CASE REPORT

Bone diseases in children receiving growth hormone

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The authors report two cases of bone disorders in children with short stature, with confirmed growth hormone (GH) deficiency treated by GH supplementation. The first patient, aged 15 years, developed avascular necrosis of the femoral head and scoliosis. The second one, aged 17 years, had avascular necrosis of the femoral capital epiphysis on one side and acute slipped capital femoral epiphysis (SCFE) on the other side. All these complications were diagnosed while they were receiving GH-therapy. The exact aetiology and the role of GH in the pathogenesis of these conditions are still unknown.

INTRODUCTION

The action of growth hormone (GH) via its receptors involves many organ systems and metabolic pathways. These diverse actions may represent unwanted side effects of GH therapy for growth stimulation. Recent expansion in the use of GH has increased the prevalence of bone complications, especially slipped capital femoral epiphysis (SCFE), avascular necrosis (AVN) of the femoral capital epiphysis and scoliosis. These complications have been reported by many authors, and their exact aetiology is still unknown. The aim of this report is to focus attention on bone disorders that can occur in children receiving GH.

CASE REPORTS

Case 1 : N.B. was a 15-year-old boy who presented with dwarfism with GH deficiency and had been on replacement treatment for three years. He complained of pain in his left hip, increasing with activity. On physical examination, Trendelenburg limping and a deficit in internal rotation of the left hip were noted. Standard radiographs showed avascular necrosis of the proximal lateral part of the femoral epiphysis (fig 1). The patient was instructed to avoid weight bearing ; and GH therapy was continued. The evolution was towards complete avascular necrosis of the femoral head (fig 2). Two years later, he developed scoliosis. GH therapy was stopped, but rapid progression of the curve required a spinal fusion operation.

Case 2 : F.H. was a 17-year-old boy presenting with GH deficiency who had been on replacement treatment since he was 11 years old. He had suffered from pain in the right hip for three years, and he reported pain in the left hip, which started two weeks before consultation. Physical examination showed severe restriction of the mobility of the

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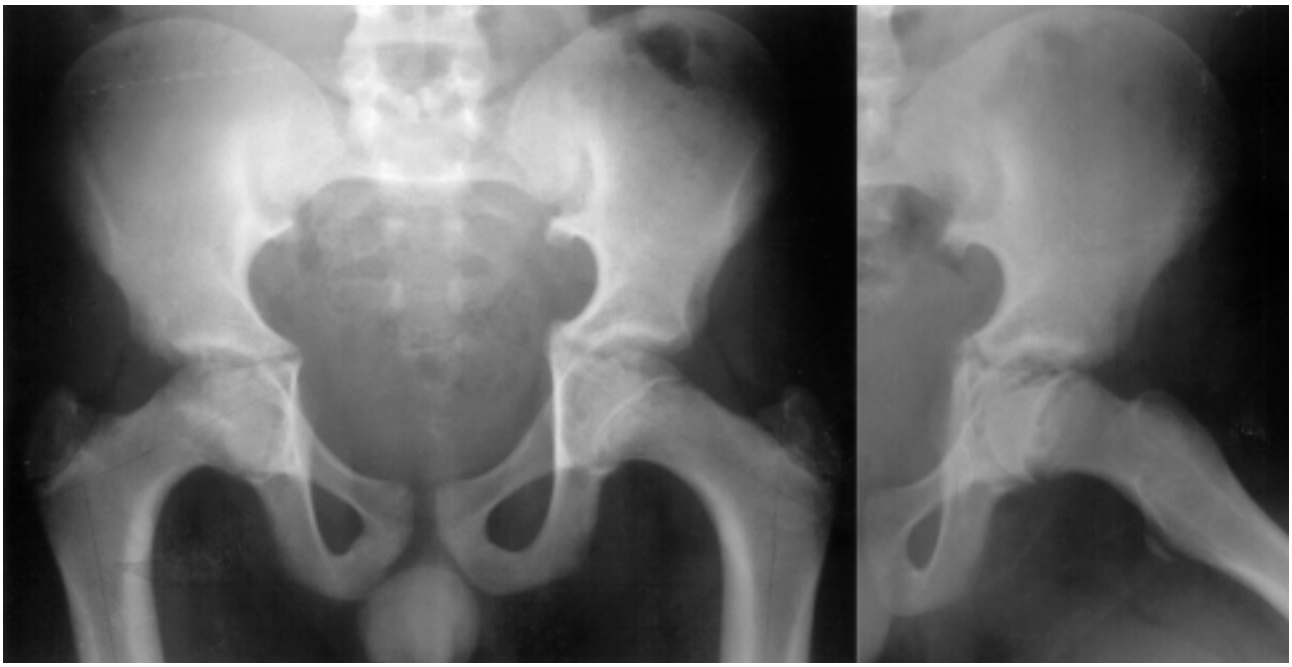

