Two Cases of Generalized Granuloma Annulare in Infants

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Generalized granuloma annulare (GGA) is characterized by disseminated necrotic dermal papules but the pathogenesis has not been fully elucidated. A 5-month and a 3-month male infant had diffusely scattered, erythematous papules on their trunks, and upper and lower extremities. Histopathological examination revealed an infiltration of histiocytes around and between altered collagen fibers in upper and mid dermis. The collagen fibers were separated by mucin, which was positively stained with alcian blue at pH 2.5. After they were treated with topical and / or systemic corticosteroid, the lesions disappeared. To the best of our knowledge, these two cases are non-perforating GGA in the youngest patients yet reported in English literature.

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INTRODUCTION

Granuloma annulare (GA) is a benign, granulomatous skin disease of unknown cause. Generalized granuloma annulare (GGA) is an uncommon variant of GA[1], which is characterized by a widespread papular eruption[2] and focal necrobiosis of collagen and granulomatous infiltration[3]. GGA is a chronic disease with a relapsing course and shows a poor therapeutic response[2].

CASE REPORTS

Case 1

A 5-month-old male infant presented with a month-long history of gradually spreading erythematous papules on his trunk, upper and lower extremities. Skin examination revealed multiple, well-demarcated, erythematous, 1- to 5-mm-sized, and firm papules on his chest, abdomen, and both arms and legs (Fig. 1). Most of the papules were diffusely scattered. In the laboratory study, the results of complete blood cell count, blood chemistry, and urinalysis were within normal limits. A skin biopsy specimen, taken from the papule on the

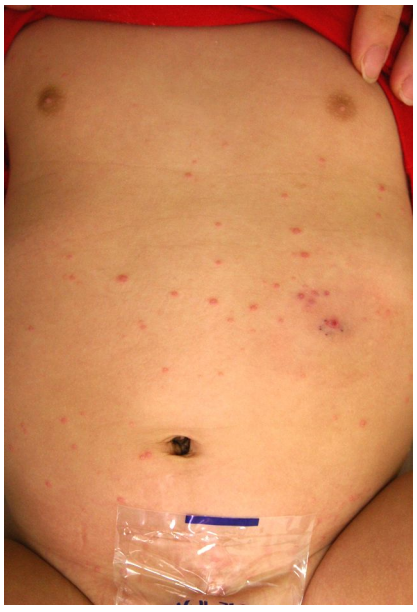

Fig. 1. Multiple 1- to 5-mm-sized erythematous papules on trunk of male patient.

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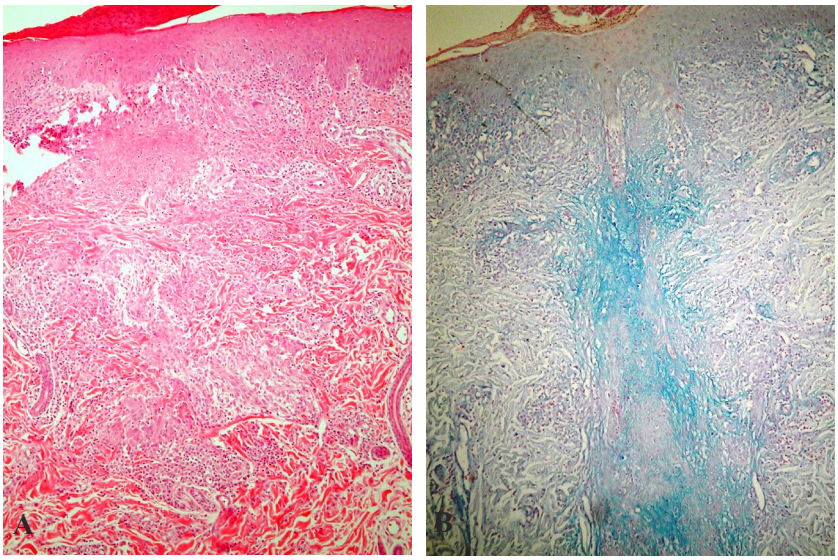

Fig. 2. (A) A central area of altered collagen is surrounded by palisading of histiocytes, lymphocytes, and multinucleated giant cells (H & E stain, × 100). (B) mucin was demonstrated within degenerative collagen bundles (alcian blue stain at pH 2.5, × 100).

abdomen, revealed an infiltration of histiocytes, lymphocytes, and multinucleated giant cells around a zone of collagen alteration in upper and mid dermis (Fig. 2A). Mucin was demonstrated within degenerative collagen bundles by alcian blue stain at pH 2.5 (Fig. 2B).

After he was treated with oral methylprednisolone 0.5 mg/kg/day for 10 days and topical corticosteroid (Dermatop® oint) for a month, the lesions disappeared leaving hyperpigmentation.

Case 2

A 3-month-old male infant presented with a 3-week history of generalized papules. Multiple erythematous papules were diffusely scattered on his face, chest, abdomen, and both arms and legs. Some of which were surrounded by erythema (Fig. 3). The laboratory study was not performed. A skin biopsy specimen taken from the papule on the abdomen revealed an infiltration of histiocytes around and between altered collagen fibers in upper and mid dermis (Fig. 4A). The collagen fibers were separated by mucin, which was positively stained with alcian blue at pH 2.5 (Fig. 4B).

After he was treated with topical corticosteroid (Lacticare-Zemagis® lotion) for a month, the lesions disappeared leaving hyperpigmentation.

