

## Two Cases of Generalized Granuloma Annulare in Early Childhood

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Generalized granuloma annulare is a rare skin disease presenting generalized eruption with a distinctive histologic picture. The age of onset of generalized granuloma annulare differs from that of localized granuloma annulare. Most of the patients with generalized granuloma annulare were in the fifth to seventh decades and cases of generalized granuloma annulare in infancy or in early childhood have been rarely reported.

We herein report two cases of generalized granuloma annulare in 45- and 18-month-old boys, who is the youngest patient yet reported in the Korean literature. The histopathologic findings were compatible with granuloma annulare and all lesions completely involuted in two months after administration of topical or systemic corticosteroids.

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Generalized granuloma annulare is a uncommon chronic benign skin disease with a distinctive histologic and morphologic picture. The characteristic lesion of generalized granuloma annulare consists of predominantly skin-colored papules with tendency to annular grouping. The histopathologic findings are focal necrobiosis of collagen and a palisading granuloma.

Generalized granuloma annulare differs from the localized form by the later age of onset and protracted course with only rare spontaneous resolution. Most of the patients with generalized granuloma annulare were in the fifth through seventh decades<sup>1-3</sup>. Few cases have been reported in the first decade and only four cases of generalized

granuloma annulare in infancy or early childhood have been reported in Korea<sup>4-7</sup>. As well as the late onset of the disease, follow up data indicated chronic relapsing characteristics of generalized granuloma annulare<sup>3</sup>.

We recently observed two cases of generalized granuloma annulare in 45- and 18-month-old boys, who is the youngest among the patients with generalized granuloma annulare reported in the Korean literature.

### CASE REPORTS

#### Case 1

A 45-month-old boy presented with a 2-month history of a generalized papular eruption. He had hundreds of 3-to 5-mm-sized, firm, slightly erythematous asymptomatic papules on his trunk and lower extremities. The papules on the trunk were diffusely scattered and the papules on the extremities showed coalescences in about 1 to 1.5cm sized annular configuration (Fig. 1). He experienced tonsillitis, otitis media, and rhinitis 2 months ago. Physical examination was otherwise normal. A 3-mm

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Fig. 1. Multiple 1 to 1.5cm sized erythematous plaques with depressed center on the lower extremities exhibit annular configuration in case 1.

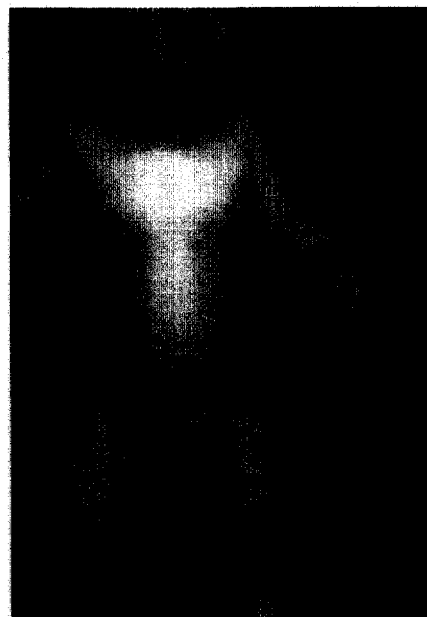


Fig. 2. Multiple 3 to 5cm sized erythematous papules with crusts are shown on the whole body in case 2.



Fig. 3A. A central area of bluish altered collagen is surrounded by a palisades of histiocytes in case 2 (H & E stain,  $\times 100$ ).

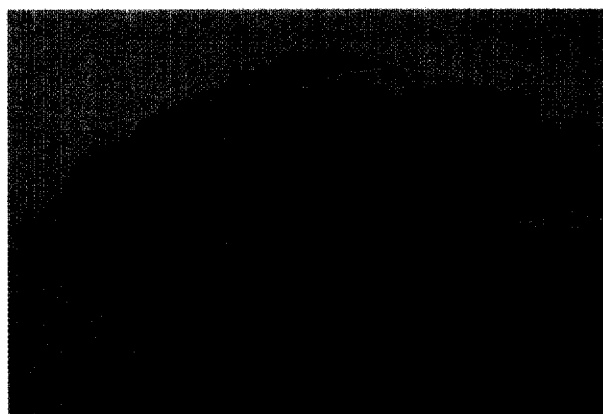


Fig. 3B. The special stain of the specimen showed the bluish zone of collagen alteration in case 2 (Alcian blue-PAS stain,  $\times 100$ ).

punch biopsy was performed and showed an infiltrate of histiocytes and multinucleated giant cells around a zone of collagen alteration. The biopsy specimen showed positive for bluish altered collagen to the alcian blue stain. The patient was treated with topical corticosteroid and the lesions disappeared in one month leaving hyperpigmentation.

