

Subchondral Insufficiency Fracture of the Femoral Head in a Pregnant Woman with Pre-existing Anorexia Nervosa

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Subchondral insufficiency fracture (SIF) is a fragility fracture secondary to osteoporosis that leads to collapse of the femoral head with no evidence of osteonecrosis. SIF of the femoral head has been reported in adults of varying ages and both sexes, but it has never been reported to occur in pregnant women. Herein, we describe a 40-year-old primiparous patient with pre-existing anorexia nervosa who developed SIF of the femoral head in the third trimester. At 29 weeks of gestation, the patient complained of sudden pain on walking in both hips. Despite the bed rest, her hip pain increased; consequently, cesarean section was performed at 36 weeks. After delivery, plain radiographs showed that the left femoral head was collapsed. Dual-energy X-ray absorptiometry indicated that the patient was osteoporotic. The magnetic resonance imaging (MRI) of her hips showed the findings that were compatible with SIF. Her left hip pain worsened during follow-up, and a radiograph showed progressive collapse of the left femoral head. The patient then underwent left bipolar hip arthroplasty 18 months after delivery, and she was diagnosed with SIF histopathologically. This is the first report of SIF in a pregnant woman that may reflect pregnancy-associated osteoporosis. SIF in pregnancy might be overlooked or misdiagnosed because the MRI findings have several overlaps with those of other hip disorders. Precise diagnosis of SIF in pregnancy may contribute to a better outcome by avoiding early arthroplasty in young women and appropriate evaluation of the osteopenic status of the patient.

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Introduction

Subchondral insufficiency fracture (SIF) of the femoral head is a relatively new entity that may cause femoral head collapse with no evidence of osteonecrosis (ON) caused by normal or physiological stress to the femoral head (Bangil et al. 1996; Rafii et al. 1997; Yamamoto and Bullough 1999). Previously thought to be a disease predominantly affecting elderly osteoporotic patients, SIF has been reported in adults of varying ages and activity levels (Yamamoto et al. 2008; Iwasaki et al. 2011; Yoon et al. 2014; Hackney et al. 2016). To the best of our knowledge, however, SIF of the femoral head has never been reported to occur in pregnant women.

On the other hand, pregnancy-associated osteoporosis is osteoporosis that occurs during pregnancy and lactation, and it rarely causes fragility fractures without trauma. Vertebral fractures are most commonly described, while

other locations are possible. The precise etiology of pregnancy-associated osteoporosis is not yet fully understood, but the maternal bone loss owing to insufficient calcium intake is generally thought to be related, especially in potentially osteopenic women (Kovacs and Ralston 2015).

In this article, the case of a pregnant woman with coxalgia and pre-existing anorexia nervosa is presented. Based on the radiological findings and histopathologic examination, it was concluded that SIF of the femoral head occurred in this primiparous patient as pregnancy-associated osteoporosis.

Case Presentation

A 40-year-old primipara presented with severe pain in both hip joints. In terms of past history, she had developed anorexia nervosa at 23 years of age and became amenorrheic. The patient was 161 cm tall, and her lowest weight and body mass index (BMI) were 30 kg and 11.6 kg/m²,

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respectively. After recovery from anorexia nervosa, she married at 31 years of age.

Since her menstrual cycles were irregular, she consulted a reproductive clinic a few years after marriage and was treated with controlled ovarian hyperstimulation drugs. After two miscarriages, she became pregnant with twins by in vitro fertilization at 39 years of age (weight, 40 kg; BMI, 15.4 kg/m²). She had no preceding history of trauma, fever, diseases other than anorexia nervosa, or smoking, and she had no predisposing factors for ON, such as steroid intake, alcohol abuse, or pre-existing ovarian hyperstimulation syndrome. No family history of severe osteoporosis was identified.

At 29 weeks of gestation, she complained of sudden pain on walking in both hips. Because the pain increased gradually, she was admitted to the Shiga University of Medical Science Hospital at 30 weeks (weight, 49 kg), and treated in the Department of Obstetrics and Gynecology and the Department of Orthopedic Surgery. The obstetricians considered that the excessive weight-bearing load on the hip joints due to the twin pregnancy might be the cause of the persistent pain. Despite inactivity owing to bed rest, the hip pain increased so much that she developed difficulty walking at 35 weeks. Cesarean section was performed at

36 weeks, and a 2,630-g girl and a 1,918-g girl were delivered.

