



Familial Transient Osteoporosis of the Hip? On Account of Three Cases from the Same Family

CASE REPORT

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ABSTRACT

Transient osteoporosis of the hip (TOH) is a rare clinical entity characterized by a spontaneous hip pain associated with a delayed appearance of osteoporosis in the femoral head. In this report, we present three members of the same family, who were diagnosed with TOH based on the radiological findings. In case 1, a 29-year-old, single, non-pregnant female presented with severe, increasing pain in the right hip with a diagnosis of TOH. In case 2, the patient is the father of the above-mentioned patient and presented with pain in the right hip at the age of 48 years, 9 years before the date when his daughter was diagnosed with TOH. In case 3, the patient is the uncle of the case 1 patient and brother of case 2 patient. He was referred to our outpatient clinic and was diagnosed with TOH 8 years before the admission of the case 1 patient. Our case 1 was an interesting case of TOH, considering the distinct features of this patient, who was a non-pregnant woman with migratory transient osteoporosis, as well as familial character of the condition when assessed in association with the other two cases. These findings suggest that genetic factors should be taken into consideration in the etiological assessment, and there is a requirement for gene studies for further clarification.

Keywords: Transient osteoporosis of hip, familial

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INTRODUCTION

Transient osteoporosis of the hip (TOH) is a rare clinical entity characterized by spontaneous hip pain associated with a delayed appearance of osteoporosis in the femoral head (1). This condition usually affects middle-aged men or women in the third trimester of pregnancy (1, 2). Although TOH is a self-limiting condition, it should be kept in mind that it may become a migratory condition, and other joints of the lower extremity, including the knee joint, ankle, and contralateral hip, may also be involved (3).

Transient demineralization of the hip was first described by Curtiss and Kincaid in 1959 in three women in the third trimester of their pregnancy (4). In association with the increasing use of magnetic resonance imaging (MRI), Wilson introduced the term “transient bone marrow edema syndrome” for the first time in 1988 (5).

The familial presentation was first reported in three brothers with TOH in 1983 (6), and Bijl et al. (7) reported a daughter and a father with TOH in 1999.

In our cases, we present three members, who are from the same family, with a diagnosis of TOH based on the radiological findings.

CASE REPORT

Case 1

A 29-year-old, single, non-pregnant female presented with severe, increasing pain in the right hip. She had been suffering with walking pain initially but started to feel pain at rest and later on. She had been working as a shopping mall salesperson 8 h per day for the last 12 years. Her body mass index (BMI) was 29.1 kg/m². She had a history of smoking 20 cigarettes per day for 13 years and had no history of alcohol intake. Among her family members, both her father and her uncle (brother of her father) had similar complaints, and they had been diagnosed with TOH in the right hip and followed up in our clinic. Right hip movements induced pain, and internal rotation of the hip was limited. Laboratory test results including complete blood count, erythrocyte sedimentation, C-reactive protein, rheumatoid factor, urinalysis, serum 25(OH)D3 level, serum calcium, phosphorus, and alkaline phosphatase levels as well as thyroid, kidney, and liver tests were within normal limits. Subsequent MRI scans of both hips revealed altered signal intensities in the right femoral head and neck with low signal intensities on T1-weighted sequences (Figures 1,2) and high signal intensities on T2-weighted sequences (Figure 3), and this suggested diffuse

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Figure 1. Coronal section of femur head and neck edema in T1 sequence

