Linear growth in prepubertal children with atopic dermatitis

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Abstract

Objective—To define the evolution of prepubertal growth in atopic dermatitis and the factors influencing that growth pattern.

Methods—Height and height velocity over two years, weight, triceps and subscapular skin fold thickness, and bone age were assessed in 80 prepubertal patients with atopic dermatitis and a control group of 71 healthy prepubertal school children.

Results—Height standard deviation scores (SDS) and height velocity SDS did not differ between patients and controls, and were not influenced by body surface area affected by atopic dermatitis, topical glucocorticoid potency, or coexisting asthma. However, height SDS ($r = -0.37$) and height velocity SDS ($r = -0.31$) correlated inversely to age in patients but not in controls. A greater proportion ($z = 2.84$) of patients than controls had year 2 height velocity SDS less than -1.96 . Patients had a mean delay in bone age of 0.22 years and 0.41 years at the beginning of year 1 and year 2 of the study, respectively. The delay in bone age correlated positively with age ($r = 0.39$) and duration of atopic dermatitis ($r = 0.39$), and negatively with height SDS ($r = -0.51$) and height velocity SDS ($r = -0.38$).

Conclusions—Prepubertal children with atopic dermatitis are not short compared with controls. However, as they approach the teenage years their height velocity decreases, the proportion of children with extremely low height velocity increases, and the delay in bone age increases. These features are consistent with the pattern of growth seen in people with constitutional growth delay.

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Keywords: atopic dermatitis; growth; height; height velocity

Cross sectional studies have reported impaired growth in children with atopic dermatitis^{1–3} and a higher prevalence of atopic dermatitis among children with short stature than those with normal stature.⁴ However, normal adult height has been seen in 35 patients with childhood onset atopic dermatitis.⁵ These observations suggest that any growth impairment in childhood is likely to be temporary. However, longitudinal growth in children with atopic dermatitis has not been studied. In addition, the contributions made by factors that might influence growth adversely in atopic dermatitis such

as the disease itself, sleep disturbance,⁶ impaired growth hormone release,⁷ topical glucocorticoid treatment, undernutrition,⁸ and coexisting asthma and its treatment have not been determined.

Our study aimed to define the evolution of prepubertal growth in atopic dermatitis and the factors influencing that growth pattern. Constitutional delay of growth and puberty is a common cause of short stature and is defined as height reduced for chronological age associated with delayed bone age and delayed pubertal development in otherwise healthy adolescents.⁹ However, this pattern of delayed growth has often been present throughout childhood.¹⁰ Thus, retarded linear growth and retarded bone age are likely in the prepubertal years in children with constitutional delay. We hypothesised that prepubertal children with atopic dermatitis would have this pattern of growth and exhibit: (1) a lower height velocity than controls, (2) a decrease in height velocity over time (retarded linear growth), and (3) delayed bone age.

Subjects and methods

We recruited 80 consecutive prepubertal children (mean age, 4.8 years; range, 2.0–10.5) attending the University Department of Child Health for atopic dermatitis from October 1992 to June 1993, referred by paediatricians or dermatologists because of the severity or intractable nature of the disease. Prepubertal patients aged 2–11 years whose atopic dermatitis appeared in the first year of life, irrespective of severity, were eligible for the study. The parents of one child declined participation. We excluded two patients treated with systemic glucocorticoids.

For each of the first 40 patients with atopic dermatitis aged ≥ 3 years, two control subjects of the same sex and age (birth date, as recorded in the school register, within one month of that of the patient) were enrolled from two local schools (there were no children under 3 years of age in the schools). Of these 80 school children, nine were excluded (two had a history of atopic dermatitis and asthma, five left the school within six months of the start of the study, and two were repeatedly absent from school). Thus, we studied 71 non-atopic children.

There were no children with a known independent cause for short stature, history of chronic systemic disease, or endocrine problem in the study or control groups. The study was approved by the local ethics committee and informed consent was obtained from parents and children old enough to understand.

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Table 1 Scores for severity of atopic dermatitis, topical glucocorticoid treatment, and coexisting asthma

Score for severity of atopic dermatitis (total 9)	1	2	3	
Body surface area involved	< 9%	9–36%	> 36%	
Erythema	Mild	Moderate	Severe	
Course	Remission > 3 months in past year	Remission < 3 months in past year	Continuous	
Score for topical glucocorticoid treatment (total 10)	1	2	3	4
Potency of preparation	Mild	Moderate	Potent	Very potent
Body surface area treated	< 9%	9–36%	> 36%	
Treatment duration	≤ 7 days in past month	< 7 days in past month	Continuous	
Score for coexisting asthma (total 8)	0	1	2	3
Number of exacerbations in a year	0	1–3	4–6	≥ 7
Interval symptoms	None	Intermittent	Continuous	–
Treatment	None	Bronchodilators	Sodium cromoglycate	Inhaled glucocorticoid

For the patients with atopic dermatitis, we recorded age of onset, percentage body surface area involved, and potency of topical glucocorticoid preparation used as described in the British National Formulary. Patients had mild to severely inflamed atopic dermatitis involving 8–95% (median, 47%) of the body surface area. The severity of atopic dermatitis, treatment, and asthma scores were based on the criteria shown in table 1. Thirty eight patients regularly used mild potency topical glucocorticoid preparations and 39 patients used moderate potency preparations. Only one patient regularly used a potent topical glucocorticoid preparation. Two patients did not use topical glucocorticoid preparations.

