular papule or plaque, tinea corporis, annular lichen planus, cutaneous sarcoidosis, erythema annulare centrifugum, and nodular tertiary syphilis can be considered. Generalized granuloma annulare can present similarly to arthropod bites, id reaction (autoeczematization), Sweet syndrome, or eruptive xanthomas. Rheumatoid nodules, subcutaneous sarcoidosis, and deep fungal infections are also included in the differential diagnosis for the subcutaneous variant. Finally, perforating granuloma annulare can be confused with other perforating diseases such as perforating folliculitis or perforating cutaneous sarcoidosis.

TREATMENT

Most cases of granuloma annulare are localized with spontaneous resolution. Approximately 50% of cases of localized granuloma annulare resolve in 2 years, and about 80% of cases resolve in 9 years (Wells & Smith, 1963). However, granuloma annulare may persist and require treatment (Mazzatenta, Ghilardi, & Grazzini, 2010). There are no standardized guidelines on the management of granuloma annulare as current literature on the efficacy of treatment options is primarily restricted to case reports and small case series (Lukács, Schliemann, & Elsner, 2015).

Topical and intralesional corticosteroids are considered first-line therapies (Brey, Malone, & Callen, 2006; Rallis, Stavropoulou, & Korfitis, 2009; Seif-El-Nasr & El-Komy, 1962; Volden, 1992). Other treatment options with reported success include psoralen and ultraviolet A light therapy, niacinamide, isotretinoin, topical calcineurin inhibitors, and pentoxifylline (Baskan, Turan, & Tunali, 2007; Buendia-Eisman, Ruiz-Villaverde, Blasco-Melguizo, & Serrano-Ortega, 2003; Harth & Richard, 1993; Hindson, Spiro, & Cochrane, 1988; Jain & Stephens, 2004; Ma & Medenica, 1983; Rigopoulos et al., 2005; Rubel, Wood, Rosen, & Jopp-McKay, 1993; Tang, Chong, & Lo, 1996).

DISCUSSION

In conclusion, although we have a limited understanding of the cause of granuloma annulare, providers should be aware of its broad clinical spectrum as it is imperative for an appropriate diagnosis. The five variants of granuloma annulare, namely, localized, generalized, patch type, perforating, and subcutaneous, lead to numerous clinical scenarios in which a diagnosis of granuloma annulare should be considered. Granuloma annulare is typically idiopathic without inciting factors and can present on visible parts of the body. Because of this, although the lesions are often asymptomatic, the clinical findings can be alarming for a patient. Knowledge of the self-limiting nature of most granuloma annulare cases and possible treatment options allows for enhanced education, counseling, and management. Future studies should aim to further elucidate the etiology of granuloma annulare and determine the effectiveness of treatment options as there are significant gaps in the literature regarding these topics. ■

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