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Current Research on Subchondral Insufficiency Fracture of the Femoral Head

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Subchondral insufficiency fracture (SIF) of the femoral head is one of the predominant etiologies of rapidly progressive osteoarthritis of the hip (RPOH). SIF is a rare disease that causes acute pain in the hip joint. It is most frequently found in elderly women with osteoporosis. It is often underdiagnosed or misdiagnosed as osteonecrosis of the femoral head. SIF is currently a well-established cause of RPOH; however, the deeper etiology of SIF is not clear. Good clinical outcomes have been reported for hip preservation therapy and hip replacement. SIF is not obvious radiologically in the early stage, and a T1-weighted magnetic resonance imaging shows a discontinuous low-intensity band under the articular cartilage convex to the articular surface as its characteristic manifestation. Some patients will lose the opportunity to preserve the hip joint due to symptoms such as progressive joint space narrowing and subchondral collapse within a very short period. Patients with progressive hip space narrowing and subchondral collapse on X-ray should be converted to total hip arthroplasty. Based on the characteristics of the disease, surgeons need to master the clinical and radiological characteristics of SIF and strive for early diagnosis and treatment.

Keywords: *Subchondral insufficiency fracture, Femoral head, Rapidly progressive osteoarthritis of the hip*

Subchondral insufficiency fracture (SIF) of the femoral head mostly occurs in older women. SIF is considered an important contributing factor of rapidly progressive osteoarthritis of the hip (RPOH) and an uncommon cause of acute hip pain in healthy adults.[1] The concept of SIF was first proposed and defined by Bangil et al.[2] in 1996 as a subchondral fracture of the femoral head usually secondary to osteoporosis or osteopenia without any evidence of osteonecrosis of the femoral head (ONFH). It was previously thought that this disease was mainly affected by osteoporosis in the elderly, but current evidence suggests that SIF can occur in adults of all ages and at different activity levels.[3-6] It has also been reported as a secondary symptom of some primary diseases in patients with renal transplantation, liver transplantation, oncologic osteoporosis, and alkaptonuria.[7-10] SIF is frequently misdiagnosed as ONFH due to an incomplete understanding of its etiology. Some patients were improved with conservative treatment to keep the disease under control,[11] while others underwent surgical intervention owing to RPOH.[12,13] Various treatment strategies for SIF have been reported, although the related literature remains scant.

The present review investigated the recent research advances in epidemiology, etiology, clinical presentation and radiographic characteristics, histopathological manifestations, diagnosis, differential diagnosis, treatment, and prognosis of SIF to enhance surgeons' knowledge about this disease. Approval was granted by the Ethics Committee of Kanazawa Medical University (No. 134). Written

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informed consent was obtained from the parents.

EPIDEMIOLOGY

SIF is most prevalent in elderly women with osteoporosis mostly in low-intensity daily life activities, but it has also been reported in younger patients. Iwasaki et al.[3] reported 5 patients, including 3 men and 2 women with a mean age of 23.4 years (range, 16–29 years). The exact incidence of SIF is still unclear, and most of the literature is case reports. However, according to Yamamoto et al.,[4] SIF was observed in 3.6% (460/7,349) of patients with a preoperative diagnosis of osteoarthritis of the hip and in 11.1% (41/369) of patients with a diagnosis of ONFH. Yamamoto et al.[6] treated 39 patients diagnosed with SIF from 2001 to 2011, 14 of whom were men and 25 were women. The prognosis of male patients was better than that of female patients based on comparison of outcomes. In contrast, male patients in Hackney's cohort[14] had significantly faster disease progression to total hip arthroplasty (THA) than did female patients, and the progressive group was significantly older than the non-progressive group.