On postpartum day 3, plain radiographs showed that the left femoral head was collapsed, while the right hip showed no remarkable findings (Fig. 1). Her left hip flexion, extension, and abduction were limited. The range of motion of flexion, extension, and abduction was 110°, -10°, and 10°, respectively.



Fig. 1. A plain radiograph on postpartum day 3. The left femoral head is collapsed, while the right hip shows no remarkable findings.

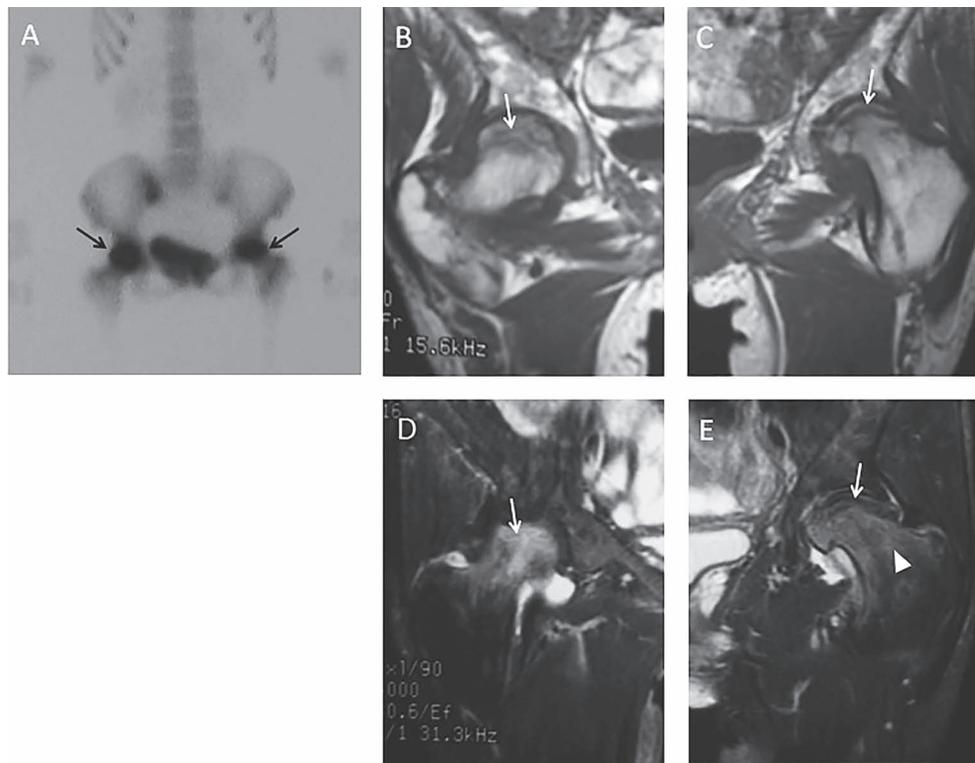


Fig. 2. A bone scintigram on postpartum day 8 and magnetic resonance imaging (MRI) on postpartum day 20.

There is strong uptake at bilateral femoral heads and femoral necks (arrows). (B) (C) T1-weighted images of the right (B) and left hip (C). There is a low-intensity band that is irregular, disconnected, and parallel to the articular surface in the subchondral area of each femoral head (arrows). (D) (E) Fat-suppressed T2-weighted images of the right (D) and left hip (E). A low-intensity band corresponding to the T1-weighted images is noted in the subchondral area of each femoral head (arrows). The left femoral head was collapsed (C) (E), and a diffuse high-signal intensity in the femoral head and neck is also seen on fat suppressed T2-weighted image (arrow head) (E).

and 20°, respectively. On postpartum day 8, a bone scintigram showed strong uptake of ^{99m}Tc in bilateral femoral heads (Fig. 2A). Dual-energy X-ray absorptiometry suggested low bone mineral density (BMD) for the femoral neck (0.544 g/cm², T score -3.0), total hip (0.62 g/cm², T score -2.6), and spine (L2-4) (0.877 g/cm², T score -2.0). The parathyroid hormone level was normal, at 22 pg/mL (normal, 10-65 mg/dL), and other laboratory investigations also showed no abnormalities. With a diagnosis of pregnancy-associated osteoporosis that involved the hips, she was treated with alendronate 5 mg per day, in addition to calcium L-aspartate hydrate 200 mg and alfacalcidol 0.5 µg per day, and she was kept non-weight-bearing. The neonates were bottle-fed.

