Chapter 7
Osteonecrosis

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Introduction

Osteonecrosis, also known as avascular necrosis, aseptic necrosis, and idiopathic necrosis of the femoral head, is not a specific disease entity but is rather a condition in which a localized area of bone becomes necrotic primarily due to an impairment of its blood supply. This may result from a number of etiologic factors acting alone or in concert. It was first described in 1738 by Alexander Munro [1], and since then has been the subject of a number of reports which have appeared with increasing frequency. This chapter will not attempt to provide a comprehensive review of osteonecrosis (ON), but will focus on our current understanding of the etiology and pathophysiology as it directly affects our ability to diagnose and treat this condition. We will be concerned primarily with non-traumatic ON in the adult hip since this is the anatomic region most often affected and most studied.

Clinical Features

The clinical picture of ON is nonspecific. The exact prevalence is unknown but it is estimated that over 30,000 new cases are diagnosed annually in the United States alone, and that approximately 10 % of all primary total hip replacements are performed for ON. The incidence is considerably higher in other parts of the world,

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especially in Asia. This condition affects primarily younger adults in their 30s and 40s. For weeks, and perhaps even months, after the initial vascular insult the affected area may remain asymptomatic. When symptoms develop, they do so gradually. The femoral head is the region most involved, followed by the humeral head, the knee, and less frequently the small bones of the wrist and foot. When one hip is affected, the other will be involved over 60 % of the time, and in 15 % of cases other regions of the body will also be involved. Symptoms do not develop simultaneously in all affected regions. In approximately 80 % of clinically diagnosed cases of hip involvement, the condition will progress without specific treatment, and will usually result in flattening of the femoral head and eventually degenerative changes in the joint. Pain and disability increase gradually, often becoming severe, and may be associated with a limp and decreased range of motion. However, small areas of necrosis, especially if not close to a weight bearing articular surface, may remain asymptomatic and heal spontaneously. Known etiologic factors can be identified in approximately 80 % of cases if searched for carefully and are important in leading to the diagnosis. This is usually confirmed by a characteristic radiograph appearance. If radiographs fail to confirm the diagnosis or if they show involvement of only one region, it is essential that other suspected areas, especially the opposite hip, be examined with MRI. This is a very sensitive and specific test for ON. If an area appears normal on MRI, the chance that ON will appear later is less than 10 % [2].

Other conditions which may resemble ON, such as transient osteoporosis of the hip (TOH) or bone marrow edema syndrome (BMES), cystic lesions within the femoral head, subchondral insufficiency fractures, and rapidly progressive osteoarthritis, must be ruled out. Other imaging studies, such as computerized tomography (CT), are of limited value. Positron emission tomography (PET) might eventually allow us to identify areas of ON even before MRI, but at present these techniques are not routinely employed. Laboratory tests are generally within normal limits, but may help to diagnose certain associated conditions such as Sickle Cell disease, hyperlipidemias, and certain coagulopathies. In selected instances genetic testing might indicate patients at risk for developing ON.

Early diagnosis, before femoral head collapse, is essential as it will allow early treatment with better results.

Etiology

The most common cause of osteonecrosis is trauma, such as a dislocation or displaced fracture of the femoral neck. In these cases the etiologic factor is mechanical injury to or compression of the vessels which supply the femoral head. In nontraumatic ON of the femoral head, a number of etiologic factors have been identified. The relative frequency with which they are encountered varies considerably and depends upon the demographics of the population from which the patients are drawn. In most series excessive alcohol consumption and prolonged corticosteroid

administration are by far the leading causes. The mechanisms involved are not entirely clear, but it is presumed that they involve alterations in blood coagulability and circulating lipids. This in turn results in intravascular thrombosis and/or embolization by red blood cells or lipid droplets [3]. In patients with hemoglobinopathies, such as Sickle Cell disease, emboli composed of clumps of abnormal red blood cells are formed, and in "Caisson disease" or dysbaric osteonecrosis, intravascular and perivascular nitrogen bubbles are responsible for interfering with the circulation. A number of other factors have been identified in patients with ON including local vascular abnormalities, gout, smoking, liver disease, systemic lupus erythematosus (SLE), and myeloproliferative disorders but etiologic associations are difficult to establish. Early in the investigation of this condition, an increase in the intraosseous pressure of the involved femoral head was noted and was considered to be a primary cause of osteonecrosis. However, later studies found increased pressure to be present in a number of other conditions unrelated to osteonecrosis and most investigators now consider this to be the result, rather than the cause, of ON.

