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PROGRESSION OF A STRUCTURAL SCOLIOSIS DURING TREATMENT WITH GROWTH HORMONE

A Case Report

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A diagnosis of panhypopituitarism was made in an infantile male at the age of 22. Skeletal age was estimated to be 14 years. Thyroxin, corticosteroid and later testosterone was administered. Growth hormone was given initially over a period of ten weeks and later for two and a half years. The standing height increased from 143 to 158.5 cm. During periods of growth induced by growth hormone a progression of a thoracic scoliosis from 15° to 62° was observed. In this case growth hormone or the associated substances seem to be the more probable cause of the progression of scoliosis than growth rate *per se*.

Key words: growth; growth hormone; panhypopituitarism; scoliosis

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A connection between the velocity of growth and the progression of structural scoliosis was demonstrated already in the beginning of the nineteenth century (Bampfield 1824). The risk of an increase of the spinal deformity is particularly high during periods of rapid growth, for instance, during the prepuberal growth spurt at the age of 11 to 13 years in girls and 13 to 15 years in boys.

This case report illustrates the connection between progression of a thoracic scoliosis and two periods of growth hormone treatment in a man with panhypopituitarism.

CASE REPORT

The patient is a male born in 1946. The family history is non-contributory. His mother had moderate hypertension and albuminuria during pregnancy. At parturition he was born in breech presentation. Immediately after delivery he was noted to have muscular cramps in the right arm and the right side of the face. He also developed a hematoma of the right sternocleidomastoid muscle and eventually torticollis.

In 1957 he was admitted to a pediatric department and a diagnosis of pituitary nanismus was made. In 1968 he was referred to an endocrine department. At admission he had a height of 143 cm and a span of 146 cm. He weighed 31.5 kg. He appeared infantile and there were no secondary sex characteristics. The thyroid was not palpable and blood pressure was 105/80 mm Hg. He had a slight anemia, but normal serum electrolytes and normal liver and kidney function.

Thyroid function: PBI was 4.1 μg/100 ml and T_3-resin uptake 91 per cent, serum cholesterol 273 mg/100 ml. Iodine uptake increased from 26 per cent to 56 per cent after administration of thyrotropin. On scanning the thyroid gland appeared small but otherwise normal. A provisional diagnosis of secondary hypothyroidism was made and thyroxin administration was started with a

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dosage of 0.1 mg daily which was gradually increased to 0.2 mg daily. This dosage was maintained throughout the reported studies.

Adrenal function: Urinary steroids and plasma cortisol were subnormal under basal conditions, but increased following ACTH. No increase was demonstrable following metyrapone. Following the demonstration of ACTH deficiency the patient was put on cortisone acetate perorally 5 mg twice daily. This dosage was increased to 5 mg three times daily in November of 1970.

Gonadal function: Urinary gonadotrophins and later plasma FSH and LH determined radioimmunologically were low. During the time of observation there were no spontaneous signs of puberty and in November of 1970 treatment with testosterone was started.

Growth hormone: Growth hormone levels were low or undetectable and did not increase in connection with insulin induced adequate hypoglycemia. Growth hormone (Kabi 1620 DqP7) was administered 2 mg daily for 1 week. Under metabolic ward conditions this caused a decrease of urinary nitrogen excretion from an average of 9 to an average of 4 mg daily. Thereafter the same preparation was given by injections of 2 mg twice a week from September 28 to December 3 of 1968 (10 weeks).

Growth hormone therapy was resumed with the same preparation (Kabi 1620 DqP27) in February of 1970, that is after 14 months, in a dosage of 3.7 mg twice weekly and thereafter growth hormone was given continuously until September of 1972 (31 months). The dosage was increased to three injections weekly in April of 1971.

CLINICAL COURSE

On admission at the age of 22 this man was severely retarded physically. The skeletal age was estimated as 14 years. Standing height was 143 cm (compared with the average height of Swedish adult males of 179 cm). A structural scoliosis of 15° according to Cobb (1948) was known to have remained constant for more than 3 years.

Growth hormone therapy induced rapid growth. Simultaneously, the structural scoliosis progressed from 15° to 27° over a period of 10 weeks. Because of this progression of the scoliosis, growth hormone therapy was stopped. After cessation of growth hormone therapy, growth continued at a slower rate. During this period of 13 months the scoliosis remained stationary.

