# The Pathology of Osteonecrosis of the Femoral Head

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## 19.1 Introduction

Although the precise etiology of nontraumatic osteonecrosis of the femoral head (ON) is still unclear, this condition has generally been considered to result from an ischemia to the bone and bone marrow tissues. The first pathologic description of the femoral head osteonecrosis was reported in a case of caisson disease in 1888 [1]. In 1915, the microscopic appearances of the necrotic bone caused by a circulatory disturbance (ischemia) were described by Phemister [2], who also described that reparative process was observed around the dead bone (creeping substitution) [3]. Thereafter, both alcohol- and corticosteroid-related osteonecrosis have been reported clinically, and their pathologic appearances have also been described based on the histological examinations [4, 5].

## 19.2 Pathologic Characteristics of Osteonecrosis

One of the most characteristic pathology in ON is a zone formation, comprising necrotic, reparative, and viable tissue (Fig. 19.1) [6]. A wedge-shaped necrotic area is seen in a subchondral area, which is surrounded by the reparative tissue. This reparative tissue continues to the normal viable bone and bone marrow tissue. This zone formation is quite similar such as seen in myocardial infarction and brain infarction, and thus osteonecrosis is also recognized as bone infarction [4, 5].

In the early phase of ON, the reparative tissue generally consists of infiltration macrophage, granulation tissue, and fibrous tissue (cellular repair tissue), which can only be recognized on MRI. Thereafter, bony repair such as an appositional bone formation or creeping substitution occurs, when radiograph can detect these bony changes as a sclerotic change (Fig. 19.1). MRI is thus useful for the detection of ON in the early phase. In another word, MRI is useful for the detection of early reparative tissue formed around ON [7].

## 19.3 Pathology of Osteonecrosis

Macroscopically, the articular surface generally undergoes flattening (Fig. 19.2). On the cut section, opaque yellow, wedge-shaped osteonecrosis is observed in a subchondral region, which is bordered by an irregular reparative zone, comprising granulation and fibrous tissue as well as the sclerotic cancellous bone (Fig. 19.3). In general, a fracture (crescent sign) is present at the subchondral region [8].

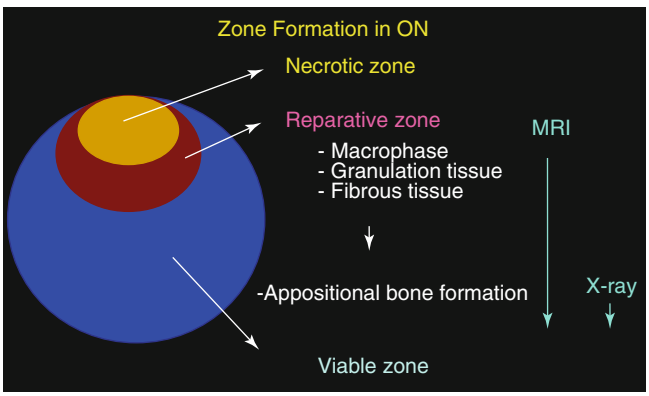


**Fig. 19.1** Zone formation in ON. A wedge-shaped necrotic area is seen in a subchondral area, which is surrounded by the reparative tissue. This reparative tissue continues to the normal viable bone and bone marrow tissue. In the early phase of ON, the reparative tissue generally consists of infiltration macrophage, granulation tissue, and fibrous tissue, which can only be recognized on MRI. Thereafter, bony repair such as an appositional bone formation or creeping substitution occurs, when radiograph can detect these bony changes as a sclerotic change