Fig. 1. — Polar superolateral avascular necrosis of the left femoral epiphysis (case 1)

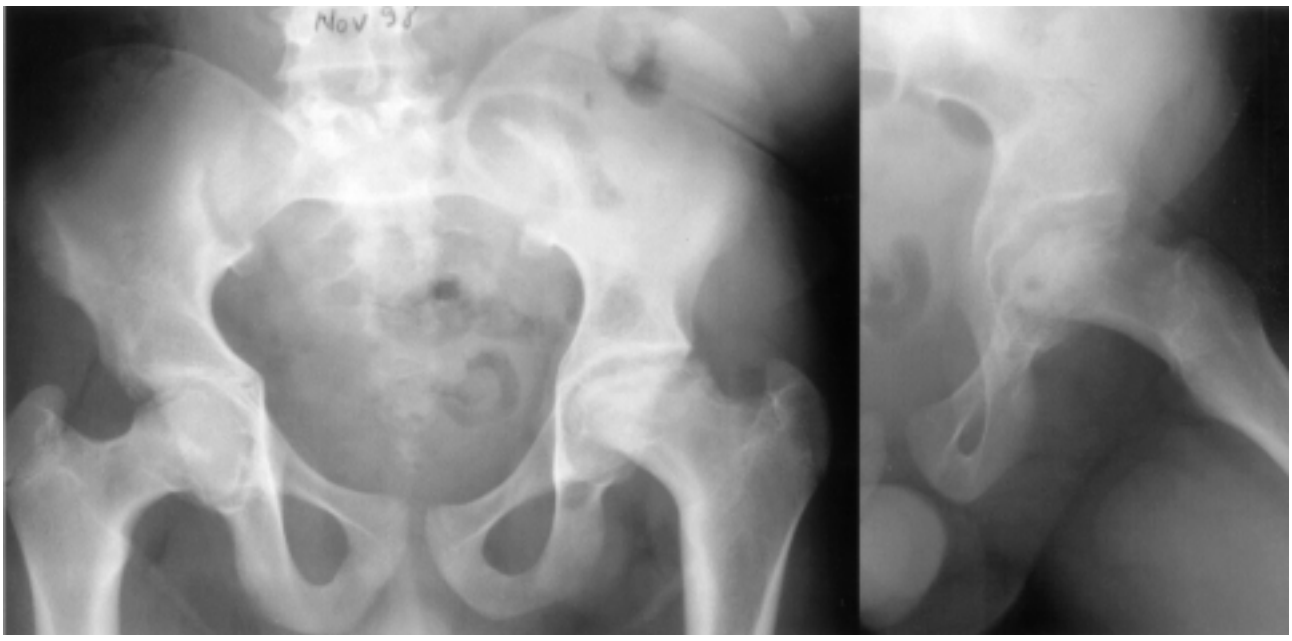

Fig. 2. — Complete avascular necrosis of the left femoral epiphysis (case 1)