ETIOLOGY

Age-related osteoporosis including oncological osteoporosis is the most prevalent cause of SIF, and pregnancy-related osteoporosis has been reported to lead to SIF onset.[10,15] Some other possible etiologies of SIF have also been demonstrated in the literature. Kubo et al.[16] treated 48 patients diagnosed with SIF and classified them into two groups: younger (< 40 years old) and elderly (≥ 40 years old). In the younger group, the patients had a posterior pelvic tilt. Kubo et al.[16] suggested that posterior pelvic tilt may be partially involved in the mechanism of injury in SIF. Ishihara found a higher degree of hip dysplasia in patients with SIF than in control patients, and he suggested that excessive pressure on the acetabular rim due to dysplasia may be associated with SIF incidence.[17,18] Fukui et al.[1] investigated SIF cases and found that patients with SIF had an inverted glenoid labrum, which is inserted between the femoral head and the acetabulum. The inversion of the glenoid labrum causes a stress concentration that contributes to SIFs and progressive joint space narrowing. Wang et al.[19] validated the hypothesis of acetabular labral inversion as the cause of SIF by demonstrating that subchondral fractures occurred in femoral neck fractures in the absence of labral inversion. The results also showed that the stress on the femoral head increased only 1.3 times when the pelvis was tilted posteriorly up to 20°. In a retrospective study of 9 patients with SIF, Uchida et al.[20] found symptoms of acetabular labral tears in all patients, and they suggested that SIF may be associated with bony deformities and acetabular labral tears. SIF has also been reported in patients with alkaptonuria,[9] renal and liver transplantation,[7,8] and systemic lupus erythematosus.[18,21]

CLINICAL PRESENTATION

The most common symptom of SIF is an acute onset of severe hip pain, usually without any aura or a minor injury. Moreover, this pain is persistent and is not relieved by rest or at night.[22] Patients may suffer pain, needing crutches or even having complete loss of mobility. In some case reports, patients had no history of corticosteroid use and alcohol abuse. The patients' movement of the hip joint was affected in all directions. Some patients can achieve relief with conservative treatment. In contrast, some patients develop joint collapse, narrowing, or even loss of joint space within a few months, resulting in impaired joint function and the need for joint replacement.

RADIOGRAPHIC CHARACTERISTICS

Plain Radiographic Findings

Plain radiographs are unremarkable in some patients in the early stages of the disease (Figs. 1 and 2), except that there may be a decrease in bone density. When the patient develops secondary osteoarthritis, there may be cystic degeneration of the femoral head, collapse, or slight narrowing of the joint space several months after the onset of pain, or only a faint linear patchy osteosclerotic area can be seen in the superior portion of the femoral head or crescentic sign (Figs. 2 and 3).[23]

Magnetic Resonance Imaging Findings

Magnetic resonance imaging (MRI) is one of the most effective diagnostic techniques for SIF. The diagnostic criteria regarding MRI can identify joint effusion with extensive bone marrow edema in the femoral head, neck, and/or acetabulum at the early onset.[24] According to Rafii et al.,[25] on T1-weighted MRI, all hips had a low-intensity band that tended to be irregular, disconnected, and convex to the articular surface. In SIFs, the low-intensity band on T1-weighted images matched histologically the fracture line and associated fracture repair tissue (Figs. 1 and 3).

In contrast, the low-intensity band in osteonecrosis is generally smooth and circumscribes all the necrotic segments because it represents repaired tissue. By observing MRI findings in 51 patients with SIF, Hackney et al.[14]