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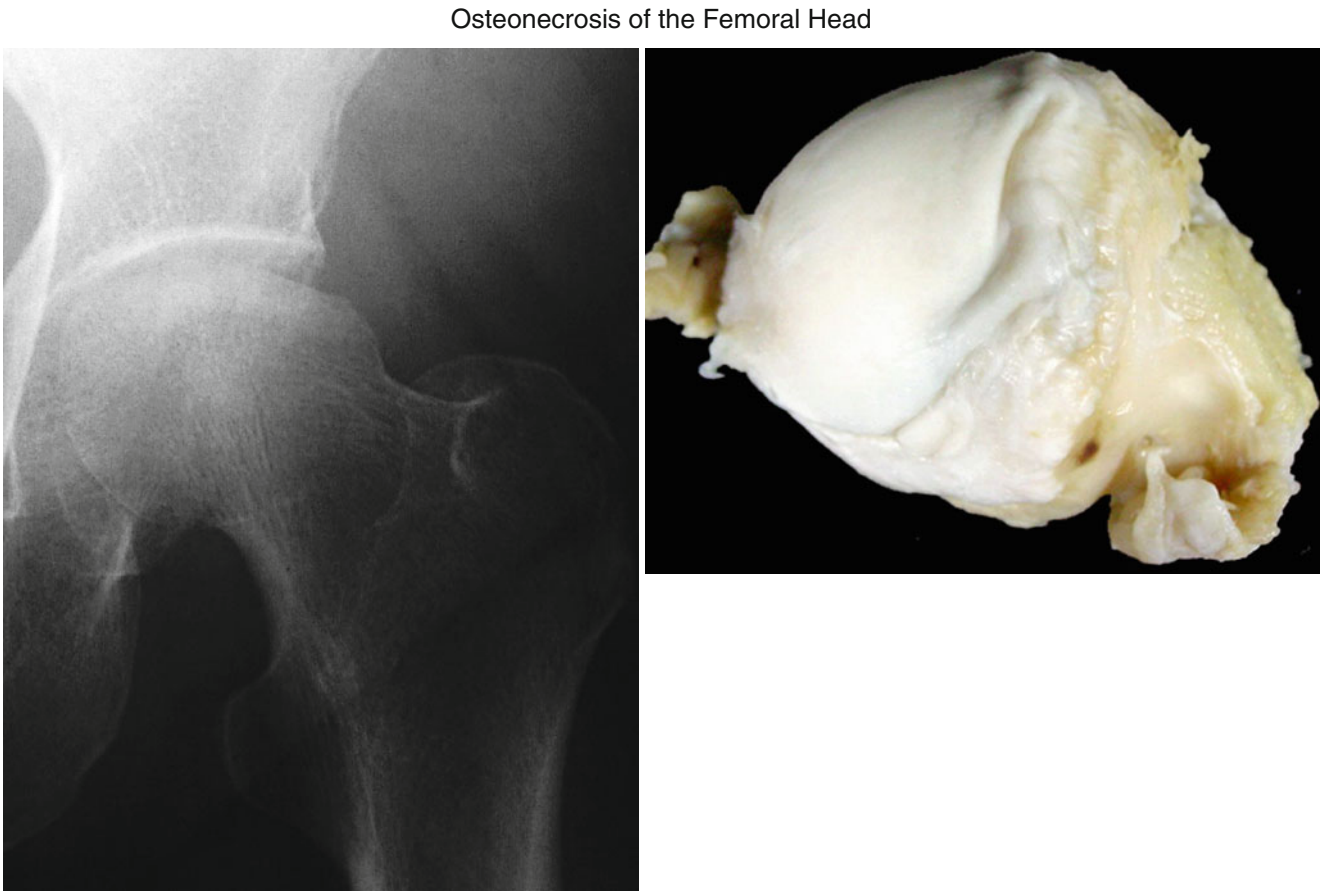


**Fig. 19.2** ON often undergoes subchondral collapse, and the resected femoral head also shows the collapsed lesion at the lateral portion of the femoral head