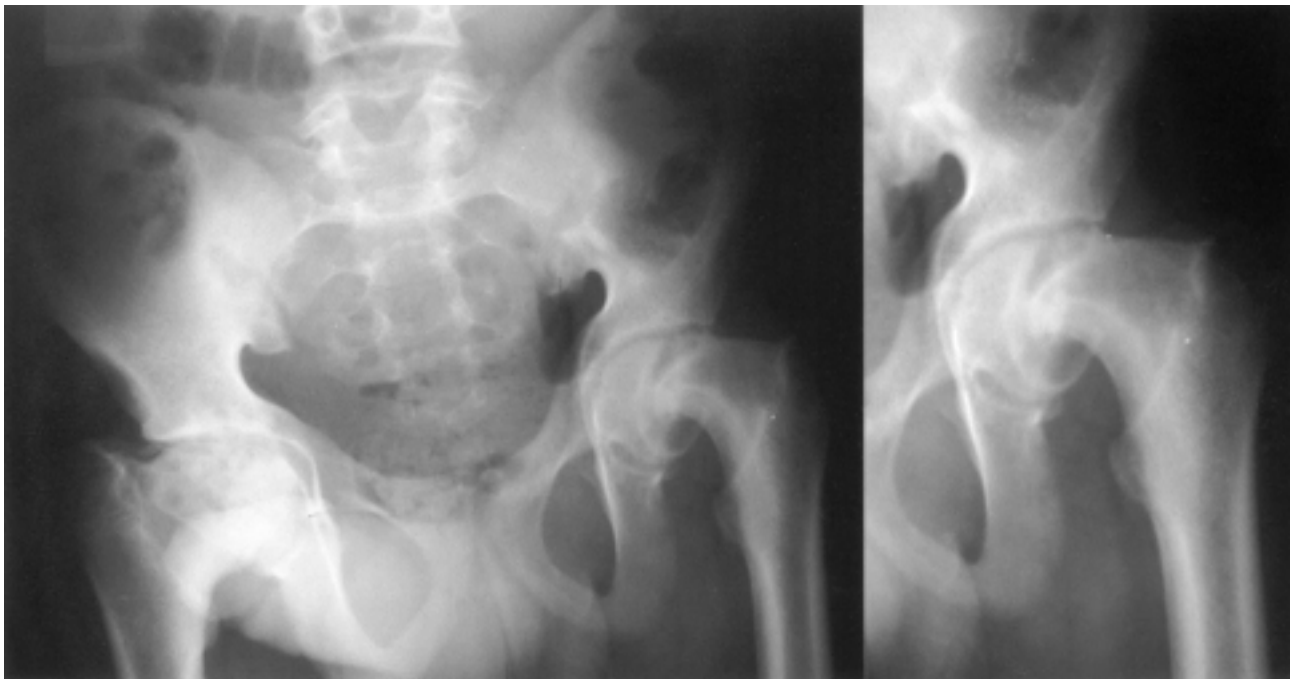

Fig. 3. — Coxa vara and complete avascular necrosis of the right femoral head associated with acute SCFE on the left side (case 2)

right hip, with a 3-cm shortening of the right lower limb. The left hip was held spontaneously in flexion and external rotation, and physical examination showed a lack of internal rotation and abduction of the left hip. Roentgenograms of the left hip showed a slipped capital femoral epiphysis, with avascular necrosis affecting the whole femoral epiphysis, and a coxa vara deformity (fig 3). After a few days of traction, the left capital femoral epiphysis was pinned after reduction, but no specific action was taken with respect to the right hip (fig 4).

DISCUSSION

Growth hormone was initially used for growth stimulation in children with short stature secondary to GH deficiency or with Turner syndrome (9). In the last two decades, GH has been used for a number of other indications, especially in children with chronic renal failure (11). This increased use of GH and its monitoring in large multicenter international databases have showed the occurrence of some adverse events, including on bone. As a result, paediatric orthopaedic surgeons are now more likely to encounter patients receiving GH.

SCFE as a complication of GH therapy has been reported by many authors, but its incidence and the relationship with GH therapy are controversial (3, 8, 9, 11). Loder *et al* (7) performed a search of the entire English literature from 1938 to 1993 and found that 92% of patients with GH deficiency developed SCFE during supplemental therapy. Blethen and Rundle (3) studied the correlation between SCFE and GH treatment in 16,514 children. They found that 15 children had SCFE prior to receiving GH therapy, 26 developed SCFE on one side prior to GH treatment and on the controlateral side while receiving GH. They concluded that children with GH deficiency, Turner syndrome and other known causes of short stature are more likely to develop SCFE before or during GH treatment than children with idiopathic short stature. Rappaport and Fife (8) believed that the risk of developing SCFE is significantly greater in GH-deficient children, whether on substitutive GH therapy or not, than in the general population. Job (6) did not find any cases in 2312 children receiving therapy.

