

Granuloma Annulare: Clinical and Laboratory Findings in a Pediatric Group of Patients

Sir,

Despite the frequency of granuloma annulare (GA) in children, we were only able to find studies involving the pediatric population regarding rare clinical variants (1–4), or large case studies including both adult and pediatric patients (5–7). The purpose of this work was to evaluate the onset, localization, clinical aspect and course of GA in a pediatric population.

PATIENTS AND METHODS

Our case study includes 63 children (33 males and 30 females, aged 7 months–12 years, mean 5 years) affected by GA, seen between January 1989 and January 1995.

We gathered data on age of onset, family history and associated diseases of the patients and possible precipitating factors, duration and clinical appearance of the lesions. Based on the morphology and distribution of the lesions, we identified the following clinical types: (1) the localized form with a single lesion, defined by the presence of only one GA on the whole body; (2) the localized form with multiple lesions, defined by the presence of 2 or more lesions localized in one or more cutaneous regions (face, limbs, buttocks) but absent on the trunk; (3) the generalized form (GGA), defined by the presence of more than 10 lesions, either in non-annular or in annular configuration, distributed according to Dabski & Winkelmann (6), either on the trunk alone or on the trunk and one or more limbs; (4) the subcutaneous or deep form (pseudorheumatoid nodules) with nodules involving the deep dermis and hypoderma; and (5) the perforating form with umbilicated papules, which may ulcerate with production of creamy discharge.

Follow-up was obtained through periodic examinations and the administration of a telephone questionnaire.

RESULTS

The duration of the lesions at time of presentation varied from 15 days to 5 years (mean 10 months). The mean age at onset was 5 years in boys and 4 years and 7 months in girls. Only 2 of the 63 patients had a family member with GA, namely the mother in one and the sister in the other.

Distribution of lesions and clinical variants

The localized type with a single lesion was present in 17 patients (13M, 4F), and 33 (15M, 18F) had multiple lesions.

One patient presented with both a localized form with multiple GA and also umbilicated papules typical of the perforating form, located on the dorsum of the hands.

Subcutaneous GA was present in 8 patients, of which 4 (2M, 2F) had multiple lesions, while GGA was seen in 5 patients (2M, 3F).

Precipitating factors

Fifty-eight patients were evaluated for possible precipitating factors. Friction from shoes (7 patients), insect bites (6 patients) and prolonged sun exposure (6 patients) were all mentioned. An association with stressful events was possible for 9 patients.

Associated diseases

These were found only in 18 cases (17 had the localized type of GA): 9 children were atopic; 5 patients had recurrent tonsillitis; 2 had growth hormone deficiency; 1 had insulin-dependent diabetes mellitus and 1 had familial hypercholesterolemia.

Treatment

Forty patients were treated by their referring physician or by us. Although it is difficult to assess the efficacy of treatment for GA, since this may resolve spontaneously, we found rapid regression of lesions in patients treated with cryotherapy and a significant improvement in 1 of the 3 patients treated with nimesulidum. Moreover, skin biopsy performed in 31 patients was enough to induce regression of GA in 21 of them (67.7%). All 5 cases with GGA experienced spontaneous resolution of the lesions within some days after the biopsy. In all cases the biopsy confirmed the diagnosis.

Clinical course

Of the patients with the localized form, 36 cases were followed up for a period ranging from 14 months to 7 years.

Of the 8 patients with subcutaneous GA, follow-up longer than 1 year was available (average 4 years, range 31 months to 7 years). The main data of our 44 patients with follow-up are summarized in Table I.

One patient with localized form with multiple lesions and 2 patients with deep GA had a clinical course characterized by multiple short-lived relapses over a period of about 2 years; in these patients the lesions lasted each time for a shorter period and finally resolved permanently.

DISCUSSION

The analysis of our data yielded some comments.

It appears that in children GA does not have the increased incidence in females observed in adults (8). In fact we had 33M and 30F. Males far outnumbered females in the localized form with a single lesion, of which we had 13 males and 4 females for a M/F ratio of 3.25 to 1. This result is intriguing and needs to be validated by further studies.