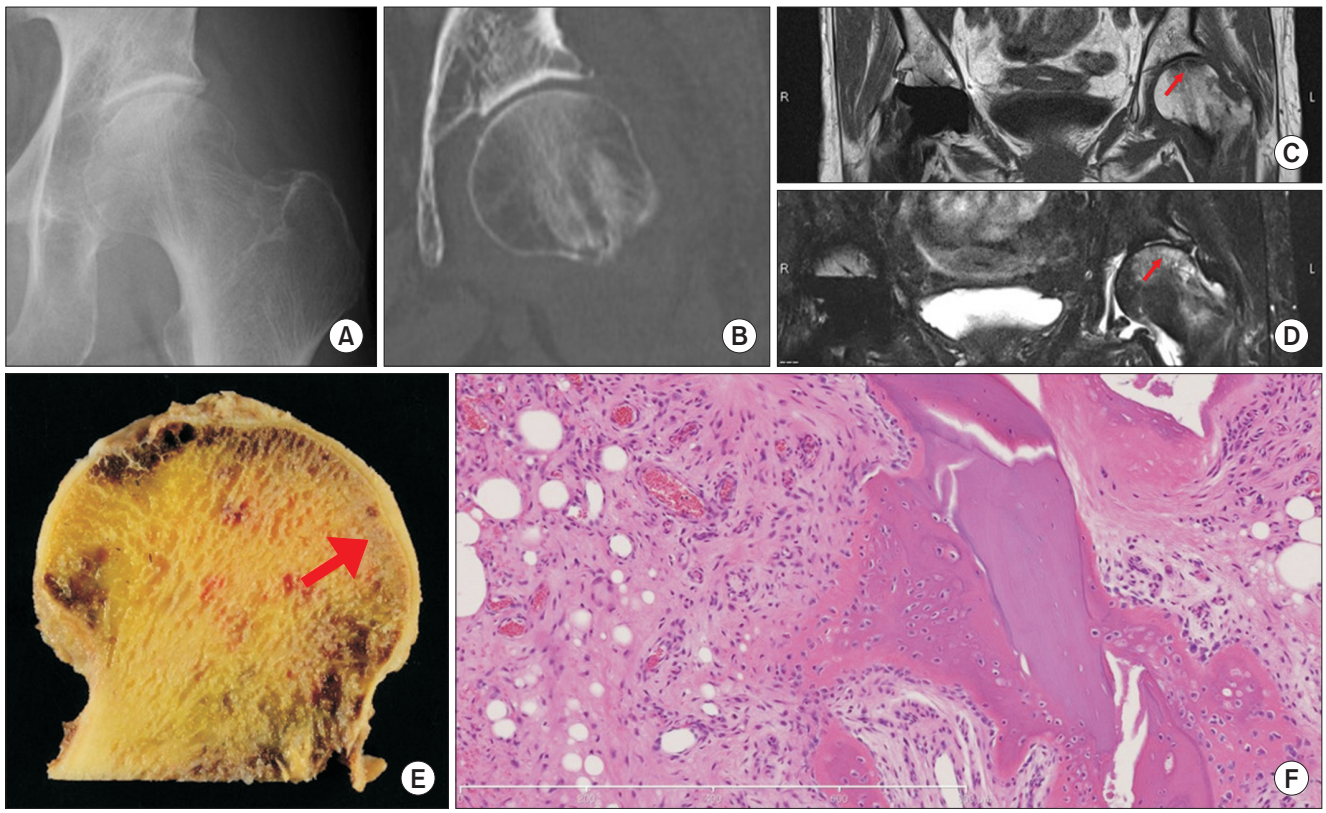

Fig. 1. A 91-year-old woman with a subchondral insufficiency fracture of the left femoral head. She had difficulty turning after the onset of pain and increased pain with weight-bearing and walking. (A) Preoperative X-ray 6 weeks later showed narrowing of the joint space and sclerosis of the weight-bearing region with slight collapse of the bone. (B) Computed tomography and the X-ray findings were consistent. Magnetic resonance imaging showed diffuse bone marrow edema in the weight-bearing area and neck, with a low signal intensity (arrow) on the T1-weighted image (C) and a high signal (arrow) on the T2-weighted image (D). (E) On the resected femoral head section, a greyish white subchondral tissue was observed in the lesion area, with loss of normal trabecular structures (arrow). (F) Histology of the lesion showed dead bone fragments, proliferating granulation tissue, osteoblasts, and new bone (H&E, × 50).

found that approximately two-thirds of patients (64.7%, 33/51) had subchondral fractures in the anterior or middle femoral head, whereas only 21.1% of patients (11/51) had them in the posterior femoral head. Hackney et al.[14] also found that cartilage defects on SIF significantly affected progression to THA. Each 1 mm increase in the size of the cartilage defect resulted in a 17.7% increase in the risk of progression to THA. T1-weighted images of SIF patients tended to have a consistent presentation, but T2-weighted images showed inconsistencies. Sonoda et al.[24] observed different intensities of subchondral deposits on fat-suppressed T2-weighted images of SIF patients, which were classified as high intensity, heterogeneous intensity, and low intensity; different intensities were associated with clinical outcomes. By retrospectively reviewing contrast-enhanced MRI in patients with SIF compared with ONFH patients, Miyanishi et al.[26] found that 90% of SIF patients had increased contrast in the proximal part of the low-intensity band after intravenous gadolinium administration, whereas none of the ONFH patients showed enhancement. Therefore, contrast-enhanced MRI can be used as a supplemental diagnostic measure.

