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NECROSIS OF THE FEMORAL CAPITAL EPIPHYSIS OCCURRING DURING HUMAN GROWTH HORMONE THERAPY

INGJALD BJERKREIM & OLAV TRYGSTAD

Sophies Minde Orthopaedic Hospital, University of Oslo, and
Department of Pediatrics, Rikshospitalet, Oslo, Norway.

A girl with growth hormone deficiency developed a necrosis of the femoral capital epiphysis 6 months after the start of human growth hormone treatment. The compensatory growth spurt is believed to have caused an insufficient blood supply to the epiphysis, resulting in necrosis.

Key words: growth hormone; femur head; epiphysis; necrosis

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The treatment of growth hormone deficiency with human growth hormone was first introduced by Raben (1958). Since then several hundreds of patients have had replacement therapy, some for more than 10 years. Except for the production of growth hormone antibodies with therapy resistance, only a few complications have been reported. Recently slipped femoral capital epiphysis occurring during growth hormone therapy was reported in three patients (Fidler & Brook 1974, Rennie & Mitchell 1974).

At the Department of Pediatrics, Rikshospitalet, Oslo, we have treated 70 growth-retarded patients with human growth hormone since 1961, and 12 children have been treated for more than 5 years. No therapy resistance because of antibody production has been observed. Two boys, 12 years of age, with a rapid compensatory growth spurt of 12 cm a year, suffered a transitory flexion contracture in the knee joints.

The purpose of the present paper is to report on a patient who developed necrosis of the left femoral capital epiphysis.

CASE REPORT

A girl (A.A. born 18.7.55) aged 14 $^{9}/_{12}$ years was seen in the clinic in April 1970 because of failure to grow and mature. Her parents and sister were about average height. The patient had an infantile appearance, doll-like face, was moderately overweight, and of normal proportions. The height was 131.8 cm, body weight 35 kg, and the bone age was somewhat less than 11 years. Growth hormone stimulation tests, and a metabolic test with administration of human growth hormone revealed growth hormone deficiency. The adrenocorticotropin and thyrotropin secretion was considered normal, whereas the luteotropic hormone and follicle stimulating hormone as well as the oestrogen levels in serum were prepubertal. The kariotype was normal feminine.

From August 1970 the patient was treated with human growth hormone, 2 mg (i.e. 4 i.u.) intramuscularly three times a week. At the start of treatment the height of the patient was 132.0 cm. The response to the treatment is given in Figure 1. During the first 6 months of treatment