On postpartum day 20, magnetic resonance imaging (MRI) of the hips showed a focal low-intensity band in the subchondral area on T1-weighted images (Fig. 2B, C). There was a low-intensity band that was irregular, disconnected, and parallel to the articular surface, typical of SIF (Rafii et al. 1997; Yamamoto and Bullough 1999; Yamamoto et al. 2008). Fat-suppressed T2-weighted imaging showed the corresponding area with a diffuse area of high-signal intensity in the left femoral head and neck (Fig. 2E). A low-intensity band corresponding to T1-weighted images was noted in the subchondral area, typical of SIF (Sonoda et al. 2016) (Fig. 2D, E).

During the follow-up period, serum estradiol and gonadotropin levels were normal, and menstruation resumed spontaneously at 8 months after delivery. Nevertheless, her left hip pain was not relieved, but it rather worsened, making it impossible for her to walk without crutches. A radiograph showed marked collapse of the left femoral head, and a slight collapse in the lateral portion of the right femoral head (Fig. 3A). The patient then underwent left bipolar hip arthroplasty 18 months after the delivery (Fig. 3B). Fig. 4A shows the macroscopic findings of

the left femoral head. A thin cleft was formed just beneath the articular cartilage of the femoral head. Inside the cleft were yellowish fragile tissue fragments that were focally continuous to whitish-gray cartilaginous tissue in the underlying bone. Microscopically, there were necrotic bone fragments in the subchondral cleft (Fig. 4B) and newly formed cartilage, bone, and granulation tissue adjacent to the necrotic bone (Fig. 4C). The cancellous bone of the femoral head consisted of thinner bone trabeculae than those of the same generation. There were no foci of necrosis, except in the subchondral area with cleft formation. Based on the radiological findings and histopathologic examination, the diagnosis of the left hip was SIF. On the other hand, the right hip became asymptomatic and showed no progression of radiographic femoral head collapse 6 months after arthroplasty (Fig. 5).

Administration of alendronate was continued for 2 years after arthroplasty.

The patient was informed that the case would be submitted for publication, and her written, informed consent was obtained.

Discussion

In this report, a case of SIF of the femoral head that occurred in a primiparous patient with pre-existing anorexia nervosa was presented. To the best of our knowledge, this is the first report of SIF in a pregnant woman.

The subchondral fracture that affected the present patient was considered to be pregnancy-associated osteoporosis, a transient osteoporosis on the basis of general low BMD prior to pregnancy. Her past history of anorexia nervosa and chronic very low BMI could have caused juvenile osteoporosis that could have lasted to her late 30s, while this patient did not suffer from a fracture before pregnancy. This patient with potentially low BMD undoubtedly suffered SIF of the femoral head associated with pregnancy.