We observed a greater frequency of GA in the 3–6 age group, with 27 cases under 3 years of age at the time of onset. This observation suggests that GA occurs prevalently in young children.

All the major clinical variants were represented; the most common being the localized form with multiple lesions, which occurred in more than half of our patients, with a ratio of 2:1 between multiple lesions and single lesion cases.

We had 8 cases of subcutaneous GA (pseudorheumatoid nodules of childhood), equal to 12.7% of our cases. Subcutaneous GA is relatively rare and occurs almost exclusively in the pediatric age group (9, 10).

The most common locations were the legs, in particular the shins, ankles and dorsum of feet, both for the localized form and the subcutaneous one. These data appear typical of the

Table I. Main clinical data of patients with follow-up ≥ 1 year

Variety of GA	Follow-up ≥ 1 year (cases)	No resolution of GA (cases)	Resolution of GA (cases)	Average duration of GA before initial resolution (months)	Relapse (cases)	Average time from initial resolution to relapse (months)	Average duration of the relapse (months)
Localized GA with single lesion	11	5	6	12	2	11 (range: 1 m-2 y)	7
Localized GA with multiple lesions	25	0	25	14	11		
Subcutaneous single GA	4	0	4	7	6	16 (range: 2 m-6 y)	5
Subcutaneous multiple GA	4	0	4				

* In 2 children no change occurred after 18 and 30 months of follow-up, respectively; in the other 3 cases there was partial resolution of the lesions after 2, 2.5 and 3 years, respectively.

pediatric population, while acral distribution on hands and feet is more common in adults (7, 11).

GGA was present in 5 patients (7.9%). This incidence is similar to the one reported by Dabski & Winkelmann in patients with GGA seen at the Mayo Clinic (6). The perforating form was present in only 1 of our patients. This confirms the rarity of this particular form (2, 4).

We had 2 cases of GA manifesting in family members of the index case (mother and sister, respectively). This agrees with reports of rare familial involvement (12). In Wells' case study, only 2 out of 208 patients were consanguineous (7).

The most interesting findings emerging from our case study resulted from the follow-up. All of the 5 patients with GGA had rapid and complete resolution within 8 months. This result is substantially different from those reported in studies of adults (5, 6). Takigawa & Aoshima (13) and Kaji et al. (14), however, described 2 cases of GGA in girls aged 15 months and 3 years, respectively, both of which resolved within a few months. Regarding the two different configurations of GGA (annular and non-annular form), we observed a marked preponderance of the latter in our patients (4 out of 5). Unfortunately, none of our patients with GGA had a follow-up longer than 1 year in order to properly evaluate possible relapses.

We found that subcutaneous GA also had a short clinical course, lasting a mean of only 7 months. However, 6 patients experienced relapses. This higher incidence of relapse in deep GA was also reported by Evans et al. (9). Other authors (15) found rapid regression of deep GA.

We noticed a high percentage of spontaneous resolution in patients with the localized form of GA, with an overall regression rate of 88%, ranging from 100% in patients with multiple GA to 54.5% in patients with single GA. However, in 38% of cases there was a relapse of lesions after an average of 11 months from the previous resolution. These relapsed lesions lasted for only 7 months, on average, before undergoing spontaneous resolution. There was no correlation between the age of onset and the incidence of relapse, or between the interval from the first and second crop of GA and the number of lesions present initially.

The mean duration of GA in our study appears to be 2.5 years. In fact, no patients have had a relapse after 2 years from resolution of the original lesion in the localized form, while for the subcutaneous form relapses were observed up to 6 years from the original lesion.

In conclusion, GA in the pediatric age group appears to occur equally in both sexes and to affect predominantly younger children, under the age of 6. By far the most common type is the localized form with multiple lesions. The clinical course is characterized by spontaneous resolution with frequent relapses in the short term in the superficial forms and relapses occurring even after many years in the subcutaneous form. The types of GA with more extensive and numerous lesions appear to have a shorter duration. In particular GGA appears to behave like an exanthematic eruption with very rapid onset and resolution within a few months.

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