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ORIGINAL ARTICLE

A retrospective analysis of 44 patients with granuloma annulare during an 11-year period from a tertiary medical center in south Taiwan

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ABSTRACT

Background: Granuloma annulare (GA) is a benign, usually self-limited, inflammatory skin disease. Although there have been several studies that review pathoclinical features about GA, the relevant epidemiological study in Taiwan was lacking. The purpose of this study is to evaluate the pathoclinical features and treatment outcome of GA in Taiwan.

Methods: This study was performed by retrospective review of medical records and pathological slides of the patients diagnosed as GA in a tertiary referral medical center in Taiwan. Fisher exact test was performed to compare remission rate between adults and children, treatment and nontreatment groups.

Result: The study included 44 patients with GA: 23 male and 21 female. The incidence of GA showed a bimodal age distribution (peaks below 20 years and above 50 years). Localized type is most common, followed by generalized variant. Perforating GA is the rarest subtype and was exclusively found in children. The pathology of GA is characterized by necrobiosis (100%), palisading granuloma (81.8%), and mucin deposition (93.2%); 13.6% and 6.8% of GA patients had history of diabetes mellitus and dyslipidemia, respectively.

Conclusion: In contrast to the reported studies, the incidence of GA showed a bimodal age incidence with slight male preponderance. Our patients had higher prevalence of diabetes mellitus than the general Taiwanese population but had no increase in incidence of dyslipidemia. Whether patients received treatment or not does not affect the disease outcome. Overall, children have better prognosis than adults.

Introduction

Granuloma annulare (GA) is a benign, and usually self-limited, inflammatory skin disease. The disease incidence is estimated[1] to be between 0.1% and 0.4%. The clinical manifestations vary, from localized, erythematous to flesh-colored papules with annular arrangement to the more generalized form. GA can develop in any skin areas, but it tends to occur on the lateral or dorsal surfaces of the hands and feet. GA is usually self-limited. The pathogenesis of GA remains unclear although abnormal repair in vascular injury or aberrant responses in delayed-type hypersensitivity may be involved. The diagnosis is made clinically or by skin biopsy with the typical histological findings of eosinophilic necrobiosis and palisading lymphohistiocytic infiltrates.

GA was reported to commonly affect children and young adults with a female preponderance based on hospital based studies performed in USA, Singapore, Switzerland, and UK.[2–4] However, a recent study in Korea reported a bimodal distribution of onset age

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and a slight male predominance among patients with generalized GA.[5] The mixed clinical and epidemiological pattern of GA might depend on the variations in clinical categorizations, races, and associated triggering factors. In Taiwan, several individual cases of GA have been reported; however, a comprehensive study to delineate the clinical categorizations, treatment outcome, associated disease, and histopathological features of GA is lacking. Therefore, we herein aimed to evaluate the clinical findings, histopathological features, associated diseases, and treatment outcomes in Taiwanese patients of GA.

Method

This study was performed by a retrospective review of medical records and pathological slides of the patients diagnosed as GA in Kaohsiung Chang Gung Memorial Hospital, a tertiary referral medical center from January 2002 to January 2013. In total, 44 patients were identified. Information including sex, age of onset, location, number and type of lesions, onset duration, clinical morphology, associated diseases, treatment and outcome were collected. Children were defined as those younger than 18 years. Skin specimens were fixed in formalin, later embedded in paraffin, and sectioned with 4-μm thickness. Sections were stained with hematoxylin and eosin and Alcian blue (pH = 2.5). Histopathological features including distribution patterns of inflammatory cells, mucin deposition, and infiltrative cell type were analyzed. The microscope slides were reviewed independently by one board-certified pathologist and one board-certified dermatologist. The diagnoses were made according to the constellation of clinical and pathological findings.

Based on clinical manifestations, the disease was classified into localized, generalized, subcutaneous, and perforating types. Solitary or a few lesions on a single anatomical site were defined as localized form. Generalized GA was defined as affecting at least the trunk and either upper, lower, or both limbs, based on the criteria initially stated by Dabski and Winkeiann.[6] Subcutaneous GA was characterized by granuloma predominantly affecting subcutaneous tissue while perforating GA was featured by superficial umbilicated papules and transepidermal elimination of necrobiotic collagen. Representative clinical features for subtypes of GA are shown in Figure 1.