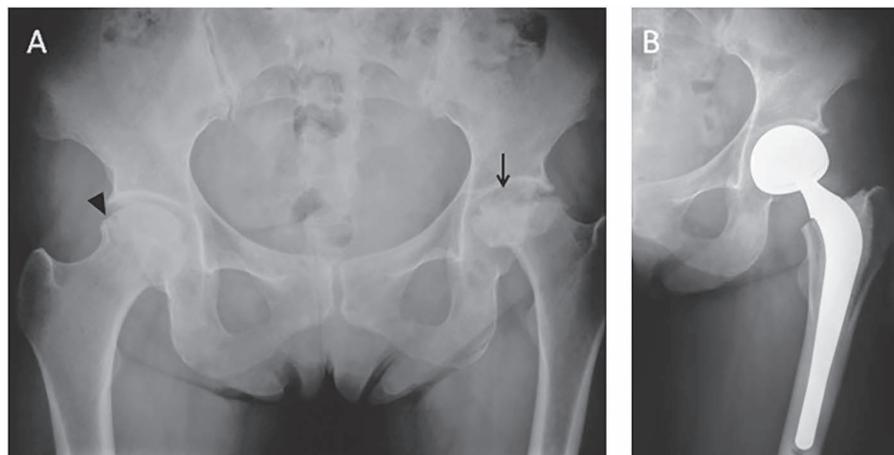


Fig. 3. Radiographs showing the left femoral head before and after arthroplasty. (A) A radiograph obtained 17 months after the delivery. The left femoral head is severely collapsed (arrow), while the lateral part of the right femoral head is slightly collapsed (arrow head). (B) A radiograph of the left hip following bipolar hip arthroplasty 18 months after the delivery.

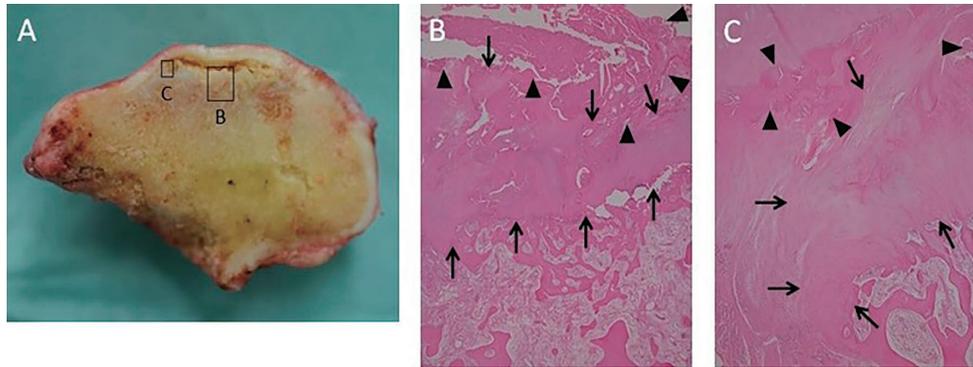


Fig. 4. Macroscopic and histopathological findings.

(A) The cut section of the resected femoral head. A thin cleft is seen in the subchondral area. The large and small squares represent the portions from which Fig. 4B, C, respectively, were obtained. (B) A photomicrograph obtained from the collapsed region. Callus formation (arrows) adjacent to the necrotic bone fragment (arrow heads) in the subchondral cleft (hematoxylin and eosin $\times 20$). (C) Callus formation consisting of cartilage and bone (arrows). There are no foci of necrosis (arrow heads) except in the subchondral area with cleft formation (hematoxylin and eosin $\times 40$).

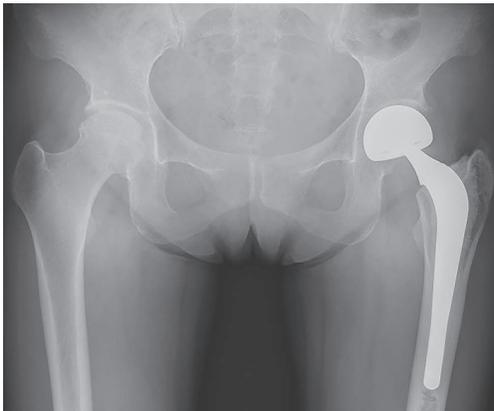


Fig. 5. A radiograph obtained 6 months after arthroplasty. The right femoral head does not show advanced collapse.

In this case with twin pregnancy, not only the weight-bearing load on the maternal hip joints, but also the fetal demand for calcium would have been greater than in a singleton case. The latter might provoke increased maternal skeleton resorption during the third trimester, when the fetal skeleton undergoes rapid mineralization (Kovacs and Ralston 2015).

