Radiologic and Clinical Features of Misdiagnosed Idiopathic Osteonecrosis of the Femoral Head

WATARU ANDO, MD, PHD; KENGO YAMAMOTO, MD; TSUYOSHI KOYAMA, MD, PHD; YOSHICHIKA HASHIMOTO, MD; TAKASHI TSUJIMOTO, MD; KENJI OHZONO, MD, PHD

abstract

Idiopathic osteonecrosis of the femoral head (ONFH) can be correctly diagnosed in accordance with the established criteria. However, some general orthopedic physicians have misdiagnosed patients as having ONFH. The goal of this study was to clarify the radiologic and clinical features of misdiagnosed patients. This study included 50 patients who were referred to the authors’ hospital by general physicians with a diagnosis of ONFH. The correct diagnosis was made based on the Japanese Investigation Committee diagnostic criteria for ONFH. Demographic data were compared between patients with and without ONFH. Of the 50 patients, 24 were diagnosed with other diseases: 10 with osteoarthritis, 7 with transient osteoporosis of the femoral head, 4 with rapidly destructive coxopathy, and 3 with subchondral insufficiency fracture. Seventeen patients who did not have ONFH had magnetic resonance imaging findings that showed a bone marrow edema pattern at the femoral head. The mean age of 62.9 years among patients without ONFH was significantly higher than that of 45.2 years among patients with ONFH. There were 18 female patients in the non-ONFH group and 5 female patients in the ONFH group. Bilateral disease was found in 1 patient in the non-ONFH group and 17 patients in the ONFH group. No patients in the non-ONFH group had a history of systemic steroid administration compared with 11 patients in the ONFH group. Clinical features associated with the non-ONFH group were female sex, older age, unilateral disease, and no history of systemic steroid administration. For patients with these features, the diagnosis of ONFH should be made carefully. [Orthopedics. 2017; 40(1):e117-e123.]

idiopathic osteonecrosis of the femoral head (ONFH) is a common cause of acute hip pain in the early stage, and it leads to progressive collapse of the femoral head, with joint destruction. It is important to make an early diagnosis of osteonecrosis to allow prompt selection of an effective joint-preserving treatment, including potential nonoperative pharmacotherapy and joint-preserving surgery. The Japanese Investigation Committee diagnostic criteria for ONFH are among the proposed diagnostic criteria for early diagnosis of ONFH with high sensitivity and specificity. Conversely, some diseases are associated with hip symptoms and/or imaging findings that resemble those of early stages of ONFH. Characteristic magnetic resonance imaging (MRI) findings in the early stage of ONFH have been reported. Some patients were diagnosed as having ONFH by general orthopedic physicians or radiologists and were referred to hip specialists based on MRI findings. However, some of these patients were misdiagnosed and rediagnosed as having other diseases by hip specialists. In these patients, the incidence and the cause of misdiagnosis were unclear.

The authors are from the Department of Orthopaedic Surgery, Kansai Rosai Hospital, Amagasaki, Hyogo, Japan.

The authors have no relevant financial relationships to disclose.

This study was supported by a Health Labour Sciences Research Grant, Ministry of Health Labour and Welfare, Japan.

Correspondence should be addressed to: Wataru Ando, MD, PhD, Department of Orthopaedic Surgery, Kansai Rosai Hospital, 3-1-69 Inaba-so, Amagasaki, Hyogo, 660-8511, Japan (w-ando@umin.ac.jp).

Received: June 19, 2016; Accepted: August 25, 2016.

doi: 10.3928/01477447-20161013-03
The current study investigated the frequency of incorrect diagnosis of ONFH to clarify the clinical and diagnostic imaging features of these patients.

Materials and Methods

This retrospective case series was approved by the ethical committee at the study institution. Patients and families were informed that data from the case would be submitted for publication and gave their consent. This study included 50 patients who were diagnosed as having ONFH by general orthopedic physicians and were referred to the study hospital for surgical intervention from May 2010 to December 2014. These patients were reclassified in accordance with the Japanese Investigation Committee diagnostic criteria for ONFH. Briefly, 5 criteria were selected, including (1) collapse of the femoral head without joint space narrowing or acetabular abnormality on radiographs (including the crescent sign); (2) demarcating sclerosis in the femoral head without joint space narrowing or acetabular abnormality; (3) “cold in hot” on bone scans; (4) a low-intensity band on T1-weighted MRI (band-like pattern); and (5) trabecular and marrow necrosis on histologic evaluation. The diagnosis of ONFH is made for patients who meet 2 of these 5 criteria.

