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Bone growth in thalassaemic children

The recent interest in various aspects of growth of thalassaemic children resulted in studies of body growth (Kattamis *et al.*, 1970; Pantelakis *et al.*, 1978) and bone density (Johnston and Roseman, 1967; Lapatsanis *et al.*, 1976; Liakakos *et al.*, 1976). As the individual height is related to the length of the long bones, a reliable index of longitudinal bone growth is the increase in length of the metacarpal bones (Exton-Smith *et al.*, 1969; Ikkos *et al.*, 1972). We have therefore studied the metacarpal growth in thalassaemic children.

Materials and methods

Sixty-one children with homozygous β -thalassaemia and 35 controls were studied. The control group consisted of children admitted to the ENT department for tonsillectomy or adenoidectomy. The age

range in both groups was 5-13 years. Thalassaemic children had hepatosplenomegaly, anaemia, and bone lesions, and were transfused every 4-8 weeks. Pretransfusion blood Hb was 6-8 g/dl for at least one year before the study; 24 hours after transfusion it was 11 g/dl or more. The total and medullary widths of the 2nd, 3rd, and 4th metacarpal bones were measured using the method of Horsman and Simpson, 1975. The axial length of the 2nd, 3rd, and 4th metacarpal bones was also measured. All measurements were made by two of us (A.D. and H.G.). Denoting total bone width by TW, medullary width by MW, cortical width by CW, and bone length by L for each metacarpal, the following were evaluated (Horsman and Simpson, 1975).

$$TW = \frac{1}{2} (TW_1 + TW_2)$$

$$MW = \frac{1}{2} (MW_1 + MW_2)$$

$$CW = \frac{1}{2} (CW_1 + CW_2)$$

$$L = \frac{1}{2} (L_1 + L_2)$$

The averages for the 6 metacarpal bones of TW, MW, CW, and L denoted by $\overline{TW}$, $\overline{MW}$, $\overline{CW}$, and $\overline{L}$ were evaluated.

Results

Table 1 shows the mean values and standard deviations (SDs) of the average length of the 6 metacarpal bones in the two groups of children. The length of the metacarpal bones was no different in the two groups between the ages of 5 and 11 years ($P > 0.1$). After age 11 years however, there was a difference ($P < 0.0025$).

Table 2 shows the mean values and SDs of the average total, medullary, and cortical widths of the 6 metacarpal bones ($\overline{TW}$, $\overline{MW}$, $\overline{CW}$), in the two groups. $\overline{TW}$ was greater in the thalassaemic children aged 5-11 years but this difference was not observed after age 11 years ($P > 0.1$). $\overline{MW}$ was greater in thalassaemic than in control children, and thalassaemic children had lower $\overline{CW}$ between ages 5 and 13 years.

Table 3 shows the bone age retardation in thalassaemic children. For each age group the number of children with bone retardation and the range of retardation in months are shown. In the group 5-7 years half the children showed bone age retardation (> 6 months), whereas after this age bone retardation was found in almost two-thirds of the cases.

Discussion

Some authors (Johnston *et al.*, 1966; Johnston and Roseman, 1967; Lapatsanis *et al.*, 1976) have observed that the cortical width is smaller in thalassaemic children than in controls, but Liakakos

Table 1 Mean values and SDs of the average length of the 6 metacarpal bones in thalassaemic children and controls

Age group (years)	n	Control children		n	Thalassaemic children		Statistical analysis	
		Mean (cm)	SD		Mean (cm)	SD	t	P
5-7	9	3.92	0.25	35	3.96	0.3	0.41	>0.1
8-9	12	4.49	0.43	7	4.47	0.33	0.1	>0.1
10-11	7	4.87	0.42	10	4.7	0.49	0.7	>0.1
12-13	7	5.45	0.38	9	4.87	0.25	3.57	<0.0025

Table 2 Mean values and SDs of the average total, medullary, and cortical widths of the 6 metacarpal bones in thalassaemic children and controls

Width	Age group (years)	n	Control children		n	Thalassaemic children		Statistical analysis	
			Mean (mm)	SD		Mean (mm)	SD	t	P
Total	5-7	9	0.57	0.052	35	0.61	0.07	1.5	0.1>P>0.05
	8-9	12	0.61	0.069	7	0.67	0.068	1.74	<0.05
	10-11	7	0.62	0.048	10	0.7	0.07	2.51	<0.0125
	12-13	7	0.7	0.12	9	0.73	0.149	0.32	>0.1
Medullary	5-7	9	0.34	0.04	35	0.42	0.09	2.35	<0.01
	8-9	12	0.35	0.05	7	0.46	0.07	3.45	<0.0025
	10-11	7	0.34	0.06	10	0.46	0.1	2.82	<0.01
	12-13	7	0.38	0.1	9	0.50	0.1	1.4	0.1>P>0.05
Cortical	5-7	9	0.22	0.01	35	0.19	0.03	2.69	<0.01
	8-9	12	0.25	0.03	7	0.21	0.02	3.38	<0.0025
	10-11	7	0.28	0.04	10	0.23	0.04	2.04	<0.05
	12-13	7	0.33	0.04	9	0.23	0.05	3.99	<0.0005

Table 3 Retardation of bone age in thalassaemic children

Age group (years)	n	Children with bone retardation	Range of retardation (months)
5-7	35	18	10-22
8-9	7	5	8-22
10-11	10	7	12-24
12-13	9	6	7-44

et al. (1976) found no such difference. In the present study we found that the cortical width in the thalassaemic children with pretransfusion Hb 6-8 g/dl, was smaller than that of controls.