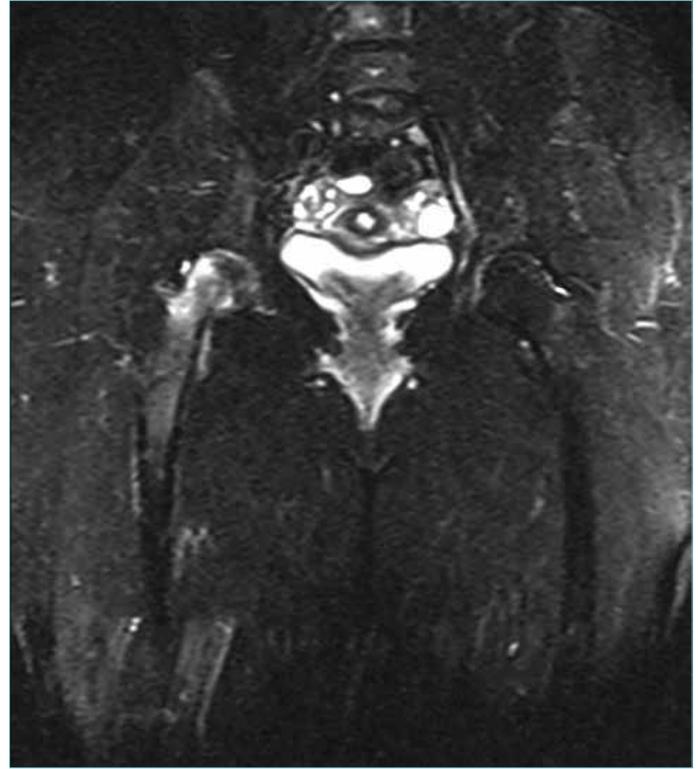


Figure 3. Coronal section of femur head and neck edema in T2 sequence

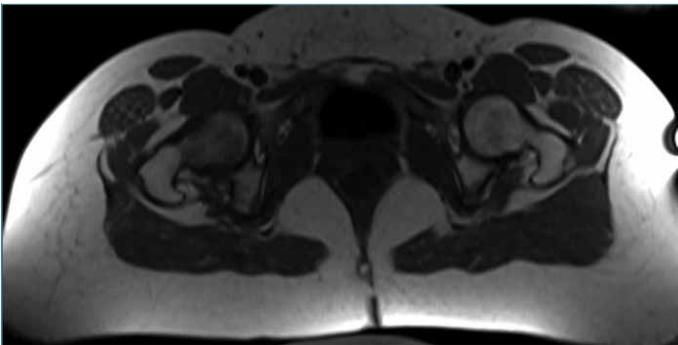


Figure 2. Axial section of femur head and neck edema in T1 sequence

bone marrow edema, and a large effusion was seen in the right coxofemoral joint. Whole body bone mineral densitometry (BMD) was normal. Based on those findings, the patient was diagnosed with TOH. She was advised not to bear weight on the right hip and was prescribed a forearm crutch. An exercise program, including strengthening the muscle groups and increasing the range of motion around the hip and knee, was devised. She was prescribed a non-steroidal anti-inflammatory drug (NSAID) (diclofenac sodium 50 mg twice a day). During her follow-up visit at month 3, right hip pain was almost completely resolved, but she defined right medial knee pain. MRI scans of the right knee revealed bone marrow edema (Figure 4). Follow-up MRI scans of the hip revealed radiological improvements. Tc-99m labeled triphasic whole body bone scintigraphy showed a marked focal activity in the right femoral head and in the medial condyle of the right distal femur on the delayed bone phase images (Figure 5). These findings suggested migratory

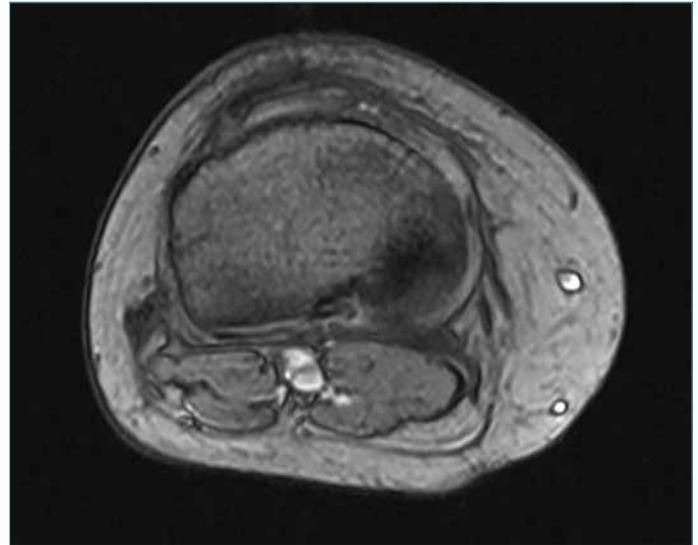


Figure 4. Axial section of knee medial malleolar edema in T1 sequence and right medial plateau of tibia

transient osteoporosis. She was advised not to stand for long time periods and do her exercises accompanied by anti-inflammatory medication. During her follow-up visit at month 7, hip and knee pain was partially resolved.

Case 2

This patient is the father of case 1 patient and had presented with pain in the right hip at the age of 48 years. His pain had started 2–3 weeks ago without a prior history of trauma. Rotational motions of the hip induced significant pain. He had a his-