HISTOPATHOLOGICAL MANIFESTATIONS

A notched liner-shaped or circular greyish white tissue under the cartilage can usually be found in the coronal gross view (Figs. 1 and 3).[27,28] There was no well-demarcated, wedge-shaped opaque yellow necrotic region, as seen in osteonecrosis. Microscopically, fractured bone scabs, granulation tissue, and fractured bone trabeculae are usually observed, corresponding to a low-intensity band on T1-weighted images. Edematous changes and vascular-rich granulation tissue can be seen around this fracture lesion.[29,30] The histological findings of SIF are different from those of ONFH. In ONFH, a characteristic appearance is

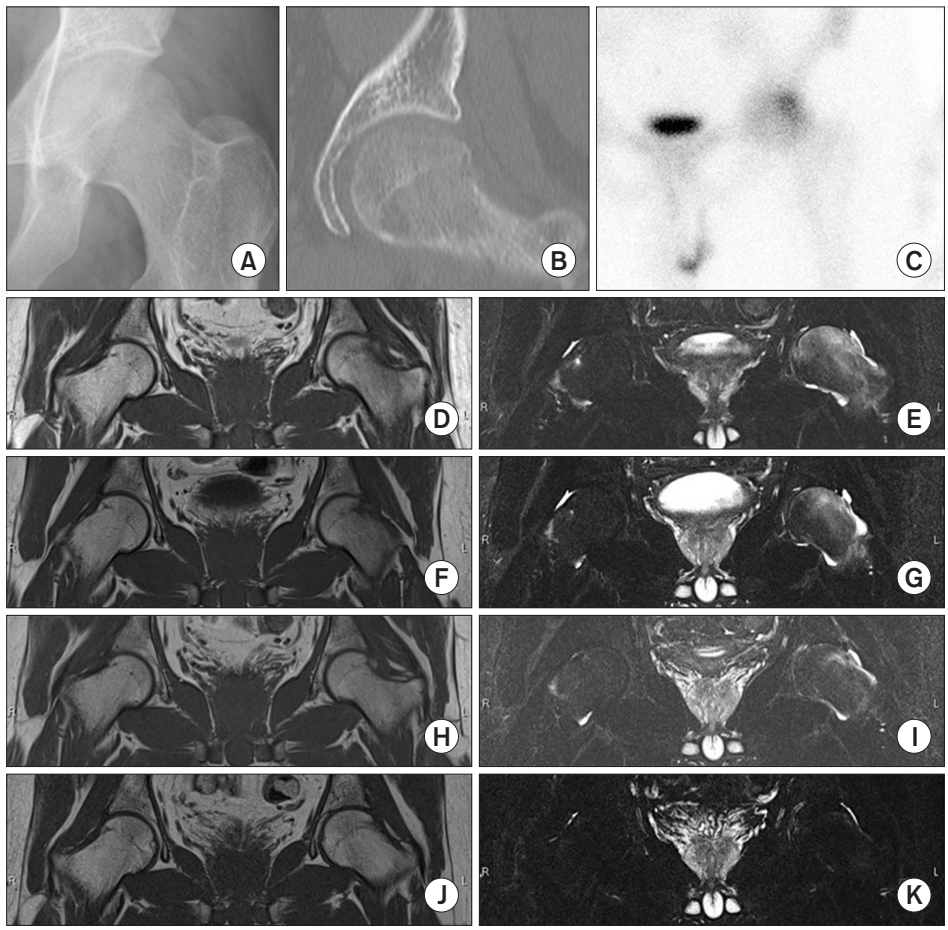

Fig. 2. A 27-year-old man with a subchondral insufficiency fracture of the left femoral head and a history of congenital osteogenesis imperfecta. After a change from a clerical to an auto mechanic career, the patient had pain in his left hip, which subsequently progressed into claudication. Five months after the onset of symptoms, a hip arthroscopic rim trimming and labral re-fixation was performed. (A) Preoperative X-ray obtained 3 weeks before surgery showed the slight collapse of the femoral head in the weight-bearing region. (B) Computed tomography and radiography findings were consistent. (C) Bone scintigraphy showed diffuse increased uptake in the femoral head. Preoperative magnetic resonance imaging (MRI) obtained 3 weeks before surgery (D, E) and 10 days before surgery (F, G) showed diffuse bone marrow edema and joint effusion in the left hip joint. (H, I) Four-week postoperative MRI scans showed reduced bone marrow edema and joint effusion. (J, K) MRI at 14 weeks after surgery showed resolution similar to that of bone marrow edema and effusion.

a zonal pattern comprising necrotic, repaired, and viable regions.

DIAGNOSIS, CLASSIFICATION, AND PROGNOSIS

Diagnosis

Early diagnosis is vital for patients with SIF, as the disease often progresses rapidly within a few months. When collapse progresses and pain increases, surgical intervention may be required. Early diagnosis and conservative treatment can preserve the function of the hip and slow the progression of the disease. The diagnostic criteria for SIF are as follows: (1) hip pain without any apparent history of trauma at the start; (2) radiographs normal or showing the collapse or joint space narrowing of the femoral head; (3) a fracture line parallel to the articular surface on a computed tomogram (CT); (4) a bone marrow edema pattern in the femoral head and/or neck on MRI; and (5) a subchondral low signal intensity band on T1-weighted MRIs, which is either serpiginous or parallel to the articular surface.[31]

Classification and Prognosis

New diagnostic techniques and staging methods have been reported. By classifying patients in more detail, the prognosis of patients can be better determined so that more appropriate and accurate therapy can be given to patients. Uchida et al.[20] used an innovative classification strategy[32]