Johnston *et al.* (1966) and Pantelakis *et al.* (1978) have reported a delay of the bone maturation in thalassaemic children. According to Johnston *et al.* (1966) this may be due to absence of the adolescent growth spurt in thalassaemic children. In the present study a similar delay in bone maturation was observed. The proportion of children with bone age retardation was greater after age 7.

There are no reported studies of bone growth in thalassaemic children. In our study we observed that longitudinal bone growth was equal in thalassaemic children and controls until age 11 years. After this age, bone length was shorter in thalassaemic children. The growth of total bone width in thalassaemic children was greater than that of the controls until age 11 and then it became equal. The medullary width was greater in thalassaemic than in normal children. Johnston *et al.* (1966) and Flynn *et al.*

(1976) suggested that the retardation of skeletal maturation in thalassaemic children is due to hormonal disturbances resulting from chronic anaemia, or to chronic iron deposition in the glands responsible for the growth spurt. The retardation of bone growth in thalassaemic children found in the present study, which was more obvious as the children became older, could be attributed to the same factors. As however the pre- and post-transfusion Hb levels were the same in all age groups it is more likely that chronic iron overload is the responsible factor. If so, effective control of iron overload by new methods of desferal administration could correct the retardation of bone growth, and this should be the first clinical sign of effective treatment in children treated from early years.

Summary

X-ray measurements were made of the length and width of the 3 middle metacarpal bones of both hands, in 61 thalassaemic and 35 control children of both sexes aged 5-13 years. Growth in length of the bone was normal until age 11 years but after this it was smaller in thalassaemic children. The growth of total width in thalassaemic children was greater than that of the controls until age 11 years and then became equal. The proportion of children with bone age retardation was greater after 7 years.

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Epileptic laughter with precocious puberty

Gelastic (laughing) epilepsy may be defined as complex co-ordinate movements with grinning, giggling, or joyful weeping. The disorder is rare and may arise from lesions in the temporal lobe, limbic system, or hypothalamus. We report a case of gelastic epilepsy which preceded the onset of precocious puberty.

Case report

A girl aged 2.2 years was referred with a long history of bouts of unusual behaviour. The perinatal and neonatal period were normal. From age 3 weeks she had had repeated episodes of crying during which she

would draw up her knees, clench her fists, and micturate frequently. As the child grew older the nature of the episodes changed; they would begin with a characteristic cry or giggle, she would then frown, appear vacant, and become pale and there would be slow rotatory eye movements, drooping of the eyelids, and repeated blinking. These episodes lasted a few seconds only but would recur about every 2 min for up to 12 hours. Throughout them she would be overexcited, aggressive in her behaviour, and repeatedly incontinent of urine. Once free of the attacks she would drink excessively and sleep for between 12 and 24 hours. Otherwise she was a happy, contented child with no other problems.

Examination was normal. However, the EEG showed paroxysmal moderate to high amplitude sharp and slow wave complexes in all areas but these were particularly pronounced in the central region. An air encephalogram showed slight hydrocephalus and a space-occupying lesion on the floor of the 3rd ventricle. On ventriculocopy a tumour occupied the whole of the floor of the 3rd ventricle. A biopsy was attempted but the tumour was too hard and fibrous to get adequate material. A bilateral ventriculocisternostomy (Torkildsen's operation) was performed to lessen the intraventricular pressure. Radiotherapy and anticonvulsant drugs were given and during the next year there were fewer fits.

During her 3rd year of life the child developed precocious puberty. On examination height was 108.6 cm (+2.1 SD) and weight 22 kg (>97th centile), pubertal development was Tanner P₄G₃ with menarche. Bone age 8.7 years. Plasma gonadotrophins were in the pubertal range; basal luteinising hormone (LH) 11.4 U/l, and follicle stimulating hormone (FSH) 4.4 U/l, after 100 μ g intravenous luteinising hormone releasing hormone (LHRH) plasma LH rose to a peak greater than 50 U/l and FSH to 24.5 U/l. Plasma oestradiol was 150 pmol/l (41 pg/ml). Growth hormone, adrenocortical, and thyroid studies were all normal. She was treated with cyproterone acetate 50 mg three times a day. Clinically, sexual maturation slowed and she lost her axillary and pubic hair. Height has continued to increase and her bone age at a chronological age of 5.8 years was 10.8 years.

At 5 years the seizures increased in frequency to at least one an hour. She would giggle or hiccup and this was followed by a brief period of apparent insecurity and uncertainty about her surroundings. Initially, these episodes occurred when she was tired or emotionally upset but later they became more common and were associated with deterioration in her school work and refusal to leave the house to play with her friends. The episodes have responded well to clonazepam 2.5 mg daily and this has