In the 1990s Glueck et al. found that up to 70 % of their patients with osteonecrosis had certain subtle coagulopathies, specifically thrombophilia or hypofibrinolysis. They later found these conditions to be caused by specific gene mutations and a familial incidence was noted [4]. For quite some time it has been recognized that there is a high prevalence of ON in populations in China, Japan, Korea, and Taiwan. Recent studies have identified certain genetic abnormalities in these patients which could affect coagulation mechanisms. These include vascular endothelial growth factor (VEGF) polymorphism [5], and endothelial nitric oxide synthase (eNOS) [6] which could affect angiogenesis. Other recent findings include increased levels of plasma cryofibrinogen which could induce thromboembolic events, and modulation of P-glycoprotein activity, known to play a role in steroid hormone metabolism [7]. The role of marrow adipocytes has received further attention. An increase in their size or number could cause vascular impairment through mechanical pressure on local vessels similar to the presumptive mechanism in Gaucher's disease. In addition to factors which can have a direct effect on bone circulation, there are others whose action directly affects cell viability. Recently adipocytes have been found to release substances that can alter the function of osteocytes, as can circulating corticosteroids. Various cytotoxic agents and chemical substances, as well as radiation, can also directly affect cell viability.

Our understanding of the etiology of ON would appear to be getting more complex as new agents and factors are being identified. In certain situations a single factor alone can cause ON, whereas under most circumstances several factors may act in concert, hence the "multifactorial" basis for ON [8]. It should be emphasized that, although a number of systemic factors may play a role in the development of ON, the local vascular anatomy of the affected region is most important in explaining why it is these regions with limited collateral circulation and not the skeleton at random which develop ON. Despite a careful search for possible etiologic factors, in most series none can be clearly identified in 15–20 % of cases. These are often categorized as "idiopathic."

Pathophysiology

Although several systemic factors have been implicated in the development of ON, in the majority of cases it is the local factors which are most important. Hence osteonecrosis develops in certain specific anatomical regions where the circulation is limited with few collaterals. Impairment of the blood supply in these regions may result in local death of marrow elements and osteocytes. Anatomic and histologic studies of the proximal femur have identified the normal vascular anatomy of the region and have shown the pathologic changes in cases of ON. These are shown schematically in Fig. 7.1. The primary blood supply to the femoral head originates from the deep branch of the medial femoral circumflex artery (MFCA) which gives rise to the superior and inferior retinacular vessels. These, in turn, branch into the superior and inferior metaphyseal and the lateral epiphyseal vessels. The obturator artery supplies the artery of the ligamentum teres which ends as the medial epiphyseal artery. The most important vessels are the superior retinacular and lateral epiphyseal vessels which supply the anterior–superior aspect of the femoral head, the main weight bearing region and the area primarily affected by osteonecrosis. The other regional vessels are considerably less important and local anastomoses are limited [9–14].

Histologic and angiographic studies of femoral heads with osteonecrosis have identified consistent involvement of the superior retinacular and lateral epiphyseal vessels. Some attempt at vascular repair can be seen with ingrowth of new vessels from the stumps of occluded vessels and from other vessels in the region. However,

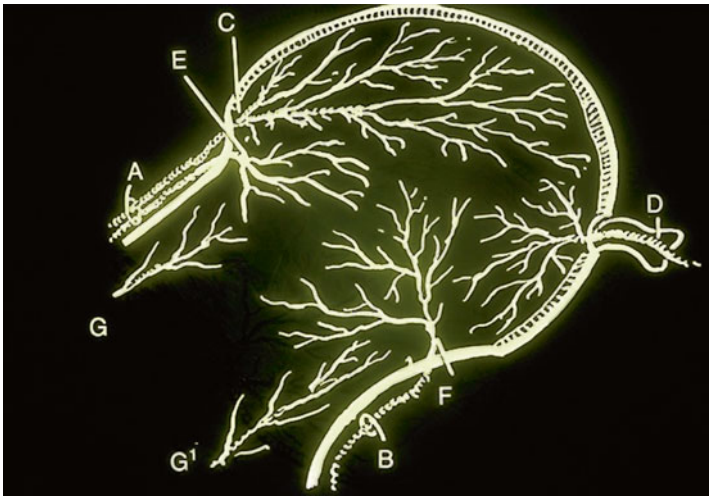

Fig. 7.1 Schematic drawing of the blood supply to the femoral head. (*A*) Superior retinacular vessels. (*B*) Inferior retinacular vessels. (*C*) Lateral epiphyseal artery. (*D*) Medial epiphyseal artery. (*E*) Superior metaphyseal artery. (*F*) Inferior metaphyseal artery. (*G*) Intramedullary vessels