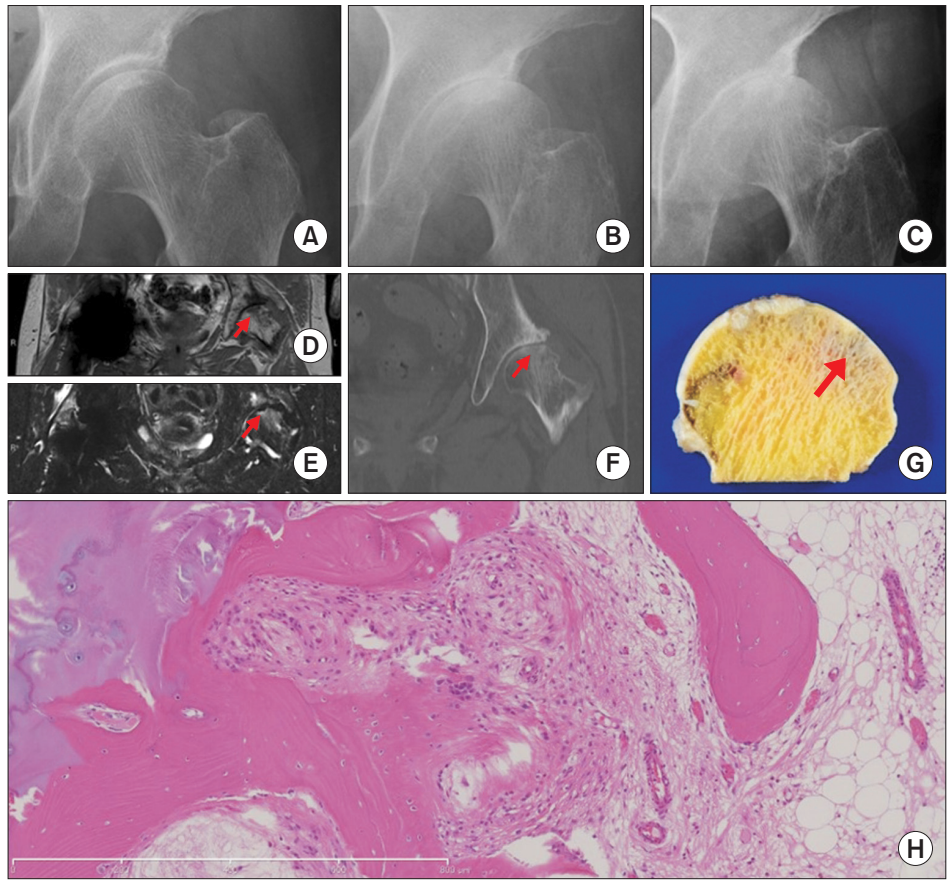

Fig. 3. A 75-year-old woman with a subchondral insufficiency fracture of the left femoral head. (A) For 9 months prior to the onset of pain, the patient's left hip joint space was normal. (B) Radiographs at the onset of pain showed narrowing of the joint space, and the patient's symptoms resolved after conservative treatment. (C) Around 4 weeks later, the patient was readmitted to the hospital with increased pain, and an X-ray showed entire joint space loss. Magnetic resonance imaging showed diffuse subchondral bone marrow edema with a low signal intensity (arrow) on the T1-weighted image (D) and a high signal intensity (arrow) on the T2-weighted image (E). A low-intensity signal band (arrow) parallel to the articular surface could be observed. (F) Computed tomography showed collapse of the subchondral bone (arrow). (G) In the resected femoral head section, the cartilage in the region of the lesion became thin, and the subchondral tissue appeared greyish white (arrow). (H) The collapsed region showed the presence of trabecular fractures surrounded by new bone formation with osteoblastic and fibroblastic proliferation (H&E, × 25).

based on the location of the SIF lesion, which was assessed using the geographical zone method, and used a different fixation method and depth according to the grade. Iwasaki et al.[33] classified 31 patients after analyzing the injured portion of SIF by three-dimensional MRI: (1) Lateral type: the contact stress between the acetabular rim and the lateral portion of the femoral head causes SIF because of insufficient acetabular coverage; (2) Central type: the contact stress between the acetabular surface and the mediolateral center of the femoral head causes SIF independent of insufficient acetabular coverage, and the prognosis of the lateral type is significantly worse than that of the central type. This finding helps us predict the clinical outcome of patients and give them a reasonable expectation. Sonoda et al.