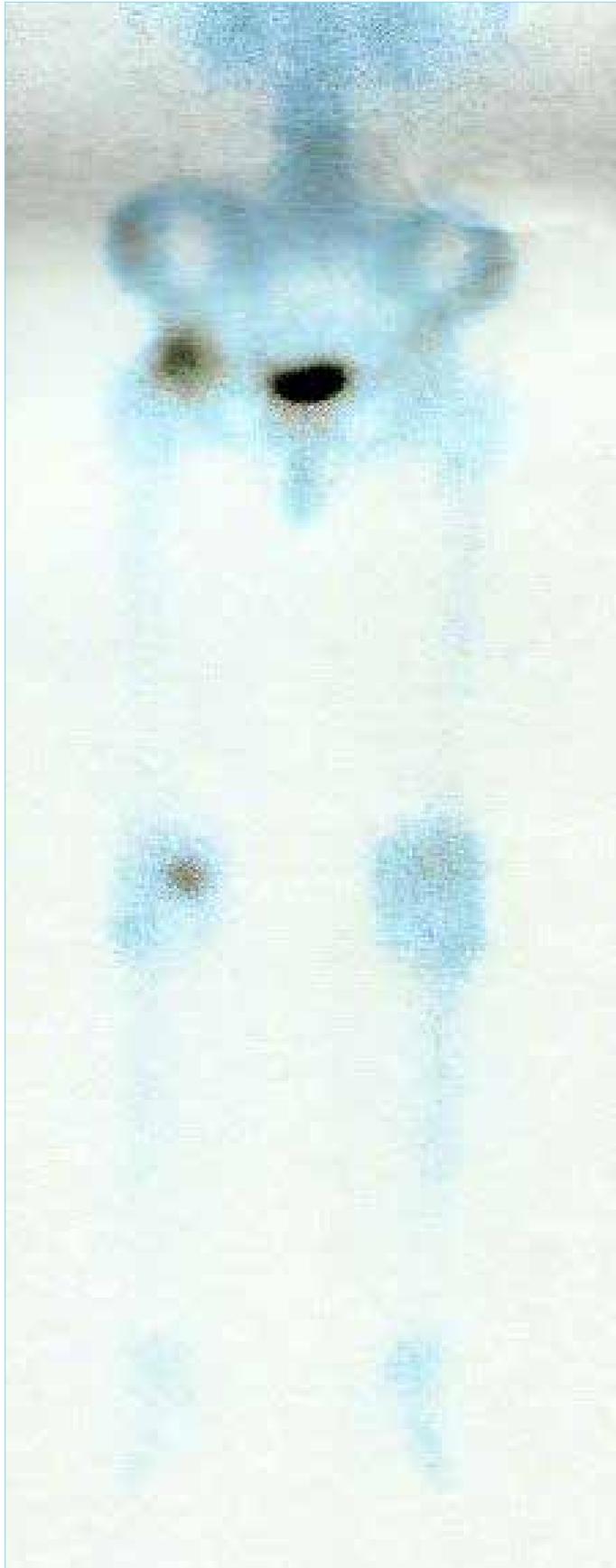


Figure 5. Tc-99 m-labeled triphasic whole body bone scintigraphy

tory of smoking 20 cigarettes per day for 28 years and had no history of alcohol intake. His BMI score was 30.3 kg/m². MRI scans of the right hip showed diffuse bone marrow edema in the femoral head and neck. In the whole body BMD, right femur t-score was -3, and left femur t-score was -2.2. He was diagnosed with TOH of the right hip and was provided with forearm crutch to prevent weight bearing on the hip. NSAID and physical therapy (transcutaneous electrical nerve stimulation, intermittent therapeutic ultrasound, and hot pack) were prescribed to provide pain relief. A treatment regimen that consisted of alendronate sodium+cholecalciferol 70 mg/week and calcium carbonate once a day was prescribed for the significant osteoporosis detected in the BMD measurements. Follow-up MRI at month 5 demonstrated an almost complete cure.

Case 3

This patient is the uncle of the case 1 patient and brother of the case 2 patient. He was referred to our outpatient clinic at the age of 47 years owing to similar complaints 8 years before the admission of the case 1 patient. He had a history of smoking 20 cigarettes per day for 25 years and had no history of alcohol intake. His BMI was 28.9 kg/m². The hip MRI and BMD findings of the patient in this case were similar to those of case 2 patient of TOH. This patient was treated in a similar way as the second patient (physical therapy and bisphosphonate therapy). At month 5 of treatment, complete cure was achieved according to the clinical and follow-up MRI findings.

None of the three cases history of corticosteroid use, and there were no findings about hypophosphatasia or osteogenesis imperfecta. Further, for cases 2 and 3, there were no findings that would cause clinical suspicion for low testosterone.

DISCUSSION

Although a number of hypotheses were suggested to define the etiology and pathophysiology of TOH, the exact cause of this condition remains unknown. Based on several theories, neurogenic compression, venous occlusion and secondary local hyperemia, proximal nerve root pathologies, ischemic bone marrow injury, and vitamin C insufficiency may play etiologic roles in the development of TOH (3). On the other hand, Miyanishi et al. (8) suggested that subchondral fractures lead to TOH.