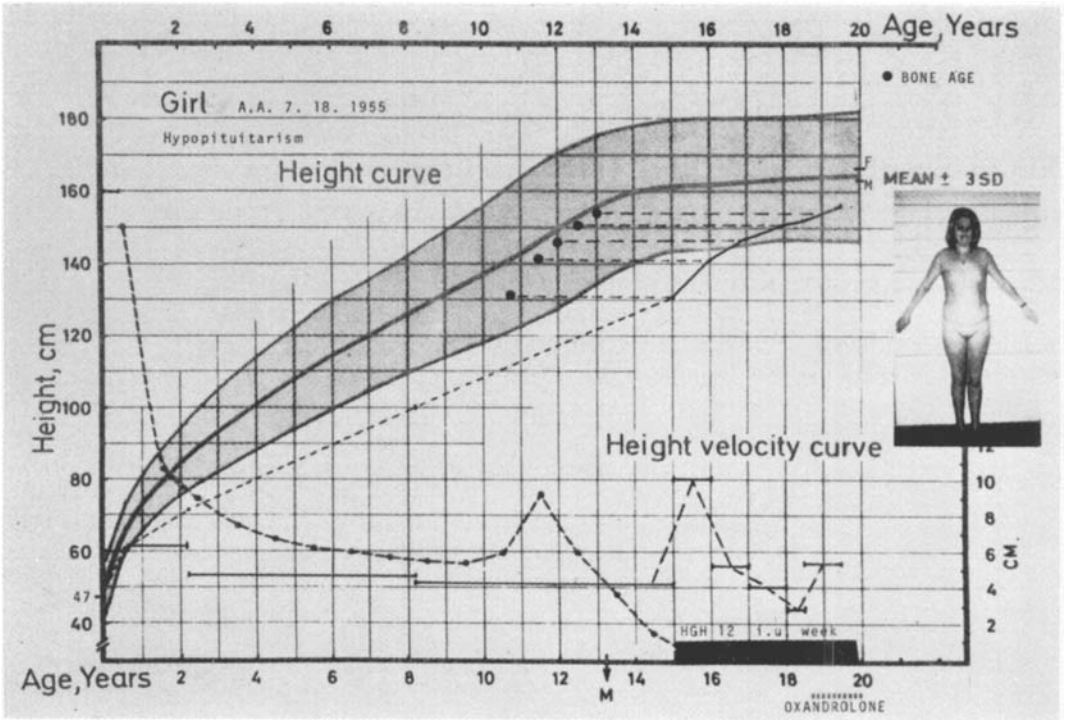

Figure 1. The growth chart of the patient prior to and after administration of human growth hormone (HGH). M denotes the height of the mother, and F the percentile height of the father.

there was a compensatory growth spurt of 6.0 cm.

In January 1971 the patient complained of pain in her left thigh over a period of about fourteen days. There had been no previous trauma. Clinical examination revealed no limitation in movement of the left hip. In April 1971 she started to limp, and after some time she could hardly walk because of pain in the left hip. On examination tenderness was found in the left groin, and movements of the left hip were markedly reduced in all directions, particularly flexion, abduction and internal rotation. Radiography showed flattening and irregular structure of the left femoral capital epiphysis with a subchondral translucent line (Figure 2). The patient was given non-weightbearing treatment on crutches. The pain vanished, but the movements of the hip continued to be markedly reduced.

A new radiographic examination in August 1972 demonstrated an extensive necrosis, involving about three quarters of the femoral head (Figure 3), and there has been little change since then. The patient was on continuous human growth hormone therapy. After starting the additional treatment with oxandrolone (an anabolic steroid) at the age of 18.5 years a deficient development of pubic hair occurred. At 20 years of age there was still no development of her breasts.

DISCUSSION

A 15-year-old girl (bone age 11 years) with growth hormone deficiency developed a left-sided hip disorder 6 months after the start of human growth hormone therapy. During this period of time she grew 6 cm. There had been no trauma. The symptoms and the radiograms 8 months after the start of treatment could well be compatible with Perthes' disease. However, Perthes' disease is seldom observed in girls of more than 11 years of age (Lauritzen 1975), and the course was also different. In spite of a marked necrosis of the femoral capital epiphysis, no affection of the metaphysis was seen,

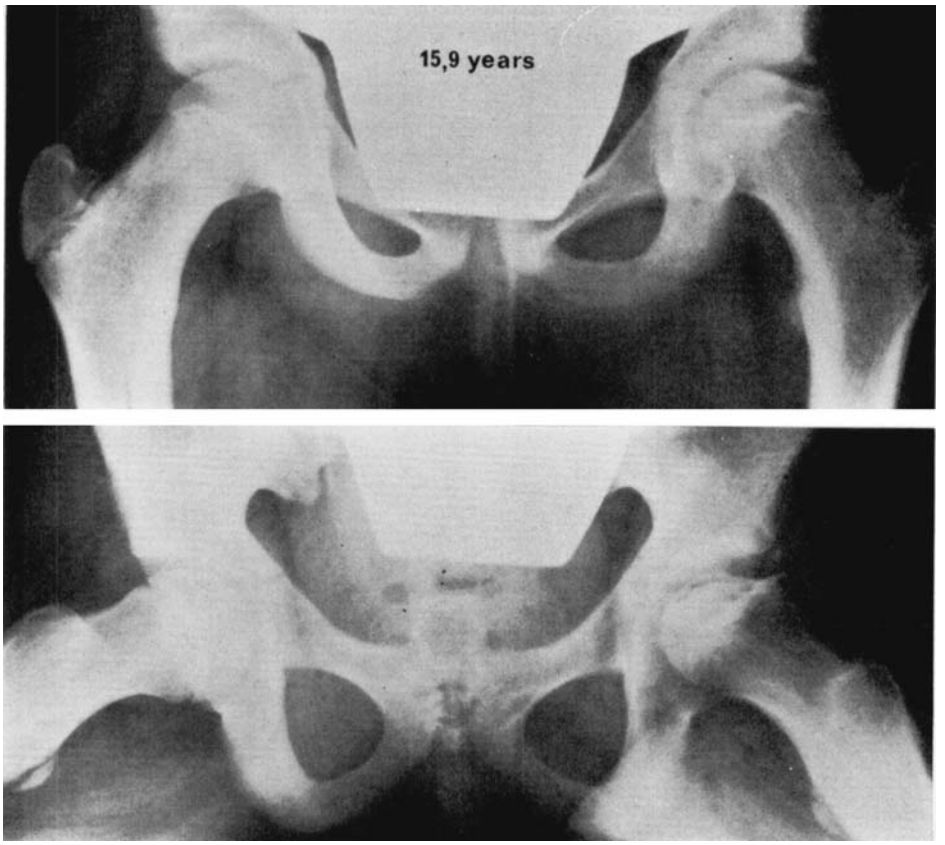

Figure 2. Radiographs of the hips 8 months after the start of growth hormone therapy showing flattening and irregular structure of the left femoral capital epiphysis.

and little rebuilding of the femoral head occurred.