[24] classified the hip into three categories by analyzing the signal intensity of subchondral bone on T2-weighted images of fat suppression in 37 patients with SIF: type 1 was high intensity, type 2 was heterogeneous intensity, and type 3 was low intensity. The results showed poor results of conservative treatment in type 3 SIF patients. This finding enables the development of more accurate treatment for patients, and patients with type 3 should be operated on as early as possible and should not waste time on conservative treatment, which increases their suffering. Miyanishi et al.[31] found a cutoff value of 71 years by analyzing SIF patients' age when they received THA (sensitivity, 77%; specificity, 64%). The survival rate was significantly lower in patients aged ≥ 71 years than in those aged < 71 years. Tartrate-resistant acid phosphatase 5-b (TRACP-5b) is widely used as a specific bone resorption marker associ-

ated with osteoclast cells. In studying osteoclast activity in the joint fluid, Kubo et al.[34] found significantly higher levels of TRACP-5b in SIF with progressive collapse than in SIF without progressive collapse. And regression analysis showed that the number of multinuclear giant cells was positively correlated with the level of TRACP-5b in joint fluid. Likewise, a retrospective analysis of 41 patients diagnosed with SIF by Shimizu et al.[35] found that hip space width was associated with the length of the band pathology, serum type 1 procollagen-N-propeptide (P1NP), and TRACP-5b. It was also determined that the levels of bone metabolic markers might reflect the local severity as a factor in determining the prognosis of SIF.