Patients were divided into 2 groups: patients reclassified as having other diseases (non-ONFH group) and patients correctly diagnosed as having ONFH (ONFH group). The incidence of non-ONFH diagnosis was calculated. The authors also analyzed several features of patients in the non-ONFH group, including the number of positive criteria for the diagnosis of ONFH, the current authors’ diagnosis, age at first visit, height, weight, body mass index, disease distribution (unilateral or bilateral), sex, history of systemic steroid administration, and treatment.

Results were reported as mean±SD. For comparison of the 2 groups, normally distributed continuous data (age, height, weight, body mass index) were analyzed with unpaired Student’s t test. For comparison of the ratio in the 2 groups for categorical data, including number of affected limbs, sex, stratified age group, and history of systemic steroid administration, Fisher’s exact test or Pearson’s chi-square test was used. Statview version 4.5 software (SAS Institute, Cary, North Carolina), was used to perform the statistical calculations. Significance was set at P<.05.

Results

Between May 2010 and December 2014, 50 patients who were diagnosed as having ONFH by general orthopedic physicians were referred to the study hospital. Of these, 24 patients were reclassified in the authors’ unit. The incidence of this occurrence was 48%. Of these 24 patients, 18 met none of the 5 diagnostic criteria and 5 patients met 1 diagnostic criterion. One female patient had positive findings on both radiographs and MRI, but she was reclassified as having subchondral insufficiency fracture based on the histologic specimen obtained at total hip arthroplasty. Of the 24 patients in the non-ONFH group, 18 were treated operatively, whereas 7 of 10 patients with osteoarthritis were treated conservatively. All patients with rapidly destructive coxopathy or subchondral insufficiency fracture underwent surgical intervention. All patients with transient osteoporosis of the hip were treated conservatively.

Patient 1: Diagnosis of Idiopathic Osteonecrosis of the Femoral Head

A 39-year-old man was seen at a general orthopedic clinic for sudden onset of pain in the left hip. He had a history of systemic steroid administration for Still’s disease. He was diagnosed as having bilateral ONFH by MRI and was referred to the authors’ unit. Radiographic examination showed preservation of the joint space bilaterally (Figures 1A-B). However, collapse of the left femoral head with demarcating sclerosis was noted (Figure 1B). On MRI examination, the high-intensity area of the right femoral head was clearly divided by a low-intensity band on T1-weighted image (Figure 1C) that corresponded to a high-intensity band on T2-weighted short-T1 inversion recovery MRI (Figure 1D). This low-intensity band in the right femoral head on T1-
weighted image is the typical band pattern seen in ONFH. A low-intensity band in the left femoral head was also observed on T1-weighted image (Figure 1E), but a diffuse high-intensity lesion was seen beneath this band on T2-weighted short-T1 inversion recovery image (Figure 1F). This patient met 2 of the 5 criteria for ONFH in both hips, and the diagnosis of ONFH made by the orthopedic physician was considered appropriate.

**Patient 2: Rediagnosed as Osteoarthritis**

A 69-year-old woman was seen at a general orthopedic clinic for sudden onset of pain in the right hip. The diagnosis of ONFH was made by MRI examination, and the patient was referred to the authors’ unit. She had no history of systemic steroid administration. Radiographic examination showed demarcating sclerosis of the femoral head, with slight narrowing of the joint space (Figure 2A). Findings of MRI examination showed a low-intensity band in the femoral head on T1-weighted image (Figure 2B), with a homogeneous high-intensity lesion inside this band on T2-weighted image (Figure 2C) that was considered a cystic change derived from the bone cyst. This patient met none of the 5 criteria for ONFH and was rediagnosed as having osteoarthritis.

**Patient 3: Rediagnosed as Transient Osteoporosis of the Hip**

A 40-year-old woman was seen at a general orthopedic clinic for sudden onset of pain in the right hip. She was diagnosed as having ONFH by a radiologist and was referred to the authors’ unit. She had no history of systemic steroid administration. Radiographic examination showed preserved joint space (Figure 3A). On MRI examination, a diffuse low-intensity lesion was seen on the femoral head on T1-weighted image (Figure 3B). A diffuse high-intensity lesion inside this band was seen on T2-weighted short-T1 inversion recovery image (Figure 3C) and was considered bone marrow edema. None of the