Treatment options with either systemic or topical medication were recorded. The treatment response was assessed by the dermatologist and by the patient. Follow-up was carried out by either medical charts or telephone interviews. Treatment response was classified as poor (no response), partial, or good (complete or nearly complete resolution).

Fisher exact test was performed to compare remission rate between adults and children, with or without treatment.

Results

Demographic data and clinical features of GA

In this study, 44 patients with GA were identified, of whom 23 were male and 21 female. The age of onset widely distributed, ranging from 2 years to 75 years (average age = 36.55 ± 24.86 years, median age = 40 years). Sixteen patients were children (36.4%) and 28 were adults (63.6%). A bimodal age distribution (peaks below 20 years and above 50 years) was noted (Figure 2). Nearly half of the patients (43.2%) had the disease in their 5th decade. Among the four clinical variants, the localized type is the most common, followed by the generalized variant. Subcutaneous GA occurs most often in children and young adults. Perforating GA is the rarest subtype and exclusively occurred in children. The majority of the lesions exhibited the clinical pattern of annular arrangement and papular morphology (Table 1). The mean disease duration is 9.5 months.

Association of metabolic diseases and GA

Among the 28 adult GA patients, six had diabetes mellitus (DM: exclusively noninsulin dependent DM), four had hypertension, three had dyslipidemia (1 had hypertriglyceridemia and 2 had hypercholesterolemia), one had history of ischemic stroke, and one

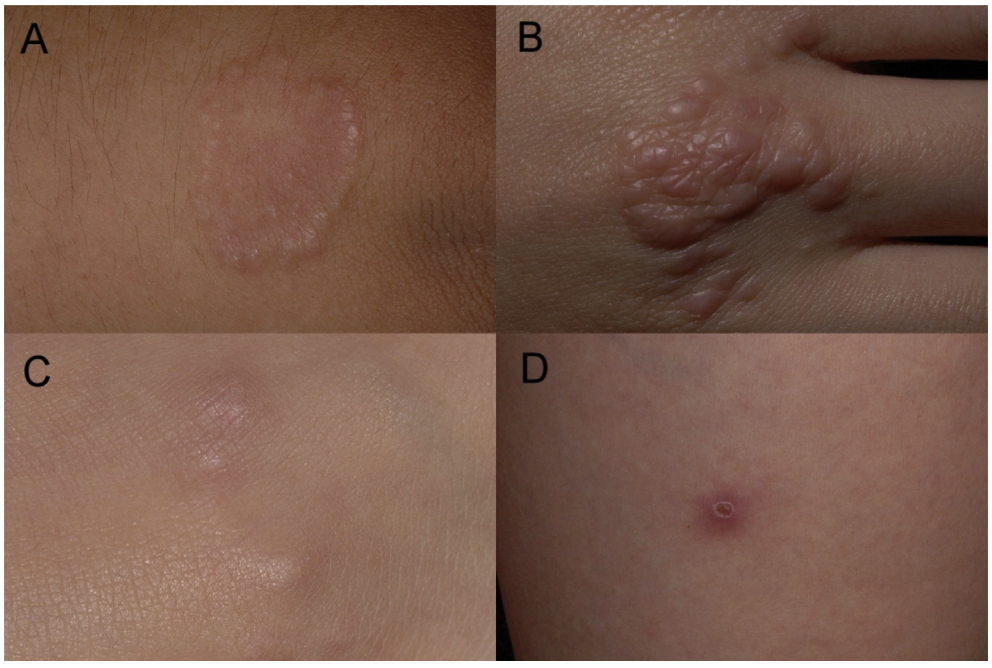

Figure 1 Clinical variants of granuloma annulare: (A) annular lesion; (B) papular lesion; (C) subcutaneous lesion; and (D) perforated lesion.