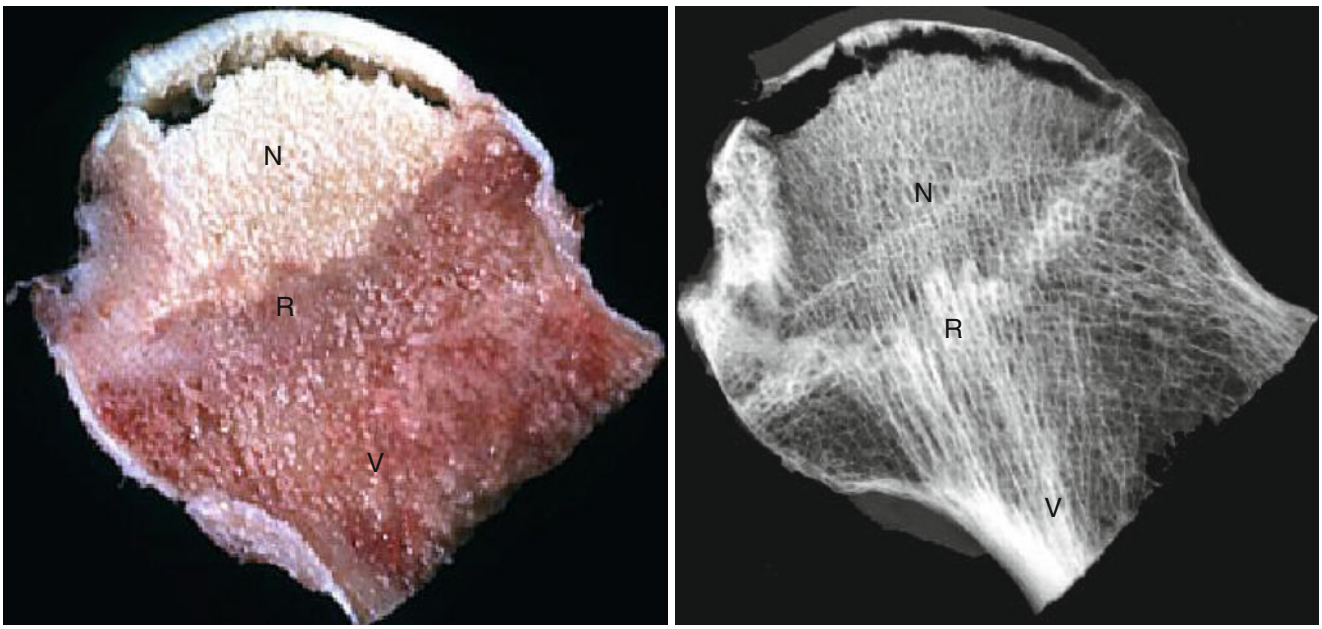


**Fig. 19.3** The cut section shows wedge-shaped yellowish necrotic area (N), which is surrounded by the somewhat whitish reparative tissue (R). The reparative tissue continues to the viable normal area (V). The specimen radiograph also demonstrates the zone formation, comprising necrotic (*N*), reparative (*R*), and viable area (*V*)

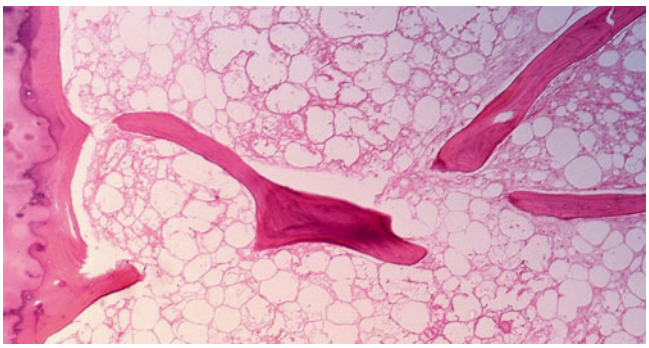

**Fig. 19.4** Histology of the necrotic area. Necrotic area shows an accumulation of bone marrow cell debris and bone trabeculae demonstrating empty lacunae occasionally containing some pycnotic nuclei of osteocytes (HE ×100)

Microscopically, typical necrotic area shows an accumulation of bone marrow cell debris and bone trabeculae demonstrating empty lacunae occasionally containing some pycnotic nuclei of osteocytes (Fig. 19.4). At the periphery of this necrotic lesion, repair process such as vascular-rich granulation tissue and appositional bone formation is observed. This appositional bone formation caused the thickening of the bone trabeculae in the reparative area (Fig. 19.5) [5, 6].