Differential Diagnosis

There are no significant differences between subchondral insufficiency fracture of the femoral head (SIFFH) and ONFH patients regarding gender, age range, or body mass index. There are also many similarities in symptoms, so it is very difficult to differentiate the two diseases. However, there may be differences in patient history, such as alcohol abuse and corticosteroid therapy.[26,36] Yamamoto[37] has clearly described the differential diagnosis between SIF and ONFH, and the difference between the two in terms of age, etiology, laterality, and imaging histopathology is well established. However, not every individual patient's symptoms are typical. For instance, in the MRI view of ONFH, the low-intensity band is often smooth and concave, whereas in the MRI view of SIF, the low-intensity band is irregularly discontinuous and convex to the articular surface. However, a case of SIF with a concave low-intensity band similar to that of ONFH was recently reported in the literature.[38] Ikemura et al.[39] recently reported a differentiating indicator between SIF and ONFH on MRI: the ratios of the distance from the articular surface of the femoral head to the T1 low-intensity band to the femoral head diameter (band depth ratio) on a mid-coronal slice of MRI. The results showed that all coronal slices in the SIF group were significantly lower than those in the ONFH group.[39] There is a statistically significant difference between SIF and ONFH indeed. Kawano et al.[40] used 20 histopathologically diagnosed SIF and ONFH femoral heads with a cubic region of interest selected in each collapsed and nearby uncollapsed region on one side and compared the microstructural parameters of both by Micro-CT, including bone volume fraction, trabecular thickness, and bone mineral density. It was found that the bone volume fraction, bone trabecular thickness, and bone mineral density in the collapsed area were significantly lower than those in the nearby uncollapsed area in ONFH. On the other hand, in SIF there were no significant differences between the region of interests in any of these microarchitectural parameters. This finding suggests that the morphologic characteristics of the lateral collapsed lesions in ONFH and SIF are inconsistent and can be a differential diagnosis between the two. However, misdiagnosis and underdiagnosis often occur for hip physicians who are not well knowledgeable about the disease. Constant efforts are still needed for the early and accurate diagnosis of SIF.

TREATMENT

After the onset of hip pain and SIF diagnosis in patients, some cases progress to femoral head collapse within a few months.[41] During this period, a certain proportion of patients may have relief and maintain the condition for several years with conservative treatment such as nonsteroidal anti-inflammatory drugs, intra-articular steroid injections, and no or partial weight-bearing.[18,23,42] When symptoms are still persistent and conservative treatment has failed, arthroscopy may be an alternative treatment option if the patient does not exhibit femoral head collapse and the primary associated lesions are bony deformities and glenoid labral tears (Fig. 2). However, there is still no consensus on its outcomes. Uchida et al.[20] reported 9 patients with SIF who underwent arthroscopic acetabular labral repair and arthroscopic fixation of SIFFH lesions using hydroxyapatite poly-lactate acid composite threaded nails in the absence of femoral head collapse. One year after surgery, all patients had complete disappearance of bone marrow edema and successful healing of SIF lesions. When the femoral head collapses, it seems that only THA can be performed, but in young patients, preservation of the hip is important. Patel and Kamath[12] reported a case of a 48-year-old man with SIF who was treated with core hip decompression and bone void filler as a hip-preserving alternative considering the patient's age. The patient was followed up at 8 weeks postoperatively, and a repeat T1-weighted MRI showed resolution of the low-intensity band and no surrounding bone marrow edema. The patient had no pain in the left hip at the 1.5-year postoperative follow-up and returned to all his prior recreational activities, including running, weight-lifting, and swimming. This procedure can provide good clinical results and can be a preservation option for young patients. Yamamoto et al.[43] described a transtrochanteric rotational osteotomy to treat young patients with SIF. The patients' postoperative Harris hip score improved significantly (71.6 preoperatively vs. 97.2 postoperatively). Radiographically, the fractured lesion healed, and no progression of collapse was observed

in their 4 patients. Sonoda et al.[13] also reported a significant improvement in Harris hip score in 7 young patients treated with transtrochanteric anterior rotational osteotomy (51.6 preoperatively vs. 91.9 at 1 year postoperatively). However, THA or hemiarthroplasty is more applicable in elderly patients.

FUTURE PERSPECTIVES

The etiology of SIF is not yet fully understood, but it has attracted increasing attention. There are some limitations in the current studies. First, the level of evidence is generally low, with most being case reports and including a small number of cases. Second, the follow-up time of cases is generally short. Third, there are fewer basic studies on the etiology of the disease. In the future, it is hoped that more researchers will be available to investigate SIF in greater depth and that SIF can be diagnosed at an earlier stage so that the patient's disease process can be slowed to the maximum extent possible and the hip joint function can be preserved.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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