The incidence of necrosis of the femoral head is relatively high in patients receiving long-term corticosteroid treatment, in alcoholics, and in Gaucher's disease. An alteration in the fat metabolism in these patients, resulting in fat embolisms has been associated with the necrosis of the femoral head (Brit. med. J. 1972). Human growth hormone has generally been considered to be lipolytic. However, our patient was treated with a human growth hormone preparation that has been deprived of the lipolytic activity (Trygstad & Foss 1968).

The mechanism of the necrosis of the femoral capital epiphysis in the present patient is not clear. In two patients on growth hormone therapy we observed that the growth of the soft tissue did not keep up with the bone growth, resulting in temporary flexion contracture of the knee joints. We consider that the necrosis of the femoral capital epiphysis in the girl described here was related to her rapid compensatory growth spurt, and an insufficient supply of blood to the epiphysis.

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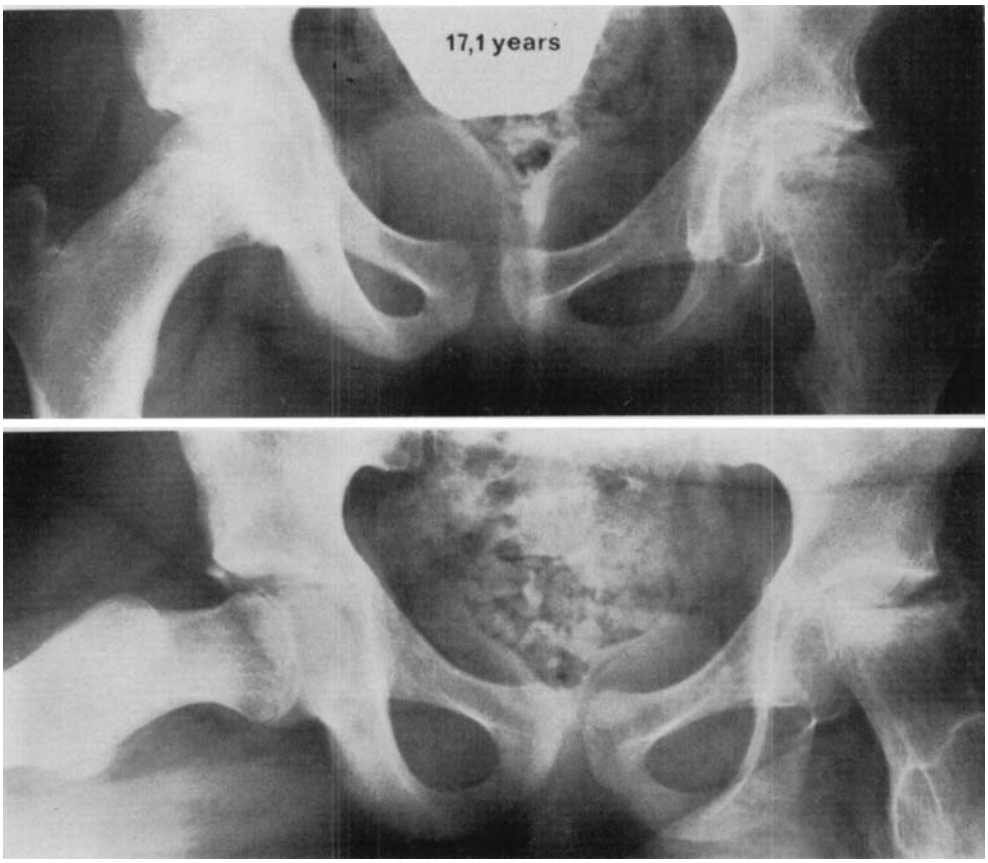

Figure 3. Radiographs two years after the start of treatment show extensive necrosis of the femoral head.

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Correspondence to: Ingjald Bjerkreim, Sophies Minde Ortopedisk Hospital, Trondheimsveien 132, Oslo 5, Norway.