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Non-ONFH Group (n=24)</th>
<th>ONFH Group (n=26)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD, y</td>
<td>62.9±17.9</td>
<td>45.2±14.2</td>
<td>.0003</td>
</tr>
<tr>
<td>Height, mean±SD, cm</td>
<td>157±8.5</td>
<td>165±8.6</td>
<td>.0010</td>
</tr>
<tr>
<td>Weight, mean±SD, kg</td>
<td>55±10.1</td>
<td>60.8±12.4</td>
<td>.0823</td>
</tr>
<tr>
<td>Body mass index, mean±SD, kg/m²</td>
<td>22.3±3.5</td>
<td>22.1±3.9</td>
<td>.8624</td>
</tr>
<tr>
<td>Affected limb, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>1 (7%)</td>
<td>17 (65%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Unilateral</td>
<td>23 (93%)</td>
<td>9 (35%)</td>
<td></td>
</tr>
<tr>
<td>Sex, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6 (25%)</td>
<td>21 (81%)</td>
<td>.0002</td>
</tr>
<tr>
<td>Female</td>
<td>18 (75%)</td>
<td>5 (19%)</td>
<td></td>
</tr>
<tr>
<td>Stratification by age group, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40 y</td>
<td>3 (10%)</td>
<td>9 (35%)</td>
<td></td>
</tr>
<tr>
<td>40-64 y</td>
<td>9 (43%)</td>
<td>14 (54%)</td>
<td>.0090</td>
</tr>
<tr>
<td>≥65 y</td>
<td>12 (46%)</td>
<td>3 (11%)</td>
<td></td>
</tr>
<tr>
<td>Steroid administration, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0%)</td>
<td>11 (42%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>24 (100%)</td>
<td>15 (58%)</td>
<td>.0003</td>
</tr>
</tbody>
</table>

Abbreviation: ONFH, idiopathic osteonecrosis of the femoral head.

Figure 1: Radiologic findings in osteonecrosis of the femoral head at the first visit to the authors’ unit. Frontal radiographs showing the right (A) and left (B) femoral head. Coronal T1-weighted magnetic resonance imaging of the right (C) and left (E) femoral head. Coronal T2-weighted short-T1 inversion recovery magnetic resonance imaging of the right (D) and left (F) femoral head.
5 criteria for ONFH were met, and the patient was rediagnosed as having transient osteoporosis of the hip. She was treated conservatively, and the hip pain resolved 6 months later.

**Patient 4: Rediagnosed as Subchondral Insufficiency Fracture**

An 82-year-old woman was seen at a general orthopedic clinic for sudden onset of pain in the left hip and a 1-month history of difficulty walking. She was diagnosed as having ONFH, based on MRI findings, and was referred to the authors’ unit. She had no history of systemic steroid administration. Radiographic examination showed flattening of the outer one-third of the weight-bearing area of the femoral head (Figure 4A). Findings of MRI examination showed a low-intensity band and a diffuse low-intensity lesion under the low-intensity band on T1-weighted image (Figure 4B). On T2-weighted short-T1 inversion recovery image, a diffuse high-intensity lesion was seen in the same area, in addition to joint effusion (Figure 4C). For this patient, 2 of the 5 criteria for ONFH were met. However, histologic examination of the femoral head at total hip arthroplasty showed different findings than those associated with ONFH, with repaired fibrous tissue under the subchondral bone (Figure 5A) and viable osteocytes in the trabecular bone (Figure 5B). This patient was rediagnosed as having subchondral insufficiency fracture.

**Discussion**

Accurate diagnosis of ONFH leads to appropriate selection of effective joint-preserving treatment.1-8 The success of joint-preserving surgery depends on the amount and progression of ONFH.7 Recently, cell therapy for ONFH was introduced with advances in stem cell research and regenerative medicine.15-18 Cell therapy for ONFH is typically used at the early stage.19 For this reason, accurate diagnosis of ONFH is increasingly important.

Sensitivity and specificity were 91% and 99%, respectively, when ONFH was diagnosed with the Japanese Investigation Committee diagnostic criteria for ONFH.9,20 However, the current study showed that approximately half of the patients diagnosed as having ONFH by general orthopedic physicians were rediagnosed as having other diseases. Some cases were diagnosed as ONFH by radiologists, based on MRI findings. Most patients in the non-ONFH group did not meet 2 of the criteria for the diagnosis of ONFH. This ratio was considered high, and these criteria should be widely known to orthopedic physicians and radiologists.

One patient in this study met 2 criteria for ONFH but was rediagnosed as having another disease, based on histologic findings. Histologic findings had sensitivity...
and specificity of 100%, whereas the other criteria had sensitivity and specificity of less than 100%. In the current study, no patients underwent bone scan and histologic examination before they were referred to the authors. It is unrealistic for patients to undergo bone scan and histologic examination in clinics. Therefore, radiographic and MRI findings are important for an accurate diagnosis of ONFH.