A Milwaukee brace was constructed and fitted, whereafter growth hormone therapy was resumed when the patient had been adequately braced. In spite of an accelerated growth rate no change in the spinal curve could be demonstrated for 18 months, that is as long as the patient wore the brace all day and all night as recommended. During the following 17 months, growth hormone therapy was continued, but the bracing was inadequate. During this period the scoliosis progressed from 26° to 56°. Growth hormone therapy was again stopped and longitudinal growth ceased, whereas there was a slight additional progression of the scoliosis to 62°.

The total increase in standing height from 143 to 158 cm should be corrected for the spinal deformity which at the time of epiphyseal closure amounted to another 4 cm according to Lind & Bjure (1975).

DISCUSSION

The connection between progression of a thoracic scoliosis and two periods of increased growth velocity induced by treatment with growth hormone has been illustrated. During the second period of treatment a Milwaukee brace, worn as recommended, seemed to be able to prevent the progression of the scoliosis. However, when the patient stopped wearing the Milwaukee brace as recommended, the scoliosis progressed rapidly during continued growth hormone therapy. To our knowledge there is no evidence that the stopping of bracing *per se* is followed by a progression of scoliosis and consequently we have interpreted the noted progression as a result of continued growth induced by growth hormone.

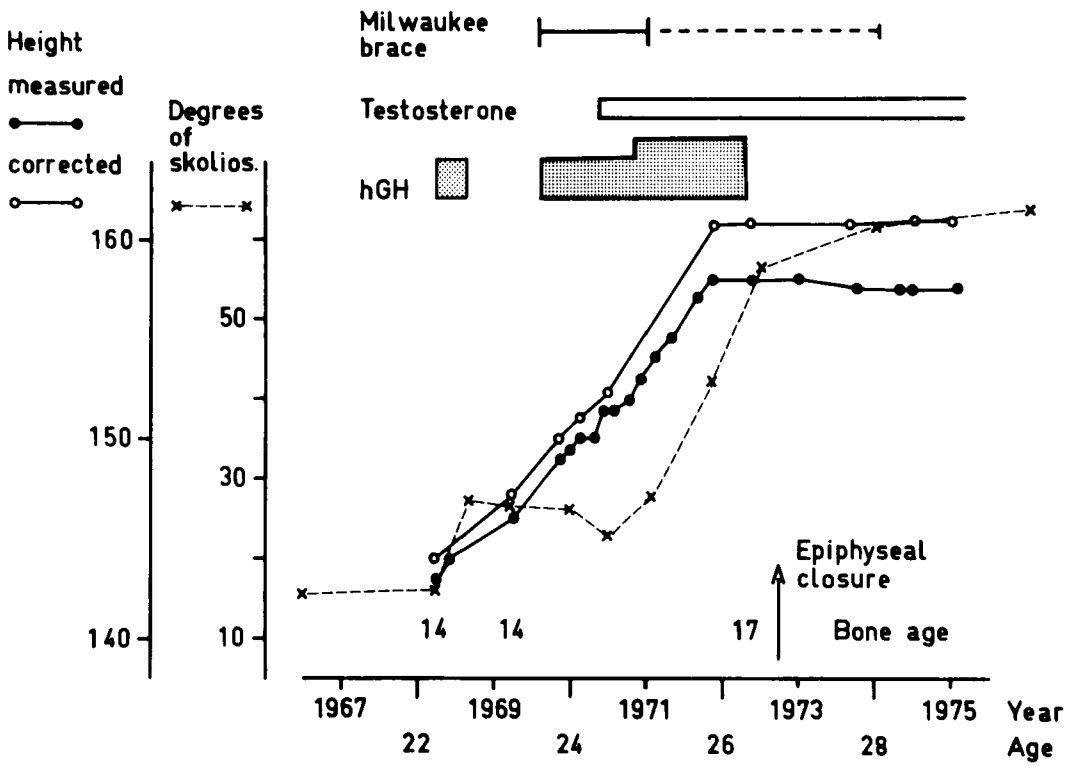

Figure 1. Longitudinal growth and progression of scoliosis in relation to therapy in a male with panhypopituitarism.

Cortisone and thyroxin were given throughout and there is no indication that either of these substances influenced the clinical course. Testosterone was given only during the latter part of the study, which partly coincided with the most important progression of the scoliosis. There is, however, no evidence that testosterone influences the course of a scoliosis unfavorably. Consequently the inadequate bracing during growth induced by the growth hormone seems to be a more probable explanation for the demonstrated progression.