Height velocity for year 1 and year 2 of the study was calculated from height measurements taken 12 months apart. Height was measured with a wall mounted Harpenden stadiometer using a standard protocol.¹¹ The standard deviation of the difference between blind triplicate height measurements of 10 children was 0.12 cm. Weight (child lightly clothed) and triceps and subscapular skin fold thickness (skin fold thickness calipers) were measured. To standardise data for age and sex, standard deviation scores (SDS) were calculated for height and height velocity (using Tanner, Whitehouse, and Takaishi standards¹²) and body mass index (BMI) (using Cole, Freeman, and Preece standards¹³). Values less than –1.96 SDS below the mean were considered to be extremely low. Bone age was assessed from left wrist radiographs using the TW2 method¹⁴ on the children with atopic dermatitis at the start of year 1 and year 2 of the study.

Variables were compared between: (1) children with atopic dermatitis who had < 50% body surface area involvement (n = 43) and those with ≥ 50% body surface area involve-

ment (n = 37); (2) children with atopic dermatitis treated with mild potency (n = 38) and moderate potency (n = 39) topical glucocorticoids; (3) children with atopic dermatitis without asthma (n = 36) and those with asthma (n = 44); and (4) the subgroup of children with atopic dermatitis aged ≥ 3 years (n = 62; mean age, 5.5 years; range, 3.0–10.5) and a control group of healthy school children (n = 71; mean age, 5.8 years; range, 3.2–9.9).

Height, height velocity, and BMI SDS were normally distributed. Triceps and subscapular skin fold thickness and body surface area involved were logarithmically transformed. The two sample *t* test was used for analysis and 95% confidence intervals are given to indicate the magnitude of the difference and to take risks of type II errors into account. Proportions were compared using the *z* statistic. Correlation and regression analysis were used to investigate the relation between the growth parameters and independent variables. The number of children completing one year and two year follow up were 53 and 36 for the patient group and 70 and 64 for the control group, respectively. The growth parameters and atopic dermatitis parameters at study entry were not different between the patients who completed the study and those who were lost to follow up.

Results

HEIGHT AND HEIGHT VELOCITY IN PATIENTS WITH ATOPIC DERMATITIS COMPARED WITH CONTROLS

There were no significant differences in age and height SDS at study entry between patients and controls (table 2). The heights at study entry of one of the 62 patients and three of the 71 controls were less than –1.96 SDS of the mean. At the end of the study, one patient

Table 2 Variables for patients with atopic dermatitis aged ≥ 3 years and controls

	Atopic dermatitis	Controls	95% CI*
Number (boys/girls)	62 (34/28)	71 (39/32)	
Mean (SEM) age in years	5.52 (0.29)	5.83 (0.26)	0.4 (–0.46, 1.09)
Mean (SEM) height SDS at study entry	0.11 (0.13)	–0.03 (0.11)	0.4 (–0.48, 0.21)
Mean (SEM) height SDS after 2 years	–0.10 (0.18)	–0.03 (0.12)	0.8 (–0.38, 0.51)
Mean (SEM) year 1 height velocity SDS	–0.10 (0.18)	–0.09 (0.11)	1.0 (–0.43, 0.43)
Mean (SEM) year 2 height velocity SDS	–0.31 (0.27)	0.06 (0.12)	0.2 (–0.22, 0.96)
Mean (SEM) body mass index SDS	0.48 (0.15)	0 (0.13)	0.01 (0.10, 0.86)
Median triceps skinfold thickness (mm) (interquartile range)	10.7 (8.2–13.9)	11.2 (9.7–13.6)	0.2 (–0.02, 0.09)
Median subscapular skinfold thickness (mm) (interquartile range)	6.2 (5.2–7.8)	5.7 (5.0–7.2)	0.4 (–0.07, 0.03)

*For difference between means/medians.

Figure 1 Relation between delay in bone age in children with atopic dermatitis and (A) age and (B) height SDS at study entry. The bold lines are the regression lines.

and three controls had height SDS less than -1.96 of the mean.