In the present case, the T1- and fat suppressed T2-weighted MR images of the left hip appeared compatible with SIF (Raffi et al. 1997; Yamamoto and Bullough 1999; Yamamoto et al. 2008; Sonoda et al. 2016). Recently, several authors have shown that the band-pattern of the femoral head that looks like SIF was also seen in transient osteoporosis of the hip (TOH) (Vande Berg et al. 1999; Miyanishi et al. 2001, 2007; Yamaguchi et al. 2017). However, we supposed that this case was far from compatible with these findings because there was no clear finding of demineralization on plain radiographs, but obvious epiphyseal collapse was seen on radiographs and MRI, and both are inconsistent with TOH (Vande Berg et al. 2008; Xyda et al. 2008). Since bone marrow edema pattern is

caused by several conditions including fractures and decreases over time (Vande Berg et al. 2008; Xyda et al. 2008; Sonoda et al. 2016), the location of bone marrow edema pattern is non-specific, and a diffuse pattern of bone marrow edema extending from the femoral head to the femoral neck or intertrochanteric region in histopathologically diagnosed SIF has been described (Yamamoto and Bullough 1999). Furthermore, her symptoms and radiological findings related to her hip did not spontaneously recover. We do understand that the pathogenesis of TOH remains controversial (Yamaguchi et al. 2017), but we assume that this case was not so-called TOH.

On the other hand, the left femoral head showed advanced collapse, which might correspond to the findings of ON. However, the diagnosis of the histopathological findings was SIF. Grossly, thin cleft formation, namely a fracture line, was seen in the subchondral area, without evidence of antecedent ON in the form of a wedge-shaped opaque yellow infarct. Microscopically, callus formation consisting of cartilage and bone with granulation tissue was observed around the fracture line, consistent with the established findings of SIF (Yamamoto and Bullough 1999; Yamamoto et al. 2008; Sonoda et al. 2016). Zone formation, characteristic of ON, was absent. Small foci of necrosis seen only in the subchondral area with a fracture line should not be interpreted as primary osteonecrosis. Thin bone trabeculae indicated the presence of osteoporosis, which is a major risk factor for SIF (Yamamoto and Bullough 1999; Ikemura et al. 2013)

It is also possible that the present patient might have developed SIF of the right femoral head considering the radiological findings, although there was no histopathological examination. The resolution of symptoms with conservative treatment was consistent with the previously reported cases of SIF (Bangil et al. 1996; Raffi et al. 1997; Yoon et al. 2014; Hackney et al. 2016; Sonoda et al. 2016). Furthermore, increased uptake in the bilateral femoral heads

on bone scintigraphy was also compatible with SIF (Rafii et al. 1997; Yamamoto and Bullough 1999; Iwasaki et al. 2011), without a “cold in hot” appearance, which is compatible with ON (Sugano et al. 1999).

As in elderly people (Ikemura et al. 2013), pregnant women who present with severe coxalgia without predisposing factors for ON should be considered to have SIF when imaging examinations show collapse of the femoral head. MRI is useful as a non-invasive modality during late pregnancy, but the MRI findings of SIF, ON, and TOH have several overlaps (Vande Berg et al. 1999; Miyanishi et al. 2001, 2007; Ikemura et al. 2013). Though it has been reported that SIF and ON each have features of a low-intensity band on T1-weighted MRI, there is considerable variation of the MRI findings, which makes differentiation of these conditions by MRI difficult (Yamamoto and Bullough 1999; Kim et al. 2000; Vande Berg et al. 2008). Histologically, SIF has been reported in 11% of patients who underwent hip replacement with a diagnosis of ON (Yamamoto et al. 2008). On the other hand, Yamaguchi et al. (2017) reported that 77% of TOH cases showed a band-like pattern of the femoral head on MRI.

SIF in a pregnant woman might be overlooked in the stage of resolution due to non-specific symptoms or misdiagnosed as ON, a well-known cause of femoral head collapse, or as TOH, a well-known entity in pregnant women. The prognosis of SIF may depend on the initial treatment, as well as the degree of osteopenia (Yamamoto et al. 2008). Restricted weight-bearing can be successful in SIF, and about a half (Yoon et al. 2014; Hackney et al. 2016) or two-thirds (Sonoda et al. 2016) of SIF cases might improve without surgical treatment. Precise diagnosis might contribute to a better outcome by avoiding early arthroplasty in young women.

Furthermore, SIF in a pregnant woman should remind clinicians of the osteopenic status of the patient, while most affected women would appear otherwise healthy, similar to other patients of pregnancy-associated osteoporosis. Bone status and potential risk factors contributing to bone loss should be evaluated carefully to reduce future fracture risk.

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Conflict of Interest

The authors declare no conflict of interest.

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