It is difficult to evaluate whether the progression of thoracic scoliosis was caused by the increased growth velocity as such, or by growth hormone and/or associated substances. An increased serum concentration of growth hormone as well as somatomedin A has previously been demonstrated in scoliotic girls (Willner et al. 1976). Girls with adolescent idiopathic scoliosis also have a different growth pattern compared with non-scoliotic healthy controls. The scoliotic girls have been found to be taller and slimmer at the time of diagnosis and they have grown more rapidly during the year before the diagnosis was made, compared with age-matched controls (Willner 1972, 1974). Skeletal maturation progressed at a slower rate in the scoliotic groups between the age of 13 and 18 years (Nordwall & Willner 1975).

In this patient the scoliosis was stationary for 3 years prior to treatment with growth hormone and for almost one and a half years between the two periods of growth hormone administration. During both these periods growth occurred but at a slower rate. Both

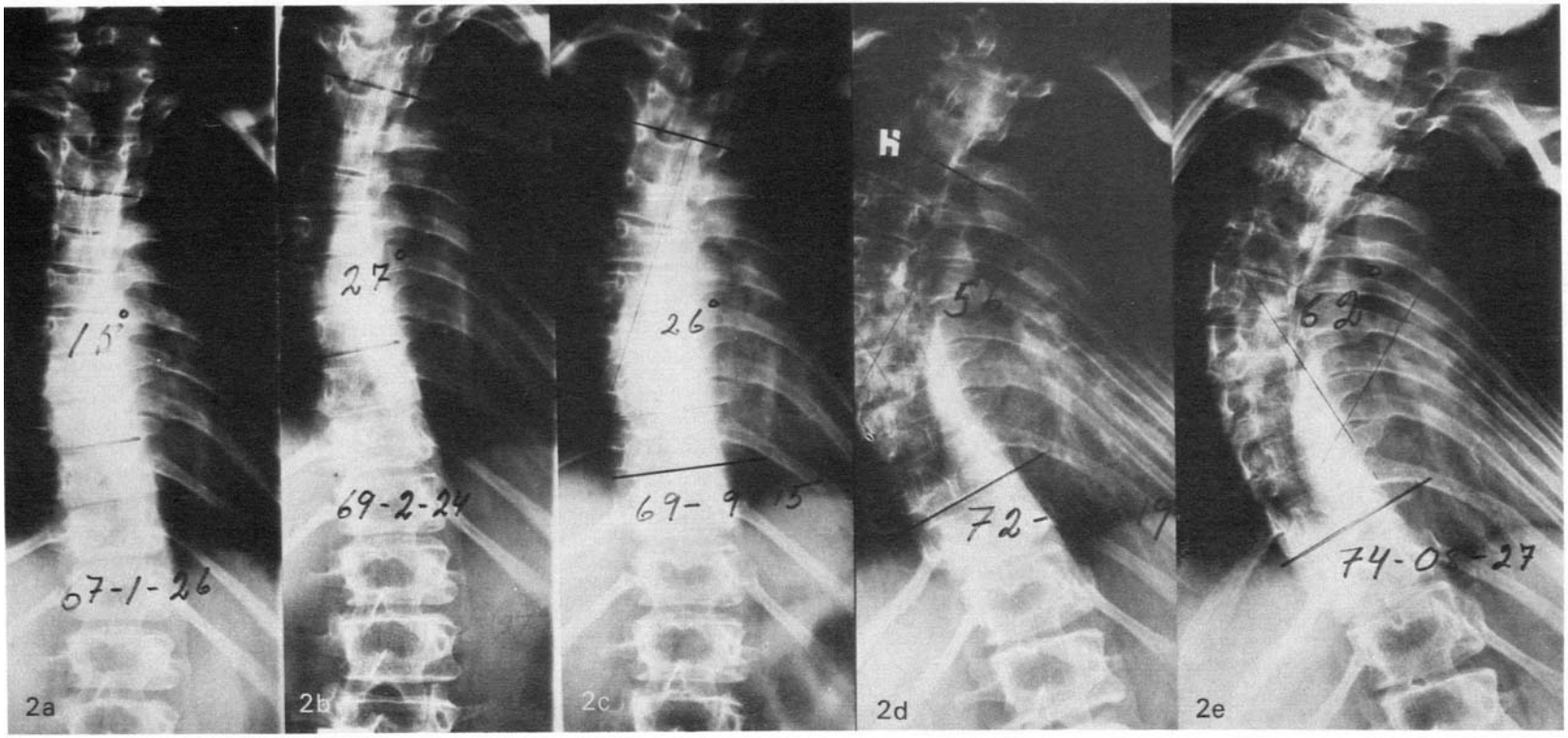

Figure 2. Progression of scoliosis determined on roentogenograms according to Cobb (1948).

these facts seem to imply that either growth hormone or an associated substance is the causative agent, rather than growth *per se*.

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