Height velocity SDS (table 2) did not differ between the two groups. Two of 70 and one of 64 controls had a year 1 or year 2 height velocity SDS of less than -1.96 , respectively. Three of 53 and six of 36 patients had a year 1 or year 2 height velocity SDS less than -1.96 , respectively. The latter number was significantly greater ($z = 2.84$; $p = 0.004$) than the corresponding number of controls.

Height SDS at study entry ($r = -0.37$; $p = 0.003$) and height velocity SDS over two years ($r = -0.31$; $p = 0.03$) correlated inversely with age in patients but not in controls.

DELAY IN BONE AGE IN PATIENTS WITH ATOPIC DERMATITIS

The mean (SD) delay in bone age compared with chronological age at the start of year 1 and year 2 was 0.22 years (0.94) and 0.41 years (1.27), respectively. The delay in bone age correlated with age ($r = 0.39$; $p = 0.001$) (fig 1A), height SDS ($r = -0.51$; $p = 0.001$) (that is, the shorter the child, the greater the delay in bone age) (fig 1B), height velocity SDS ($r = -0.32$; $p = 0.01$), and duration of atopic dermatitis ($r = 0.39$; $p = 0.001$). Of these, height SDS and atopic dermatitis duration were the best predictors for delay in bone age by stepwise multiple regression ($r^2 = 34\%$; $p < 0.01$).

INFLUENCE OF BODY SURFACE AREA INVOLVEMENT, POTENCY OF TOPICAL GLUCOCORTICOID TREATMENT, AND COEXISTING ASTHMA

Height, height velocity, and delay in bone age did not differ between patients with $< 50\%$ body surface area involvement and those with $\geq 50\%$ body surface area involvement; between patients treated with mild potency topical glucocorticoids and those treated with moderate potency ones; and between patients without asthma and those with asthma.

BODY MASS INDEX SDS IN PATIENTS WITH ATOPIC DERMATITIS COMPARED WITH CONTROLS

Patients had significantly higher BMI SDS than controls but triceps and subscapular skinfold thickness did not differ (table 2). Six patients and one control were obese (BMI SDS $> +1.96$). Five controls but only one patient were undernourished (BMI SDS < -1.96). BMI SDS of patients correlated with percentage

body surface area involved ($r = 0.28$; $p = 0.03$) and severity of atopic dermatitis ($r = 0.30$; $p = 0.02$).

Discussion

Our study shows that compared with normal children, children with atopic dermatitis begin to fail in growth towards the end of the childhood component of growth. As children with atopic dermatitis approach the teenage years their height velocity decreases, the proportion of children with extremely low height velocity increases, and the delay in bone age increases. In addition, the delay in bone age is greater in children with atopic dermatitis who have lower heights and lower height velocities. Along with data suggesting that individuals with childhood onset atopic dermatitis attain normal adult height,⁵ these findings favour the hypothesis that children with atopic dermatitis have constitutional delay in growth. Children with asthma also have constitutional delay, with impaired growth in childhood, delayed bone age, delayed onset of puberty, but attainment of normal adult height.¹⁵⁻¹⁷ This growth pattern in asthma is thought to be related to the atopic state rather than asthma itself,¹⁸ and might be influenced by impaired production of adrenal androgens.¹⁹ Reduced excretion of adrenal androgens has been found in children with asthma regardless of whether they were receiving inhaled glucocorticoids.¹⁹ With a delayed pattern of growth, short stature is likely to be more pronounced during the teenage years, owing to delayed onset of puberty and the pubertal growth spurt. This would explain the normal stature of the children with atopic dermatitis in our study, who were all under 11 years of age and prepubertal, and the short stature reported in previous cross sectional studies, which included patients with atopic dermatitis who were up to 16 years of age.^{1,2}

Although long term systemic glucocorticoid treatment is associated with growth suppression²⁰⁻²² and glucocorticoid preparations applied to the skin are absorbed into the bloodstream,²³⁻²⁶ the potential effect of topical glucocorticoid treatment on growth is unknown. In our patients, prolonged treatment with moderate potency topical glucocorticoids did not have an adverse influence on growth. In addition, as reported previously, topical glucocorticoid treatment did not suppress adrenal

glucocorticoid function in these children with atopic dermatitis.²⁷

Our observation of higher BMI SDS in children with atopic dermatitis compared with controls excludes undernutrition as a factor adversely affecting growth in children with atopic dermatitis. The systemic effect of topical glucocorticoid treatment and/or reduced daytime physical activity for reasons such as distress from itching or withdrawal because of teasing or self consciousness are possible explanations for the high BMI of atopic dermatitis patients.

We conclude that prepubertal children with atopic dermatitis are developing a pattern of growth delay, which is most obvious in those approaching the pubertal years. We anticipate that this group will tend to have delayed puberty, which may need therapeutic intervention, but our previous study⁵ suggests that final height prognosis is good.

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