#### Case 2

A 18-month-old male infant presented with a

20-day history of gradually disseminating erythematous papules. The lesions were located on the upper and lower extremities, trunk, and face. He had multiple 3-to 5-mm-sized, firm erythematous papules with crusts (Fig. 2). Some of these papules arranged ring-like pattern. The physical examination showed nothing unusual except the skin lesions. Laboratory findings were within normal limits. He had had a severe common cold one month before. Histopathological examination revealed palisad-

ing granuloma composed of mucinous degenerated collagen with surrounding histiocytes and rare multinucleated giant cells (Fig. 3A). An alcian blue-PAS stain showed a bluish tinge of altered collagen fibers (Fig. 3B). The lesions resolved clearly with systemic and topical corticosteroid in two months.

## DISCUSSION

Granuloma annulare is a chronic benign inflammatory skin disease with a characteristic lesion of small, firm, asymptomatic papules, that are often grouped in an annular or circinate fashion. Clinically two main forms of granuloma annulare are recognized; localized and generalized granuloma annulare<sup>2</sup>. Generalized granuloma annulare is an uncommon form of granuloma annulare, and the incidence of generalized granuloma annulare is unknown.

In contrast to the localized type, the generalized type has been reported mainly in the fifth through seventh decades. Dicken *et al.*<sup>1</sup> reported that only one patient was in the early childhood among 26 patients with generalized granuloma annulare. Friedman-Birnbaum *et al.*<sup>2</sup> reported that the average age of onset was 53.97 years and 84.8% of the generalized granuloma annulare patients were in the sixth and seventh decades. None had the onset of the disease in the first decade on his study. The largest series have been reported in Mayo Clinic with 100 patients with generalized granuloma annulare and the mean age of onset was 51.7 years<sup>3</sup>. Only two cases were in the first decade including 3-month-old boy. Four cases of generalized granuloma annulare in infancy or in early childhood have been reported in the Korean literature<sup>4-7</sup>. One 23-month-old girl and two 4-year-old girls and one boy aged 3 years have been reported. Our case of an 18-month-old boy was the youngest among the patients with generalized granuloma annulare so far reported in the Korean literature. It is suggested that the dermatologist should include generalized granuloma annulare in differential diagnosis in infants with annular skin lesions.

Generalized granuloma annulare is manifested by innumerable papules which are either discrete or confluent with an annular or reticulate configuration. In our cases, most lesions were discretized, scattered papules, which suggested pityriasis lichenoides *et*

varioliformis acuta or Gianotti-Crosti syndrome.

The histopathologic features of generalized granuloma annulare are the same as those of the localized form, that is, necrobiotic collagen and mucin in the dermis with surrounding inflammatory cells of histiocytes, multinucleated giant cells, and a few acute inflammatory cells<sup>8</sup>. With the histopathologic findings, we confirmed the diagnosis of generalized granuloma annulare in our cases. The alcian blue stain was used to highlight mucin.

In general, granuloma annulare appears from obscure origin. Some has been reported to follow insect bite, sun exposure, tuberculin test, ingestion of allopurinol, trauma, and viral infections including Epstein-Barr, HIV, and herpes zoster<sup>9</sup>. The possible etiologic role of insect bites was considered in our first case since the onset of the disease was in the season in which insects increased in number in Korea. Complete blood count was not performed in the first case, therefore we could not demonstrate blood eosinophilia. Viral etiology also could be considered in both cases because both had severe common colds one to two months ago.

A variety of treatment modalities for generalized granuloma annulare have been tried because it is less likely to resolve. These include topical vitamin E, cryotherapy, laser destruction, topical or intralesional injection of corticosteroids<sup>9</sup>. Systemic trials of PUVA<sup>10</sup>, dapsone<sup>11</sup>, hydroxychloroquine<sup>4,12</sup>, niacinamide<sup>13</sup>, chlorambucil, isotretinoin<sup>14</sup>, corticosteroids, salicylates, potassium iodide<sup>15</sup>, and dipyridamole have been reported but their efficacy was not very encouraging and side effects almost always outweighed benefits. In the Korean literature, 4 cases of generalized granuloma annulare in the first decade also treated with systemic corticosteroids and only one case<sup>7</sup> showed resistance to the therapy. Our two cases responded to topical or systemic corticosteroids with complete resolution. It suggests that the therapy for generalized granuloma annulare in childhood would be more successful than in adulthood.

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