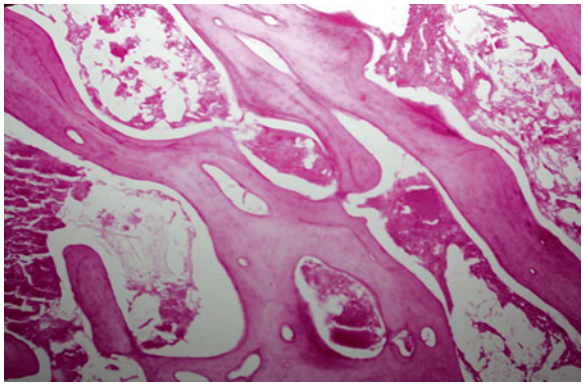

Fig. 7.2 Dead bone and marrow elements from the center of the necrotic lesion

this process is usually limited and is often blocked by the presence of necrotic material and collapsed bone (personal observation, MES).

Within hours of the vascular insult, death of marrow elements can be seen. Death of bone also takes place, but cannot be identified histologically until several days later when disappearance of osteocytes from their lacunae is noted (Fig. 7.2). Osteoclasts and phagocytic cells infiltrate the margins of the necrotic region and begin to remove dead tissue. This process is accompanied by the release of lysosomal enzymes. This is followed by the arrival of osteoblasts which attempt to repair the damage by laying down new bone directly upon the surface of dead trabeculae (Fig. 7.3). This composite of living and dead bone results in markedly thickened trabeculae which appear as radiodense or "sclerotic" regions at the margins of the infarct (Fig. 7.4). Adjacent areas from which dead bone has been removed become filled with fibrous tissue and amorphous debris, appearing as radiolucent or "cystic" areas.

(We use the University of Pennsylvania Classification of Osteonecrosis—Table 7.1). Within the first 2–3 weeks after the vascular insult, X rays appear normal but changes can usually be detected on MRI (Stage I) (Fig. 7.5a, b). However, they do not appear on routine radiographs until several weeks to months later (Stage II) (Fig. 7.6). The processes of osteolysis and bone resorption and bone repair continue, during which the affected area steadily loses mechanical strength. Because the superior retinacular and lateral epiphyseal vessels, which supply the antero-superior aspect of the femoral head, are primarily involved, and since this is also the area of maximal weight bearing, collapse of subchondral trabeculae gradually develops in this region. This often takes place before the articular surface itself is affected and may appear as a radiolucent "crescent sign" (Stage III). This stage is not always seen as collapse of the articular surface with the subchondral bone may occur more or less simultaneously. If the necrotic region is small and not close to an area of major weight bearing, the situation may stabilize and the repair process may provide it with sufficient strength so that it does not collapse. It may persist as an area of radiodensity, although occasionally it is resorbed and disappears from radiographs.

