Clinical Reports

Sequential growth hormone deficiency and acromegaly

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Summary: This is the case of a patient with a pituitary tumour presenting initially with growth hormone deficiency and requiring treatment with human growth hormone. Eight years later he represented with acromegaly. This sequence of events has not to my knowledge been reported previously.

Introduction

This, to my knowledge, is the first published case report of a patient with a pituitary tumour who presented initially with growth hormone deficiency requiring treatment with human growth hormone and 8 years later developed acromegaly.

Case report

A 16.8 year old male was first seen in January 1971 because of a 3-year history of failure to grow and frontal headaches for 18 months. His father was 180.3cm tall and his mother was 159.4cm (Figure 1). His brother and sisters were of normal stature. The patient was 149cm (Figure 1) and weighed 39.3kg; both measurements were below the third percentile for his age. Bone age was 14.9 years. Genitalia development and pubic hair were graded at stage 3 according to the criteria described by Tanner.¹ There was no axillary or facial hair. Both testes measured 8ml as assessed by comparison with the Prader Orchidometer. Visual fields were normal by perimetry. The pituitary fossa was enlarged with a double floor consistent with a pituitary tumour on X-ray. Growth hormone after 90 min of sleep was 2.2mU/l and it was 4.4mU/l before and 2.5mU/l at 30 min; 3.6mU/l at 60 min; 2.8mU/l at 90 min; 4.2mU/l at 120 min and 3.3mU/l at 180 min after 1mg of glucagon intramuscularly. Urinary luteinizing hormone (LH) was less than 0.5IU of 2nd International Reference Preparation (IRP) of human menopausal gonadotrophin (HMG) in 24 hours before clomiphene citrate 100mg daily for 5 days and 1IU 2nd IRP

Figure 1 Measurements before, during and after treatment with hGH. F = father, M = mother.

HMG in 24 hours at the end of this period.² Serum thyroxine was 83nmol/l (normal range 42-119). A metyrapone tartrate test was normal.

Full blood count, urea, electrolytes, blood sugar, urine analysis, chest X-ray, barium meal with follow through and 3-day faecal fat collection were all normal. Cobalt irradiation with a total dose of 2000rad was recommended for treatment of the pituitary tumour rather than surgery, since there was no clinical evidence of suprasellar extension.

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Accepted: 28 March 1988

In July 1972 because his serum thyroxine was 49 nmol/l (normal range 42–119) and free thyroxine index was 3.1 (normal range 3.0–9.5) he was commenced on L-thyroxine 100 µg daily. In July 1973 the L-thyroxine was stopped to reassess his thyroid status. Two months later his serum thyroxine was 37 nmol/l (normal range 42–119) and free thyroxine index was 2.0 (normal range 3.0–9.5). L-thyroxine, 100 µg daily, was recommenced.

In July 1973 his height was 153 cm (Figure 1). His growth rate of 1.9 cm/year was low (Figure 1). His bone age was 15.0 years (Figure 1). There was no stimulation of growth hormone secretion with insulin hypoglycaemia (Table I). He was therefore considered to be growth hormone deficient and was started on treatment with human growth hormone (hGH) supplied by the Health Services Human Growth Hormone Committee in the UK. His growth rate increased on growth hormone therapy which was continued until January 1976 when his height was 162.5 cm (Figure 1). The dose of growth hormone in this boy of 44 kg in weight was 10 mg intramuscularly twice weekly. This was reduced to 5 mg three times weekly in November 1975. At the commencement of growth hormone therapy his pubertal status was similar to that when he presented in January 1971. Six months after commencing treatment his testicular size increased to 10 ml (Prader orchidometer) and continued to increase in volume reaching 25 ml by October 1975. At this time genitalia were 5, pubic hair 5 and axillary hair 3 on the Tanner¹¹ scale indicating full maturation. Growth hormone antibodies were not detected during treatment with growth hormone.

From 1976 to 1981 he attended the clinic yearly. He remained well during this time. His thyroid replacement was satisfactory. A raised prolactin level of 60 ng/ml (normal less than 11) was found in 1977. In 1981 he married and fathered a child.

In May 1984 he returned to the clinic complaining of frontal headaches with nocturnal sweating for the previous 3 months. Other features noted were increase in size of hands and feet; his shoe size increased from 7 to 10 in the previous year. A change in size and shape of face was noted by his

wife. Numerous skin tags appeared on the neck and axillae. His libido had decreased markedly. A clinical diagnosis of acromegaly was made. Growth hormone response to 75 g glucose orally (Table II) and thyrotrophin releasing hormone (TRH) 200 µg intravenously (Table III) confirmed the diagnosis of acromegaly. Thyroid function tests showed adequate replacement therapy. Metyrapone tartrate and water deprivation tests were normal. His prolactin level of 570 ng/ml (normal less than 15) was increased. His serum testosterone of 1.4 nmol/l (normal male range 8.6–42) was low. X-rays of hands, feet and skull showed evidence of acromegaly and there was enlargement of the pituitary fossa. Visual fields by perimetry were normal. Computed tomographic (CT) scan showed a pituitary tumour with suprasellar extension. Hypophysectomy by the transethmoidal approach was performed. Histologically the tissue was a benign chromophobe adenoma with large areas of growth hormone producing cells. Prolactin positive cells were also found scattered throughout the sections.

Three years and six months later the patient is well on replacement with L-thyroxine, cortisone acetate, intranasal desmopressin acetate and intramuscular testosterone (as enanthate and propionate). His most recent growth hormone was 4.0 mU/l before and 3.2 mU/l at 30 min; 3.6 mU/l at 60 min and 3.8 mU/l at 120 min following 75 g glucose orally.

Discussion

This patient with a pituitary tumour, treated initially by irradiation as there was no clinical evidence of suprasellar extension, had thyroid and

Table I Insulin tolerance test (0.1 U/kg body weight i.v.), when patient had hypopituitarism

Time (min)	Blood glucose (mmol/l)	Plasma cortisol (nmol/l)	Growth hormone (mU/l)
Zero	3.8	463.7	0.6
30	1.5	560.3	1.1
60	3.0	850.1	1.4
90	3.3	656.9	1.0
120	3.8	444.3	2.0

Table II Glucose tolerance test (75 g orally) when patient had acromegaly

Time (min)	Blood glucose (mmol/l)	Growth hormone (mU/l)
Zero	5.4	66.2
30	6.7	72.7
60	6.6	74.8
120	6.8	52.1

Table III TRH test (200 µg i.v.) when patient had acromegaly

Time (min)	Growth hormone (mU/l)
Zero	54.5
30	137.0
60	92.5

growth hormone deficiency. He responded well to growth hormone replacement therapy in that he achieved an acceptable height of 162.5 cm and went through spontaneous puberty. The development of acromegaly after growth hormone therapy has to my knowledge not been reported previously. Surgical removal of pituitary tumours is more favoured than irradiation and this may be the natural behaviour of a chromophobe adenoma or possibly a change brought about by the irradiation. There was

no reason to suspect ectopic production of growth hormone releasing hormone. It is unlikely that the exogenous growth hormone in any way changed the behaviour of an irradiated chromophobe adenoma.

Acknowledgement

I wish to thank Dr J. Dinn, Consultant Neuropathologist, St Vincent's Hospital for the histopathological details.

References

1. Tanner, J.M. *Growth at Adolescence*. Blackwell Scientific Publications, Oxford, 1962.
2. Newton, J., Ramsay, I. & Marsden, P. Clomiphene as a test of pituitary function. *Lancet* 1971, **ii**: 190–191.