Case Report

Hemochromatosis and Femoral Head Aseptic Osteonecrosis: A Nonfortuitous Association?

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ABSTRACT. Chondrocalcinosis, chronic pseudo-osteoarthritis arthropathy, and osteoporosis are classic osteoarticular complications of hemochromatosis (HC). Within HC, femoral head aseptic osteonecrosis (FHAO) is not notified in textbooks. We describe 3 cases of FHAO occurring in this setting in 3 patients homozygous for the C282Y mutation on HFE gene who had no other risk factors for FHAO. FHAO was diagnosed 9 years before (Case 1), concomitantly with (Case 3), or 9 years after HC (Case 2). In one case, FHAO occurred although phlebotomies were regularly carried out. There are scarce data available in the literature on HC and FHAO. Our observations suggest FHAO may be an indicator for HC, and iron balance should be determined before considering FHAO as idiopathic. Thus phlebotomy may not be protective against the occurrence of FHAO. Studies are needed to determine the prevalence of HC in consecutive patients with FHAO. (J Rheumatol 2005;32:376–8)

Key Indexing Terms:
HEMOCHROMATOSIS FEMORAL HEAD HIP ASEPTIC OSTEONECROSIS

Femoral head aseptic osteonecrosis (FHAO) is not discussed in textbooks as a complication of hemochromatosis (HC). Osteoarticular manifestations of HC are present in 25% to 60% of cases[1], and include chondrocalcinosis, chronic pseudo-osteoarthritis arthropathy, or osteoporosis. Numerous pathologies (systemic lupus erythematosus, Gaucher's disease, connective tissue disorders, diabetes, hemoglobinopathies, hemopathies, pancreatitis) and/or exposures (alcohol, corticosteroids, hyperlipidemia, radiotherapy, trauma, hyperhomocysteinemia) are readily associated with FHAO[2]. Nevertheless, most cases of FHAO are still considered "idiopathic."

We describe 3 patients who developed FHAO in the unique context of HC; common causes such as alcoholism, hypercorticism, trauma, hemoglobinopathy, and vasculitis were excluded.

CASE REPORTS

Case 1. A man born in 1945 presented in 1991 with bilateral FHAO and astragal osteonecrosis. In 2000, HC was diagnosed according to the association of melanodermia, diabetes, hepatic cytolysis, hypogonadism, hand arthralgias, and high plasma iron (40 µg/l, normal value 9–27), transferrin saturation (1.07, normal 0.2–0.4) and ferritinemia (5946 µg/l, normal 30–300). He was homozygous for the C282Y mutation. One year later, hepatic adenocarcinoma occurred; the patient refused any treatment.

Case 2. HC was discovered in 1992 in a 37-year-old woman in the context of hand arthralgias associated with elevated iron (29 µmol/l), transferrin saturation (0.97), and ferritinemia (764 µg/l). She was homozygous for the C282Y mutation. Liver biopsy revealed ferric overload of 125 µmol/g (normal < 9); phlebotomies had been performed regularly. In 2001, she complained of bilateral hip pain. Magnetic resonance imaging (MRI) of the hip showed bilateral FHAO (Figure 1). At that time, the ferric charge was normal as assessed by hepatic MRI analysis.

Case 3. In 1998, a 46-year-old man with congenital mental deficiency developed right FHAO. Etiologic investigation led to the diagnosis of HC. Plasma iron, transferrin saturation, and ferritinemia were 30.4 µmol/l, 0.69, and 874 µg/l, respectively. He was homozygous for the C282Y mutation. Ferric hepatic load evaluated by MRI was 200 µmol/g. He underwent prosthetic hip surgery in 1999.

DISCUSSION

Hemochromatosis is a genetic disease with an autosomal recessive transmission, characterized by an abnormal iron metabolism with excessive absorption in the bowel, resulting in accumulation of iron throughout the body. It is often due to C282Y or H63D mutations. Arthropathy associated with HC typically involves the small joints of the hands, but some reports have described an increased incidence of hip involvement[3]. Chondrocalcinosis, chronic pseudo-osteoarthritis arthropathy, or osteoporosis are classical complications of HC[1]. Published data on HC and FHAO are scarce. In 1966, Jaffres, *et al* reported the first case of bilateral FHAO in a patient with HC[4]. Since then, the prevalence of FHAO associated with HC has not been accurately evaluated. Our 3 patients were found to be homozygous for the C282Y mutation on HFE gene and other risk factors for