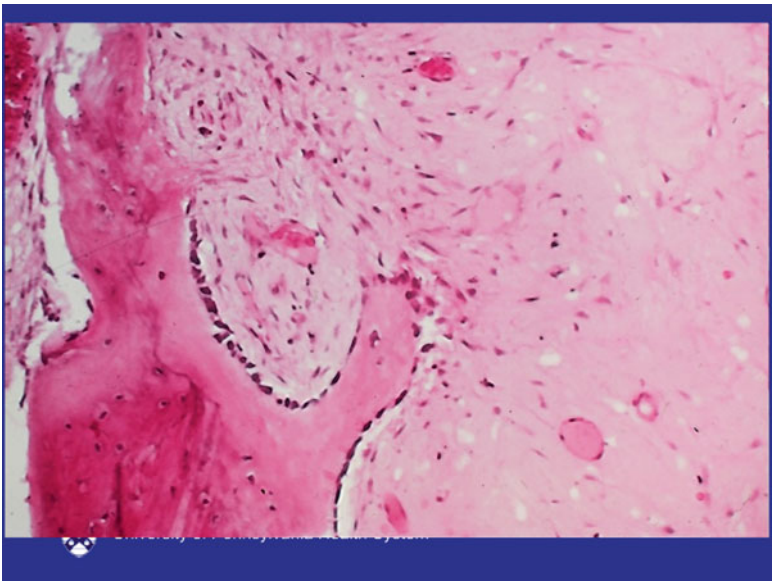

Fig. 7.3 Osteoblasts forming new bone directly on old, dead trabeculae

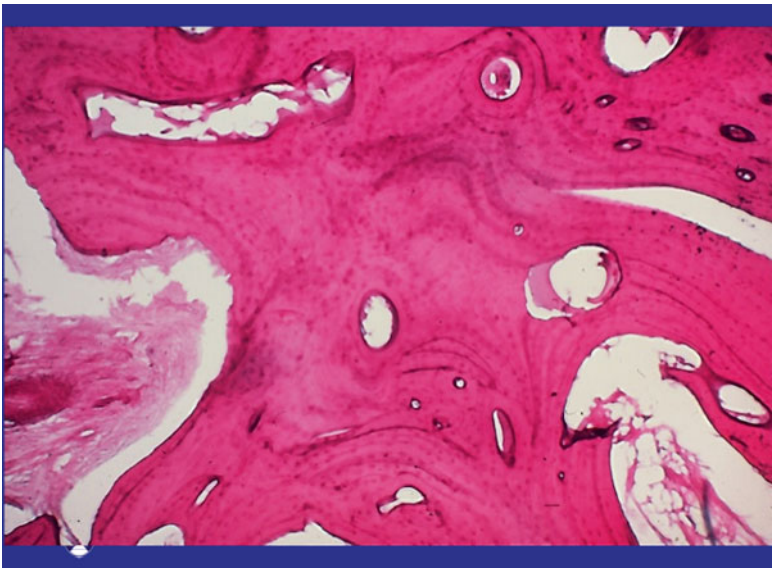

Fig. 7.4 Markedly thickened trabeculae at the margins of the necrotic region are composed of both living and dead bone

Table 7.1 University of Pennsylvania classification of osteonecrosis

Stage	Criteria	
0	Normal or nondiagnostic radiograph, bone scan, and MRI	
I	Normal radiograph; abnormal bone scan and/or MRI	
	A: Mild	(<15 % of head affected)
	B: Moderate	(15–30 %)
	C: Severe	(>30 %)
II	Lucent and sclerotic changes in femoral head	
	A: Mild	(<15 %)
	B: Moderate	(15–30 %)
	C: Severe	(>30 %)
III	Subchondral collapse (crescent sign) without flattening	
	A: Mild	(<15 % of articular surface)
	B: Moderate	(15–30 %)
	C: Severe	(>30 %)
IV	Flattening of femoral head	
	A: Mild	(<15 % of surface and <2 mm depression)
	B: Moderate	(15–30 % of surface or 2–4 mm depression)
	C: Severe	(>30 % of surface or >4 mm depression)
V	Joint narrowing and/or acetabular changes	
	A: Mild	Average of femoral head involvement as determined in Stage IV, and estimated acetabular involvement
	B: Moderate	
	C: Severe	
VI	Advanced degenerative changes	

This corresponds with the clinical observation that very small lesions, especially those located medially, have a good prognosis. However, less than 5 % of lesions meet these criteria [15, 16]. It has also been observed that the prognosis for sclerotic lesions is better than for lesions which appear cystic. This is most likely due to the fact that sufficient new bone has been formed to provide mechanical strength to the region and hence decrease the incidence of collapse [17].

With progressive collapse of subchondral trabeculae, the unsupported articular surface eventually begins to flatten. This represents an irreversible stage in the pathogenesis, Stage IV (Fig. 7.7). The articular cartilage is attached to the subchondral plate and remains viable, since it is nourished by diffusion from the synovial fluid and not by the vascular supply to the femoral head itself. However, the attached bone plate becomes necrotic (Figs. 7.8 and 7.9).

Radiographs of the hip continue to show a normal appearing acetabulum for quite some time after femoral head collapse. This can be misleading as histological changes in the articular cartilage are already taking place. In a study of 41 hips with ON which underwent total hip replacement despite a radiographic diagnosis of a "normal acetabulum," 40 hips showed gross changes in the acetabular cartilage, and

