CASE REPORT

Bilateral osteonecrosis of the femoral head in an adult man affected by congenital estrogen deficiency

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ABSTRACT. Osteonecrosis of femoral head is related to different predisposing factors. The pathogenesis is not completely understood, but an ischemic impairment seems to be one of the major determinants of bone necrosis. The association of bilateral necrosis of femoral heads and congenital aromatase deficiency is here reported. The absence of estrogen activity, as well as the persistence of unfused epiphyses for a long period of life, may be involved in the determination of bilateral necrosis of bone femoral heads. The possibility of development of bone necrosis in patients affected by congenital estrogen deficiency needs to be considered and magnetic resonance imaging can be a useful method for an early detection of this disease.

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INTRODUCTION

Osteonecrosis of the femoral head is due to different causes, however an ischemic insult seems to be the main pathogenetic mechanism. Several diseases may be associated with non-traumatic osteonecrosis of femoral head, and some predisposing factors like corticosteroids administration and alcohol abuse are often involved (1). We describe a case of avascular, bilateral non-traumatic osteonecrosis of the femoral head in a man with congenital lack of estrogen production due to aromatase deficiency. Aromatase activity is, in fact, necessary in order to transform testosterone in estradiol.

CASE REPORT

A 31-yr-old man with aromatase deficiency came to our attention because of persistent linear growth during adulthood, unfused epiphyses, a 4-yr history of skeletal pains and osteoporosis with a bone mineral density (BMD) at the lumbar spine of 0.933 g/cm² (T score = −2.07) (2). At first examination the man weighed 96.5 kg, was 187 cm tall and had a body mass index (BMI) of 27.9 kg/m². Skeletal pains were localized predominantly at the knees and at the hips, limiting his ability to walk. Physical examination revealed a restricted range of motion of the hips, consisting of a severe impairment of both abduction and internal rotation movements, which were particularly evident on the right side. Eunuchoid habitus and bilateral genu valgum were also present.

Biochemical investigations showed normal testosterone concentrations (390 ng/dl), slightly elevated FSH serum levels (13.6 IU/l), and circulating LH at the upper limit of the normal range (8.9 IU/l), together with undetectable estradiol serum levels (2). A pelvic radiograph (Fig. 1) performed at the first examination revealed bilateral osteonecrosis of the femoral heads, while unossified metaphyses of the tibias with no signs of necrosis were present in X-ray films of the knees (2). The patient had no history of previous trauma, corticosteroid treatment, alcohol and tobacco abuse or other conditions related to bone necrosis. Bilateral osteonecrosis of femoral heads was clearly confirmed by a magnetic resonance imaging (MRI) of the hips (Fig. 2), performed few years later. Both radiographs and MRI documented a more severe osteonecrosis on the right leg.
Several years later, when the patient was 39 yr old, the diagnosis of estrogen deficiency due to a point mutation in exon 9 of P450 aromatase gene was made. Then he started transdermal estradiol treatment with a 50 μg patch twice weekly for 6 months and with a 25 μg patch twice weekly for the following 9 months. The treatment led to the closure of distal femoral and proximal tibial epiphyses, to the normalization of BMD (1.275 g/cm², T score = +0.51) after 15 months of therapy (3). The patient referred a relief of skeletal pain except in the ankles where no effects were traceable in the areas of the bone necrosis at the radiological evaluation.

DISCUSSION

Non-traumatic osteonecrosis of the femoral head usually affects young people, leading to femoral head collapse in its late stage. The disease has been related to several clinical disorders, but actually it remains a poorly understood process (1, 4). An ischemic insult to bone and marrow tissues is thought to be the final mechanism involved in all cases, even though the pathogenesis is still not fully understood. Several pathogenic mechanisms have been proposed which can work jointly or individually in the different conditions etiologically related to non-traumatic osteonecrosis (1, 4).

The present case describes a bilateral non-traumatic osteonecrosis of femoral heads in an adult man affected by the congenital lack of estrogen activity due to aromatase deficiency. Congenital estrogen deficiency of the male is characterized by the presence of delayed bone age with unfused epiphyses, an eunuchoid body proportion of the skeleton and a severe osteoporosis that heals after estrogen treatment (3, 5). Recently large population studies have correlated the positive effects of bioavailable estrogens on male bone health and estrogens are becoming a new field of investigation in male osteoporosis (6).

In literature only one case in which osteonecrosis has been related to estrogen deficiency is available. A femoral head collapse was described in a 20-yr-old ballet dancer affected by anorexia nervosa, where a long state of hypoestrogenism as well as exercise have been considered as possible causes of osteonecrosis (7). Similarly to the patient here described, the ballet dancer was affected by a diffuse osteoporosis with a concomitant delay of bone age. It is possible to suppose that a delayed process of bone mineralization of femoral heads associated with estrogen deficiency may be concomitant factors etiologically related to osteonecrosis. The association between osteonecrosis and estrogen deficiency in this man fits this hypothesis even more, because femoral necrosis of this patient was bilateral and the patient never underwent stressful physical exercises. Some recent observations show a possible role of estrogen not only in the process of bone...