## 19.4 Crescent Sign

In ON, a subchondral fracture is often observed, which is generally called as a "collapse" or "crescent sign" [8]. This sign pathologically corresponds to a space formed between the fractured lesion (Fig. 19.6). Histologically, the fractures generally occur at the junction between the thickened trabecula associated with appositional bone formation and the necrotic bone trabecula [9].

As to the mechanisms of a collapse, the following three causes are proposed: (1) the cumulative effect of microfractures induced by fatigue within the necrotic zone, (2) weakness of trabeculae in the reparative front due to osteoclastic activity, or (3) focal concentration of stress at the junctions between the thickened sclerotic trabecula of the reparative zone and the necrotic trabecula [5].

## 19.5 Initial Sign of ON

There has been a confusion regarding the initial sign of ON on MRI. Some reports describe that bone marrow edema pattern is the early finding of ON [10, 11]; however, it should be noted that an initial MR finding of ON is a low-intensity band on the T1-weighted images (Fig. 19.7) [7]. In the early phase of ON, the repair tissue formed around the necrotic area consists of accumulation of serofibrinous exudate and cellular-rich granulation tissue, which can be recognized as a band-like lesion surrounding the necrotic area [6, 7].

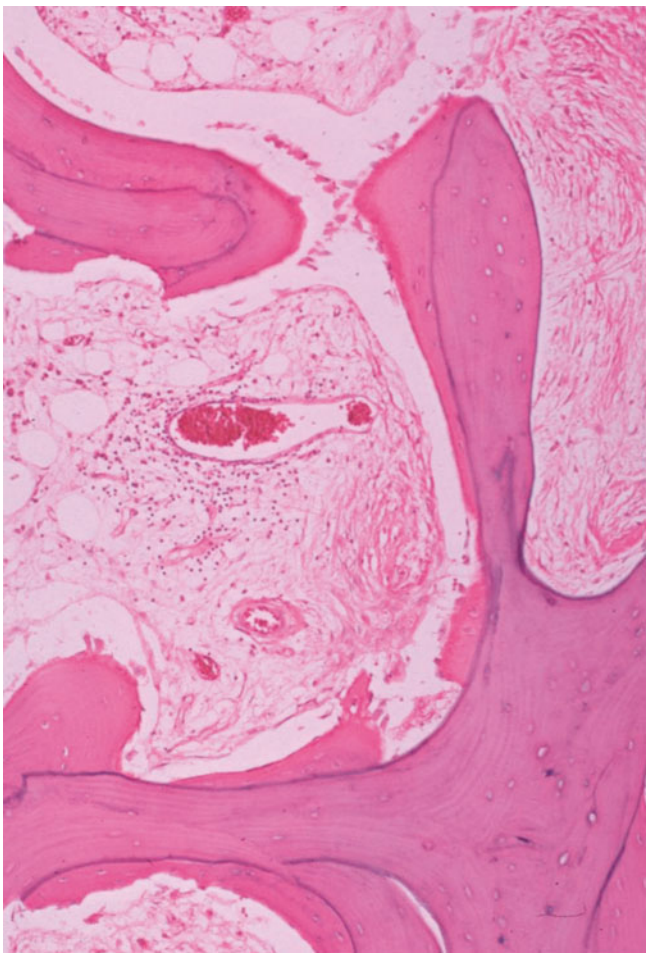

**Fig. 19.5** Histology of the reparative zone. In the repair zone, appositional bone formation is seen along the necrotic bone trabeculae, and vascular-rich granulation tissue is seen in the marrow space (HE ×200)

## 19.6 Bone Marrow Edema in ON

Bone marrow edema is frequently associated around the necrotic zone. This lesion histologically corresponds to fluid collection and hemorrhage in the marrow space [12]. The edema is seen not only in the femoral head but also in the intertrochanteric area. Based on the fine-slice pathologic examination, recurrent ON due to repeated ischemic attack, which results in a voluminous increment of necrotic lesion, is 0.3 % [6]. Therefore, the edematous lesion around the band-like reactive lesion does not progress to necrosis.