For patients with ONFH, radiographic findings of demarcating sclerosis in the femoral head without joint space narrowing or acetabular abnormality correspond to a line of low signal intensity on T1-weighted image. A crescent-shaped area of low signal intensity is seen in the subchondral area. The appearance is similar to that of necrotic tissue observed in the classic form of epiphyseal osteonecrosis. However, this low-signal band is not specific to ONFH and may be seen in insufficiency subchondral fracture. A focal low-intensity band beneath the articular cartilage was observed in some slices on T1-weighted images of patients with insufficiency subchondral fracture. Patients with osteoarthritis of the hip showed various patterns on MRI. The MRI appearance of bone cysts in osteoarthritis was diffuse low signal intensity on T1-weighted images and uniform high signal intensity on T2-weighted images within the peripheral line of low signal intensity in T1-weighted images, as shown in Figure 2C. This peripheral line of low signal intensity was similar to the band-like pattern seen in ONFH. However, the inside lesion within this line was completely different from ONFH. In the case of rapidly destructive coxopathy, no band-like pattern of low intensity was seen on T1-weighted images.

The MRI appearance of low signal intensity on T1-weighted images with matching high signal intensity on T2-weighted images extending from the femoral head to the intertrochanteric regions is known as bone marrow edema. The combination of bone marrow edema and focal ONFH is strongly associated with hip pain in the early stages of osteonecrosis, even before collapse of subchondral bone at the femoral head. In this study, 17 of 24 patients in the non-ONFH group had bone marrow edema on MRI. This edema on MRI images leads to a diagnosis of ONFH in patients with other diseases. Transient osteoporosis of the hip is a syndrome of transient demineralization that causes acute hip pain and has MRI findings similar to those of bone marrow edema. Bone marrow edema was also observed in fatigue and occult fracture as well as subchondral fracture. In addition, ONFH is usually progressive, and surgical intervention may be necessary. In contrast, transient osteoporosis of the hip is generally a self-limited condition that responds to treatment of symptoms and is protected by reducing weight bearing. Balakrishnan et al reported patients with transient osteoporosis of the hip who were referred for surgical intervention because of a previous diagnosis of ONFH. As in the current study, these patients avoided surgery because of rediagnosis. Insufficiency fracture of the femoral head was 1 cause of bone marrow edema of the femoral head, based on MRI findings. The MRI findings in transient osteoporosis of the hip and subchondral insufficiency fracture are similar, as previously reported; however, radiographic examination showed flattening of the femoral head, as shown in Figure 4A. In the current study, all of the patients with subchondral insufficiency fracture were treated surgically. The degree of bone marrow edema was also correlated with the severity of hip osteoarthritis and rapidly destructive coxopathy. In most cases, joint reconstruction is necessary for patients with progression of osteoarthritis and rapidly destructive coxopathy.

According to the nationwide epidemiologic survey of ONFH in Japan, the peak age distribution is in the 40s. The female ratio (female/total) is 42% (923/2193). Half of patients have a history of systemic steroid use and are affected bilaterally. In this study, these characteristic features of patients with ONFH were similar to those reported in a nationwide epidemiologic survey in Japan. However, in the current study, the features of patients in the non-ONFH group were significantly different from those of patients with ONFH, both in this study and in the nationwide survey. The clinical features of patients in the non-ONFH group included female sex, older age, unilateral disease, and no history of systemic steroid administration. In patients with these features, the diagnosis of ONFH should be made carefully.

**Limitations**

This study was limited because it provided an estimate of the occurrence of the disease in a limited region in Japan. The
presumed causes of ONFH were different among regions, races, and countries, according to differences in patient demographics. In Japan, the leading presumed cause of ONFH is systemic steroid administration, whereas it is alcohol abuse in Korea. Sickle cell disease is the leading cause of ONFH in some African countries. In Uganda, Ndugwa reported that the peak incidence of ONFH derived from sickle cell disease occurred in 20- to 24-year-old women. Studies in other countries are likely to show different findings.

Understanding the clinical features and radiologic findings associated with each disease, including osteoarthritis, transient osteoporosis of the hip, rapidly destructive coxopathy, and subchondral insufficiency fracture, and closely following these patients with serial clinical examination can lead to accurate diagnosis.

CONCLUSION

This study reported a series of patients referred to the authors with a diagnosis of ONFH. Of these patients, 48% were re-diagnosed with other diseases, including osteoarthritis, transient osteoporosis of the hip, rapidly destructive coxopathy, and subchondral insufficiency fracture. The notable radiologic feature of patients in the non-ONFH group was bone marrow edema on MRI. The clinical features of patients in the non-ONFH group were female sex, older age, unilateral disease, and no history of systemic steroid administration. The diagnosis of ONFH should be made carefully in these patients.

REFERENCES