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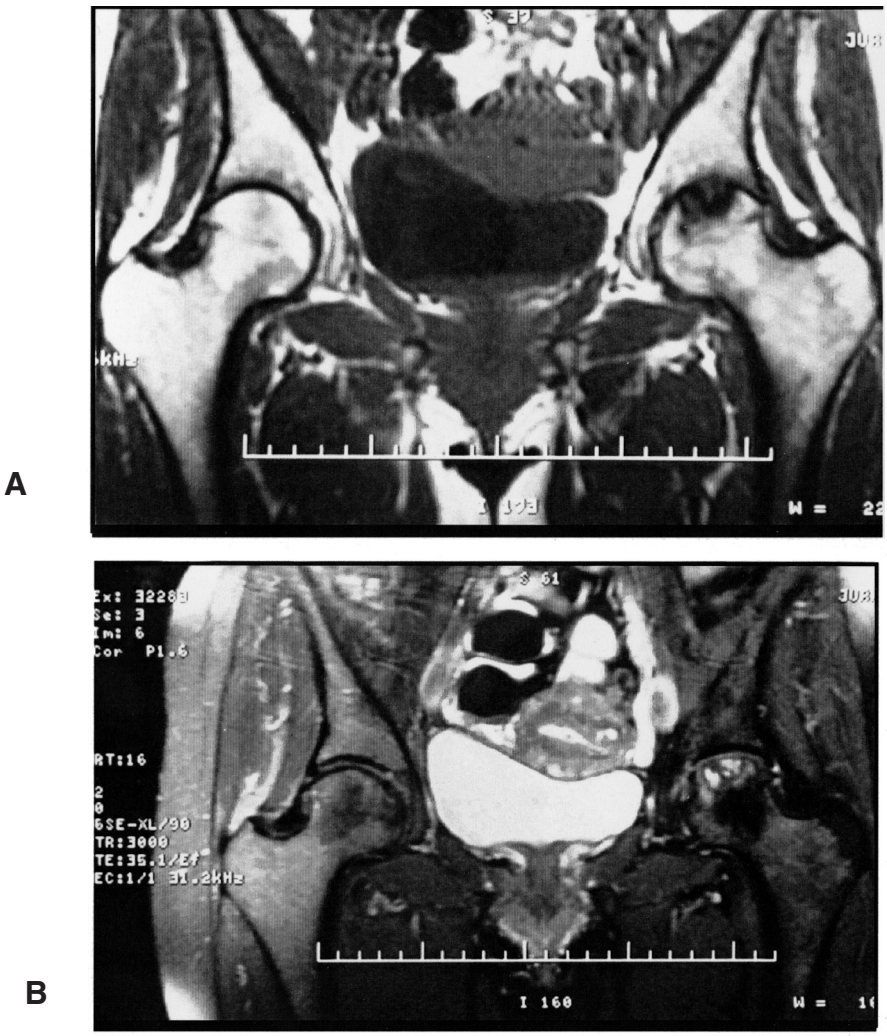

Figure 1. T1 (A) and T2 (B) sequences of hip MRI of Patient 2, with bilateral FHAO.

FHAO were excluded. Among our patients, only one was from Brittany, an area of France where prevalence of HC is particularly elevated, and none had a history of congenital hip dysplasia, with no signs on the available radiographs. No bone biopsy was performed for a possible local hemosiderosis. As well, the association with chondrocalcinosis lesions in the genesis of hip arthropathy cannot be excluded. There was no sign of chondrocalcinosis on any patient's hip MRI or radiograph, nor on the hand and foot radiographs of Patient 2, who had peripheral articular pains. Investigation in all our patients was negative for antiphospholipid antibodies, which are frequently found in various hepatic disorders[5] and are associated with occurrence of FHAO in the specific setting of systemic lupus erythematosus[6]. Finally, Montgomery, *et al* recently described evidence of bone histological lesions of FHAO in 7 out of 19 hip specimens in 15 patients with HC who underwent total hip arthroplasty[7]. These data strengthen the argument for a nonfortuitous link between FHAO and HC. Supporting this, Hamilton, *et al*, in a longterm study on genetic HC, reported radiographic evidence of hip osteonecrosis in 2 of 22 patients[8].

In our patients, FHAO was diagnosed 9 years before (Case 1), concomitantly with (Case 3), or 9 years after diagnosis of HC (Case 2). Interestingly, repeated phlebotomies did not prevent the occurrence of FHAO in Patient 2. Some investigators have suggested that the evolution of other osteoarticular manifestations of HC, such as osteopororosis or degenerative arthropathy, was not influenced by HC-specific treatment, i.e., iron depletion[9].

Femoral head aseptic osteonecrosis may reveal hemochromatosis. These observations suggest that patients' iron balance should be determined before considering FHAO as idiopathic. Phlebotomies may not be protective against the occurrence of FHAO. However, early diagnosis of HC would allow starting phlebotomies and thus avoid serious hepatic and cardiac complications, in addition to undertaking a family survey. Further studies are needed to determine the prevalence of HC in consecutive patients with FHAO.

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