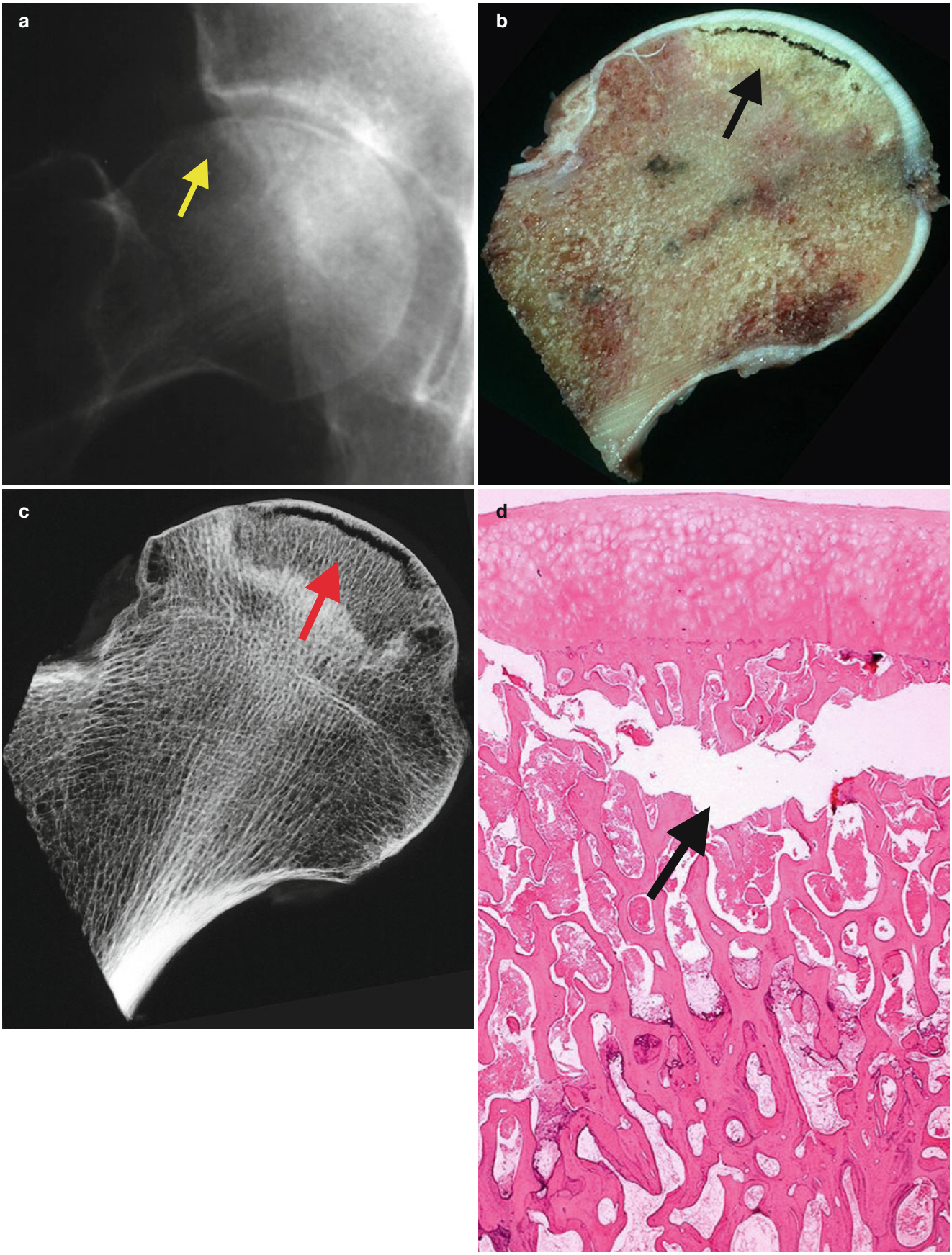


**Fig. 19.6** (**a**) Radiographic appearance of subchondral collapse or so-called crescent sign (*arrow*). (**b**, **c**) On the cut section, subchondral collapse is seen just beneath the articular cartilage (*black arrow*), and on the specimen radiograph a subchondral fracture is clearly seen in the corresponding area (*red arrow*). (**d**) This area pathologically corresponds to a space formed between the fractured lesion

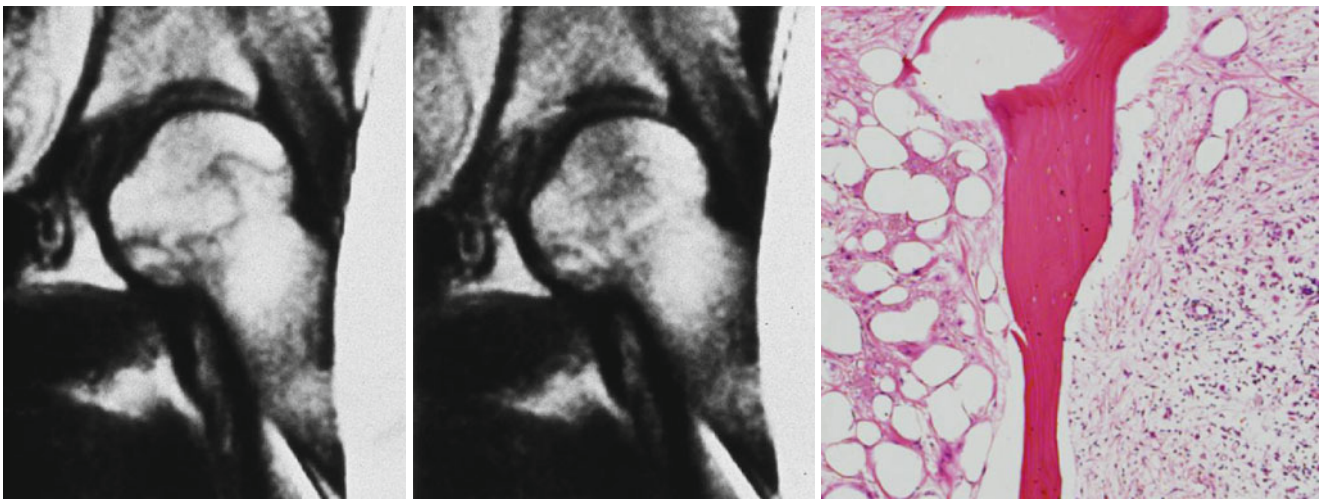


**Fig. 19.7** Initial sign of ON. The low-intensity band on T1 is the initial finding. On T2, this band shows high signal intensity, because the repair tissue consists of vascular-rich granulation tissue. Histologically, vascular-rich granulation tissue is seen in the marrow space, where appositional bone formation is not yet observed (HE ×150)

## 19.7 Differential Diagnosis

### 19.7.1 Subchondral Insufficiency Fracture

The entity of a primary subchondral insufficiency fracture (SIF) has been described in both the osteoporotic elderly and renal transplant recipients [13, 14].

At the onset of pain, plain radiographs show no obvious findings, but MR imaging reveals a bone marrow edema pattern with an associated irregular serpiginous low signal intensity line on the T1-weighted images. This irregular low-intensity line is one of the characteristic appearances of this condition, which histologically corresponds to a fracture line and an associated repair tissue such as callus and granulation tissue [15]. Before the pathologic concept of SIF was first introduced in 2000 [16], the majority of SIF cases would have been diagnosed histologically as ON, presumably based on small foci of necrosis caused by the fracture. It should be noted that since all fractures lead to some bone and bone marrow necrosis on either side of the fracture line, small segments of necrotic bone trabeculae may be observed. However, such necrotic regions will be observed only around the fracture line and such should not be diagnosed as primary ON [16].

