GROWTH HORMONE DEFICIENCY ASSOCIATED WITH ACQUIRED IMMUNE DEFICIENCY SYNDROME – CAUSE OR COINCIDENCE

F OFEI, J APPIAH-KUSI AND DELA NYONATOR
Endocrine Clinic, Department of Medicine, Korle Bu Teaching Hospital and University of Ghana Medical School, PO Box GP 4236, Accra.

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CASE HISTORY
An 18-year-old male was referred from a mission (district) hospital to the endocrine clinic of the Korle-Bu Teaching Hospital (KBTH) with a diagnosis of ‘stunted growth’ associated with primary hypothyroidism. A blood test requested 6 months earlier by the referring doctor had shown mildly elevated thyroid stimulating hormone (TSH) but normal levels of free triiodothyronine (free T₃) and free thyroxine (free T₄).

On review at the KBTH the patient complained of recurrent headaches, abdominal pain, easy fatigability and earaches. His bowel movements were regular and he had noticed weight loss and intolerance for heat. He had no problems with his vision or sense of smell. He had noticed his genitalia to be considerably smaller than that of his peers, however, he experienced regular spontaneous penile erections.

The patient was born in January 1982 from a full term normal delivery; the 12th of thirteen children of the same parents. His early developmental milestones had apparently been normal and he did not suffer from any protracted childhood illness, kwashiorkor or marasmus. However, during a brief hospital admission at the age of 6 years he received a blood transfusion for reasons that were unclear to his oldest sister who accompanied him to the clinic. He had remained well thereafter until these complaints of general ill health and a lack of growth forced him to drop out of junior secondary school at the age of 15 years. His sister indicated that both parents and the other siblings were well and either 'tall or of average height'.

On examination his height and weight were 1.24 metre (> 3 standard deviations below mean for age) and 27 kg respectively (body mass index 17.6 kg/m²). The body proportions were normal, with an arm span equal to his height. His voice was high-pitched. He had curly black hair and pallor of the mucous membranes. There was no lymphadenopathy, goitre or gynaecomastia and the rest of the general, cardiac, respiratory and nervous system physical examinations were normal. Blood pressure was 100/70 mmHg. The spleen and liver were both palpable 5 cm below the costal margins. Facial, axillary and body hairs were absent. Pubic hair was scanty while his penis, scrotum and testes were small, corresponding to Tanner stages IV and I for the pubic hair and genitals respectively. There was no hypospadias.

Results of investigations on blood samples at the time of his initial presentation showed haemoglobin of 6 g/dl and haemoglobin electrophoresis AA. Fasting blood glucose, urea, electrolytes, creatinine, bilirubin and alanine transaminase were within normal limits, while albumin, aspartate transaminase and alkaline phosphatase showed only minor alterations. X-ray films of the chest and sella turcica were normal. That of the left wrist and hand corresponded with a bone age of 13 years.

Evaluation of anterior pituitary hormone function was limited to a repeat thyroid function test, which showed normal levels of free T₃, free T₄ and TSH, and blood sampling for growth hormone (GH) and cortisol during an insulin tolerance test (ITT). The ITT, a well-established provocative test for assessment of GH status, was preceded by sex steroid priming with stilboestrol. 1 mg b.d. orally for 48 hours, and an overnight fast. Blood samples for glucose, GH and cortisol were taken immediately before, 30, 45, 60, 90 and 120 minutes after intravenous injection of 0.15 U/kg body weight of...
regular insulin (Actrapid, NovoNordisk, Denmark).