DISCUSSION

Generalized granuloma annulare (GGA) is an uncommon variant of granuloma annulare (GA), representing 8% to 15% of all cases of GA[4]. It is defined as affecting at least the trunk and either the

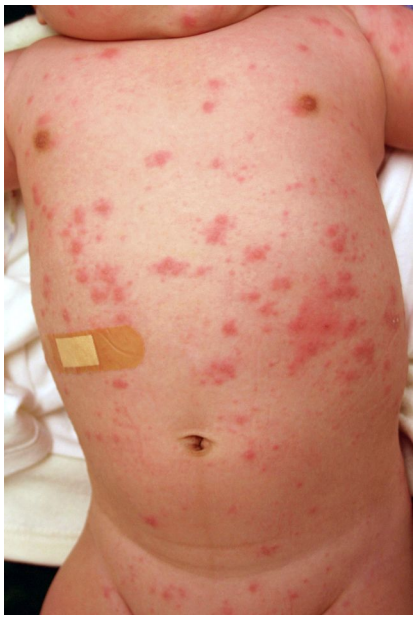

Fig. 3. Multiple erythematous papules were diffusely scattered on trunk of male patients.

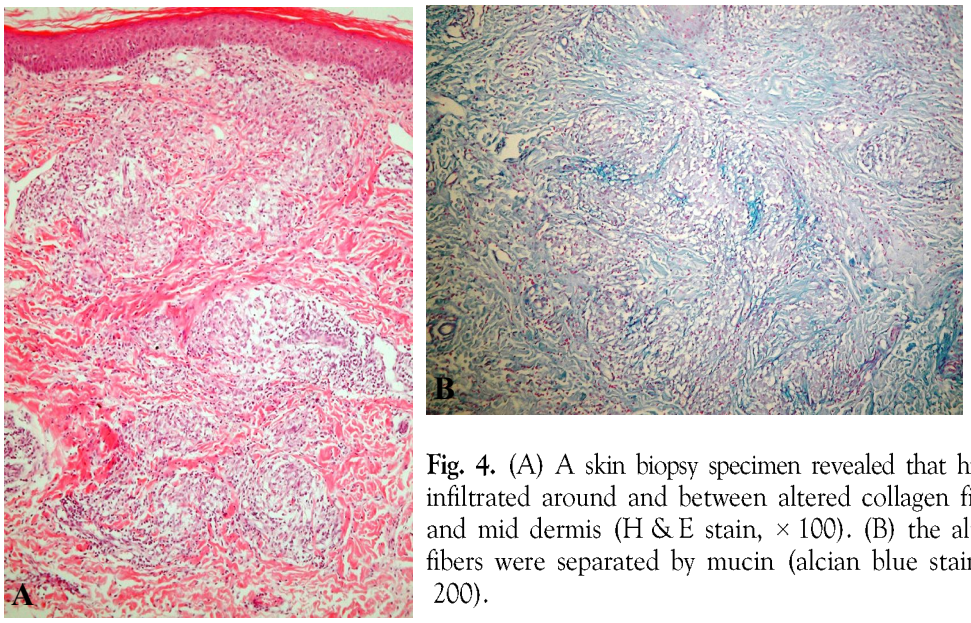

Fig. 4. (A) A skin biopsy specimen revealed that histiocytes were infiltrated around and between altered collagen fibers in upper and mid dermis (H & E stain, × 100). (B) the altered collagen fibers were separated by mucin (alcian blue stain at pH 2.5, × 200).

upper, lower, or both, extremities[2]. GGA most frequently occurs in middle-aged to elderly adults, between 30 and 60 years old[5]. However, in 20% of the cases it occurs before the age of 10 years[5] and rare cases of GGA in infants have been reported[5-7]. The clinical morphologic patterns of GGA can be divided into the annular and non-annular patterns. Among them, the non-annular pattern is composed of symmetrically scattered papules often coalescing papules[2]. It is different from the annular pattern by a nearly equal female-to-male ratio, certain laboratory abnormalities such as a lower incidence of elevated serum lipids and a more frequent occurrence of increased titers of gamma globulins and immunoglobulins. The non-annular pattern also shows positive staining for lipid more frequently[2]. In our two cases, erythematous papules were diffusely scattered on the trunk, upper and lower extremities and they are compatible with non-annular GGA.

Typical histopathologic findings of GGA are necrobiotic collagen and mucin in the dermis with surrounding inflammatory cells of histiocytes, multinucleated giant cells, and a few acute inflammatory cells[3]. Although histolopathologic differences between localized GA and GGA are minimal, collagen sclerosis, palisading pattern and decreased or absent elastic fiber in granulomatous inflammation foci occurred more commonly in localized GA than in GGA[3]. In our two cases, collagen sclerosis and palisading pattern are not prominent on the histopathology.

GGA is a chronic disease with a relapsing course and shows a poor therapeutic response[2]. These circumstances have led to numerous treatments, including systemic corticosteroid[6], isotretinoin[7], PUVA[8], potassium iodide[9], sulfone[10], hydroxychloroquine[11], niacinamide[12], topical vitamin E, topical corticosteroid, and cryotherapy. However, in our two cases, the lesions disappeared leaving hyperpigmentation after treatment with topical or systemic corticosteroid for a month. No recurrence was observed during the follow up period of 15 months and 4 months, respectively.

A 68-day-old infant with generalized perforating GA was the youngest patient with GGA. However, to the best of our knowledge, these two cases of GGA are the earliest onset of non-perforating GGA reported in the English literature.

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