Histopathological criteria for the diagnosis of subchondral fractures have been established [16]. On gross examination, a linear, narrow, irregular whitish-gray zone in the bone marrow space parallel to the subchondral bone end plate is generally seen. Microscopically, this area consists of irregularly arranged fracture callus, reactive cartilage, and granulation tissue (Fig. 19.8).

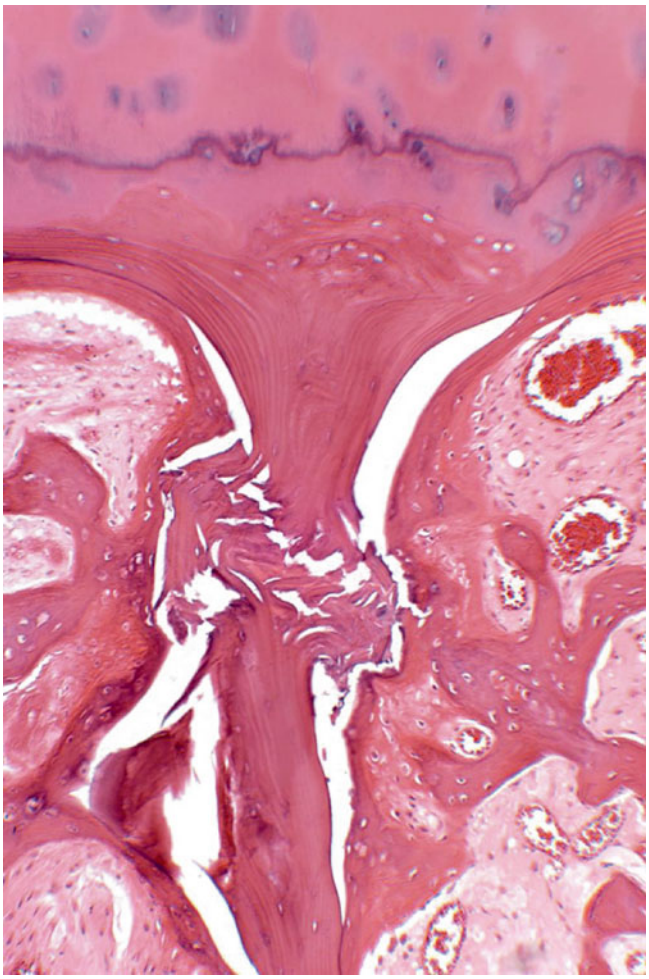

**Fig. 19.8** Histology of SIF. The fractured area consists of irregularly arranged fracture callus, reactive cartilage, and granulation tissue (HE ×400)