Blood glucose at the start of the ITT was 4.1 mmol/L, reaching a nadir of 2.1 mmol/L at 30 minutes. Plasma GH, which was 0.18 microgram/L (normal range 0 - 5.0 microgram/L) at the start, reached a peak of 2.64 microgram/L at 60 minutes, falling off to 1.32 microgram/L by the end of the test. Peak cortisol during the test was 698 nmol/L (normal morning range 138 - 690 nmol/L). The hypoglycaemia achieved was adequate and not associated with any untoward clinical event. During an ITT, a blood glucose level of 2.2 mmol/L or less provides an appropriate stimulus which should result in peak serum cortisol and GH levels exceeding thresholds of 585 nmol/L and 10 ng/ml respectively in normal individuals. This patient, therefore, had a normal cortisol response but severe GH deficiency.

Treatment with recombinant human growth hormone (rhGH) was contemplated but not initiated due to financial constraints. The patient was therefore referred to the dieticians for a high calorie diet and given supplemental oral B vitamins and folic acid in the interim.

Five months after the first clinic review his height remained the same. However, he had gained 9 kg in weight. On further review 3 months later he reported anorexia, odynophagia, recurrent diarrhoea and generalised pruritic skin lesions. Physical examination then revealed tinea capitis, extensive exfoliative dermatitis and oral thrush. An additional test for the human immunodeficiency virus (HIV), which was not considered in the evaluation of his earlier complaints, was positive for HIV 1 and 2 on a screening test (HIV-SPOT. Genelabs Diagnostics, Singapore) and subsequently confirmed by an enzyme immunoassay method (INNOTEST HIV-1/HIV-2. Innogenetics N.V., Belgium).

There was no identifiable predisposition or risk behaviour for the HIV infection except for the previous blood transfusion. The patient was given no further treatment as, for financial reasons, his family opted for counselling only, without anti-retroviral therapy. He has since died.

DISCUSSION

This report describes short stature associated with GH deficiency in a patient with HIV infection. Constitutional delay in growth and puberty (CDGP) is by far the commonest cause of short stature. However, CDGP was unlikely in this patient as he failed to produce the expected peak response of GH to provocative testing especially after pre-treatment with stilboestrol. Stilboestrol priming increases the basal, peak and incremental levels of GH during insulin-induced hypoglycaemia and distinguishes between CDGP and true GH deficiency in peri-pubertal children.

Typically children with GH deficiency present with short stature. They tend also to be overweight for their height, with increased subcutaneous fat especially around the trunk. A low body weight accompanying short stature, as was observed in this patient, is suggestive of chronic malnutrition or systemic disease.

Failure to thrive frequently accompanies HIV infection in childhood with as many as 50% of HIV-infected children showing evidence of poor growth in the long term. These abnormalities occur irrespective of whether the children were born to HIV-infected women or became infected postnatally. Levels of HIV RNA are greater in HIV-infected children with poor growth compared with similarly infected children with normal growth rates. Also, treatment of HIV-infected children with anti-retroviral drugs appears to have a favourable effect on ponderal and linear growth. Such evidence supports a direct role of the virus in the wasting and growth failure that accompany the acquired immune deficiency syndrome (AIDS).

The growth failure in HIV-infected children has been found to be related, not only to deficiencies in several micronutrients, but also to neuroendocrine abnormalities occurring as isolated or multiple defects relating to adrenal, thyroid, growth hormone and insulin-like growth factor-1 (IGF-1) function.

With regard to GH dysfunction in AIDS, most reports indicate the commonest abnormality to be a peripheral tissue resistance to the effects of normal circulating levels of GH. Only few reports suggest classical GH deficiency as the likely abnormality. The reasons for patients presenting with either abnormality is unclear.

While treatment of children with HIV-associated growth failure with rhGH can improve their growth rate and lean body mass, there is evidence that it can also improve immune function in some patients. This additional advantage of rhGH is
attractive and should make treatment of proven HIV-related growth failure worthwhile. Provided issues regarding access to, and the cost of, rhGH and anti-retroviral therapy can be adequately addressed.

As HIV infection becomes more common in all age groups, investigations for delayed or failed linear and ponderal growth in children and adolescents must consider this possibility alongside other better-known causes.

REFERENCES