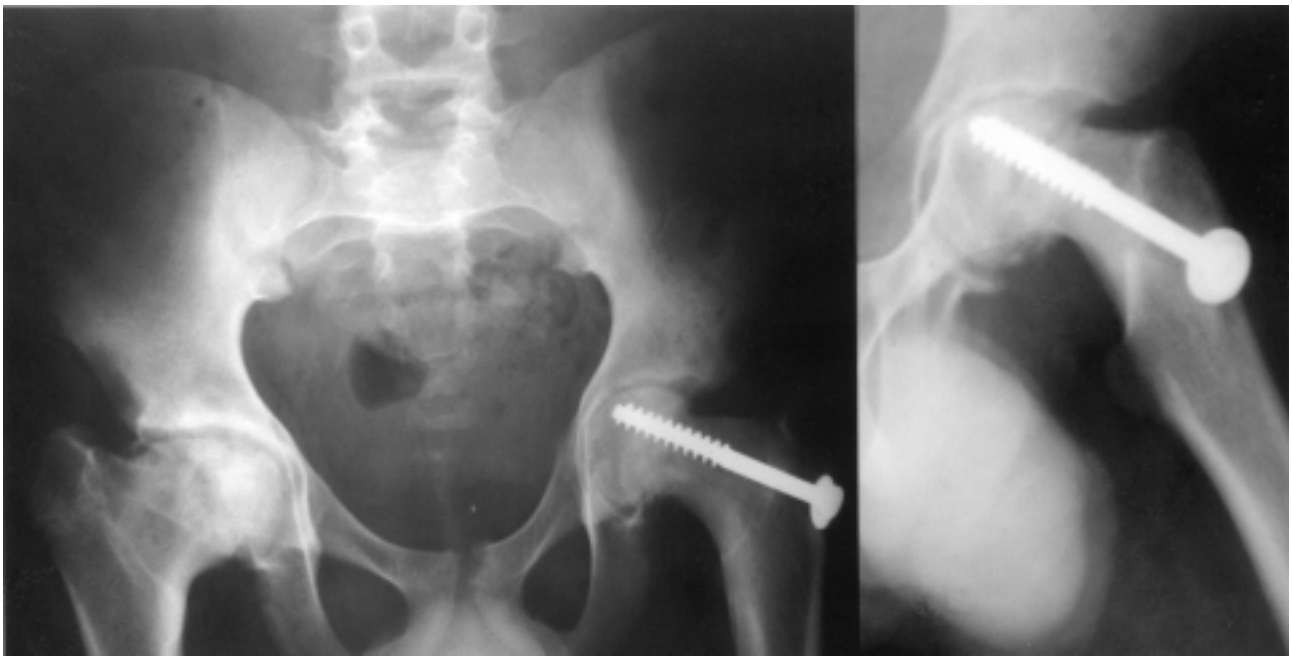

Fig. 4. — Reduction and fixation of the left epiphysis (case 2)

The pathogenesis is still unclear. In 1950 Harris (5) suggested the role of GH in the genesis of SCFE. He proposed that the resulting stimulation of cartilage cells by somatomedin allows for a pubertal-type growth spurt. The increase in the thickness of the layer of hypertrophied cartilage in the epiphyseal plate results in reduced shear strength. Therefore a patient receiving GH substitution appears to be at risk for SCFE, which can occur during or after GH therapy (3, 11).

Avascular necrosis of the femoral head has also been reported in children receiving GH. In a recent study of over 200 children with chronic renal failure, 15 cases of AVN were identified in treated patients. Eight lesions were present prior to treatment, the other seven patients were not examined radiologically prior to their treatment, and thus the relationship to GH could not be determined (11). Bjkerkreim and Trygostad (2) reported AVN of the femoral head in a girl with GH deficiency that appeared six months after the start of GH treatment. They believed that the growth spurt under treatment had resulted in an insufficient blood supply to the epiphysis, resulting in avascular necrosis.

Several studies have confirmed the relationship between GH secretion and scoliosis. Ahl *et al* (1) found that girls with adolescent idiopathic scoliosis have a higher endogenous secretion of GH than normal girls. Dymling and Willer (4) were the first authors to report the occurrence of scoliosis in a patient receiving GH therapy. Their patient had a rapid progression of his scoliotic curve while receiving GH therapy. They believed that rapid progression was a direct effect of the GH.

Wang (10) studied a group of 250 patients receiving GH therapy. Ten of them (4%) were found to have scoliosis during treatment, with rapid progression. All of the patients with scoliosis except two had accelerated growth rates at the time they were diagnosed with scoliosis. This suggested that GH therapy played a role in the onset and progression of the scoliosis.

CONCLUSION

Orthopaedic disorders during GH therapy are rare but serious. Children treated with GH should be carefully observed and monitored for avascular

necrosis of the femoral head, slipped capital femoral epiphysis and scoliosis with serial radiographs. Regular checks allow early diagnosis and treatment.

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