In a retrospective study with 23 patients with TOH, prior episodes of TOH, metabolic bone diseases, smoking, any sudden overuse of the lower limbs, osteoporosis, and osteopenia have been taken into consideration as risk factors for TOH. The average time to diagnosis was 2.8 months, and the average time to the resolution of symptoms was 7.1 months. Overuse was the common risk, and the second most common risk factor was found to be metabolic bone diseases. Overall, 30.4% of the patients were smokers who smoked >20 cigarettes per day, and seven patients had a history of TOH episodes. No associations were found between risk factors and symptom duration (9). The average time to recovery for all three patients was shorter (7 months, 5 months, and 5 months, respectively) because all them were diagnosed during their first visit (month 1) and started on treatment. Osteoporosis or osteopenia was not detected in case 1, the non-pregnant woman; the other two male patients

were diagnosed with osteoporosis. All three patients were active smokers (20 cigarettes per day). Our first patient had a job requiring prolonged standing during the day, and the other two male patients had desk jobs. None of the three patients had a history of trauma.

MRI is a specific and sensitive diagnostic tool for TOH. Bone marrow edema is a typical MRI finding. In total, 5%–41% of the cases of TOH show a migratory pattern. Migration typically occurs within the first 6 months. The most frequent clinical presentation is the involvement of the lower limb from proximal to distal (10, 11). In a study evaluating hip MRI images of 155 patients, regional migratory osteoporosis was detected in 19.4% of the patients, and bilateral TOH was detected in four postpartum patients. The site for bone marrow edema was the femoral head in 11% of the patients, femoral neck in 40% of the patients, and femoral shaft in 49% of the patients. Subchondral fractures were observed in 48.7% of the hips (12). In our cases, the homogenous distribution of low signal intensities on T1-weighted sequences and high signal intensities on T2-weighted sequences indicated a diffuse bone marrow edema in the femoral head and neck, and a large effusion was detected in the coxofemoral joint. In addition, in case 1, the disease migrated to the knee region 3 months after the involvement of the hip.

Radionuclide bone scan with Tc-99 m is a method with high sensitivity but low specificity, and this helps the early diagnosis of the disease. A diffuse and homogeneously increased radionuclide uptake is seen at the femoral head within a few days after the onset of symptoms (13). Uptake in TOH also extends into the acetabulum, femoral neck, and occasionally into the femoral shaft. Conversely, radionuclide uptake in femoral head osteonecrosis is less intense and is limited to the femur head. An important feature of radionuclide bone screening in the early stages of osteonecrosis is the presence of cold spots because of reduced isotope reuptake in the anterior superior region of the femur head (13, 14). In our case, Tc-99 m-labeled triphasic whole body bone scintigraphy showed diffuse homogeneously increased activity in the right femoral head and in the medial condyle of the right distal femur.

In a study evaluating treatments administered to 18 hips diagnosed with TOH, 18 patients were retrospectively evaluated within a period of 3 years. The patients were prevented from weight bearing by using forearm crutches and received medical treatment including diclofenac sodium, acetylsalicylic acid, and risedronate sodium in addition to hyperbaric oxygen therapy. Both clinical and radiological improvements were observed in all patients. None of the patients developed avascular necrosis of the femoral head. No treatment-related complications were reported (15). In a similar way, we controlled weight bearing on the hip joint by prescribing a forearm crutch to all three cases, and pain control was achieved by prescribing NSAIDs. We prescribed strengthening exercises for the muscles around the hip and knee regions. No antiresorptive therapy was given in case 1 because the patient did not show any findings indicating osteoporosis or osteopenia. We prescribed NSAIDs and 70 mg alendronate sodium+cholecalciferol to our other two patients along with weight-bearing control, exercises, and physical therapy. Further,

we observed a shorter time to recovery in these two patients than that in case 1. No treatment-related side effects were observed in the three cases of TOH.

Two previously reported cases have focused on genetic factors. In these case reports, human leukocyte antigen (HLA) DR7 homology was commonly detected, and it was concluded that a certain HLA phenotype constitutes the risk of developing TOH (6, 7). We cannot do HLA tissue typing in our patients. However, the etiopathogenesis of our cases, which consist of two brothers and one sister, will shed light on future research for this still unknown disease.

Our case 1 was an interesting case of TOH, considering the distinct features of this patient, who was a non-pregnant woman with migratory transient osteoporosis and familial character of the condition when assessed in association with the other two cases. These findings suggest that genetic factors should be taken into consideration in the etiological assessment and that there is a requirement for gene studies for further clarification.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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