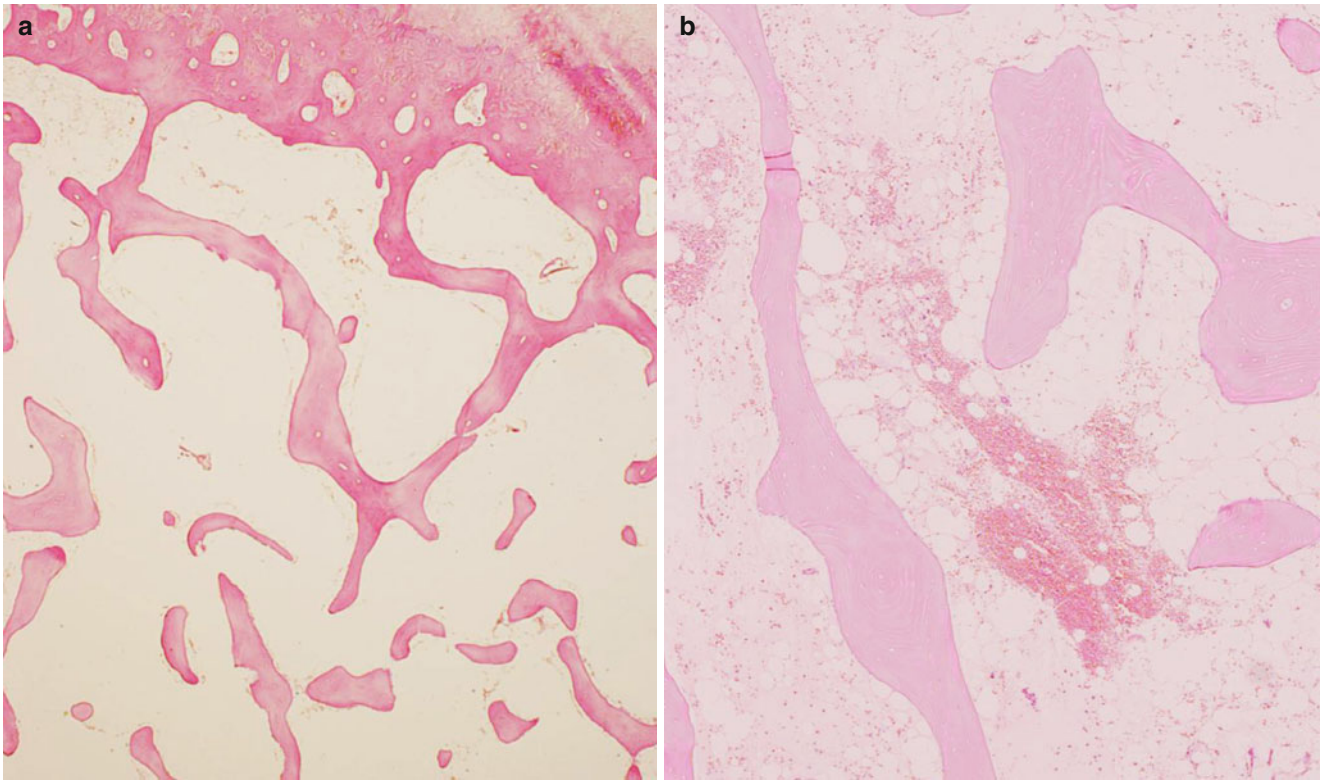


**Fig. 19.9** Histology of TOH. (**a**) Bone trabeculae are thin, disconnected, and sparsely arranged. Creeping bone substitution is not recognized (HE ×100). (**b**) In the bone marrow spaces, exudative fluid frequently associated with congestion and interstitial hemorrhage is seen (HE ×200)

## 19.8 Transient Osteoporosis

Transient osteoporosis of the hip (TOH) is a relatively rare disease seen in pregnant women and middle-aged men. It is characterized clinically by severe pain without an obvious antecedent cause and is considered as a self-limiting disease [17].

The radiological characteristics of the affected femoral head are a focal loss of radiodensity, a diffuse homogeneous uptake on bone scintigram, and a bone marrow edema pattern on MR imaging, often involving the femoral head, neck, and sometimes intertrochanteric region.

The histopathology of the affected area shows nonspecific edematous changes in the marrow space with associated hemorrhage and infiltration of vascular tissue. None of the TOH cases shows an opaque yellow osteonecrotic region or zone formation comprising necrotic, reparative, and viable zone.

Microscopically, bone trabeculae in the affected area are thin, disconnected, and sparsely arranged (osteopenic) (Fig. 19.9). These osteopenic bone trabeculae are variously covered with the osteoid seams and active osteoblasts, but creeping bone substitution is not recognized. In the bone marrow spaces, exudative fluid frequently associated with congestion and interstitial hemorrhage is seen (Fig. 19.9). In TOH cases, a wedge-shaped osteonecrotic region is not observed [18].

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