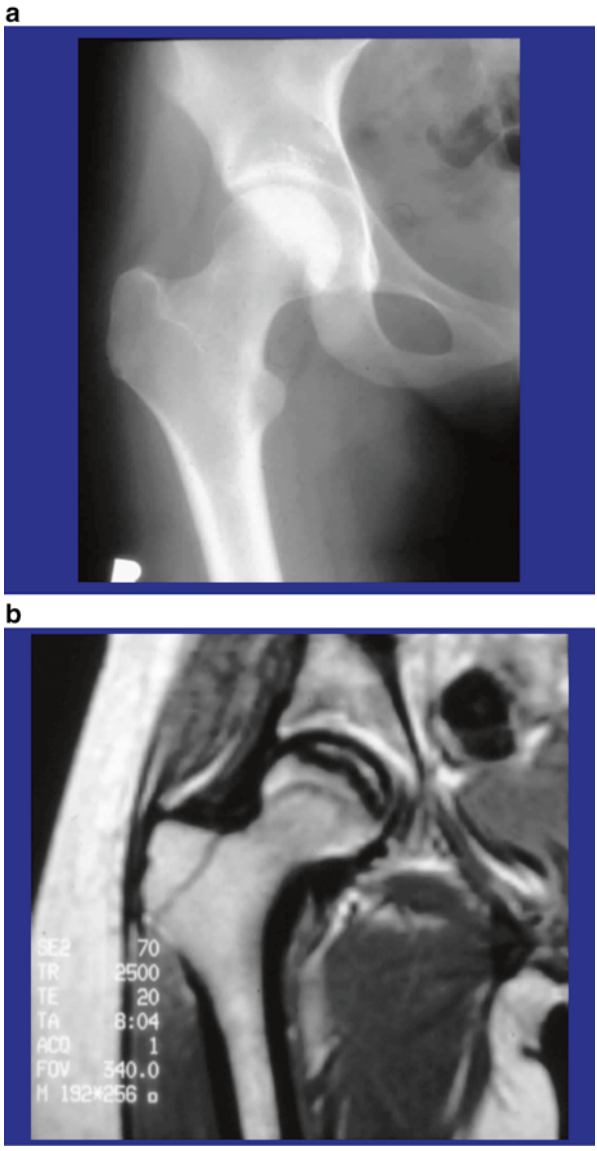

Fig. 7.5 Images of a young male with Stage I steroid-induced osteonecrosis of right hip. (**a**) Plain radiograph appears "normal." (**b**) T1 Weighted MRI shows characteristic changes of ON

all 41 showed histologic degeneration [18]. It is important to keep this in mind when considering a hemi-arthroplasty involving only the femoral head with the assumption that the acetabulum is "normal."

Progressive degenerative changes take place in the acetabulum secondary to the abnormal mechanical stresses imposed by the collapsed femoral head. Initially they involve only the articular cartilage as indicated by radiographic narrowing of the joint line. Later the underlying bone becomes affected and radiolucent and sclerotic

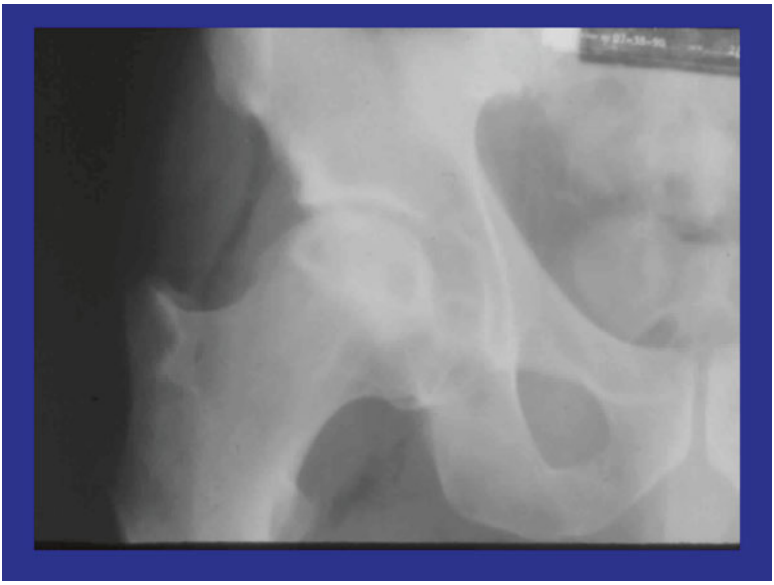

Fig. 7.6 Sclerosis and lucency within the femoral head are characteristic of Stage II ON

regions appear in the roof of the acetabulum, often accompanied by marginal osteophyte formation. This represents Stage V radiographically. In a small number of cases this process continues until the joint is almost completely obliterated, which represents Stage VI [19].

Classification and Staging

The pathophysiologic sequence of events outlined usually follows a relatively predictable course. As a result, it is possible to describe the status of the osteonecrotic hip by means of a system of classification and staging.

The first classification system for ON was described in the early 1960s by Arlet and Ficat [20] and included three specific stages. A fourth stage was added in the 1970s and this is the version most widely used today, although in 1985 six stages were described [21, 22]. MRI was not originally included as it was not available at the time, and there was no attempt to indicate the size of the infarct nor the extent of joint involvement. Other classifications followed including those described by Marcus et al. [23], Sugioka [24], and the Japanese Investigation Committee for Avascular Necrosis [15].

The University of Pennsylvania Classification was developed in the early 1980s and identified seven clearly defined radiographic stages. It was the first to employ

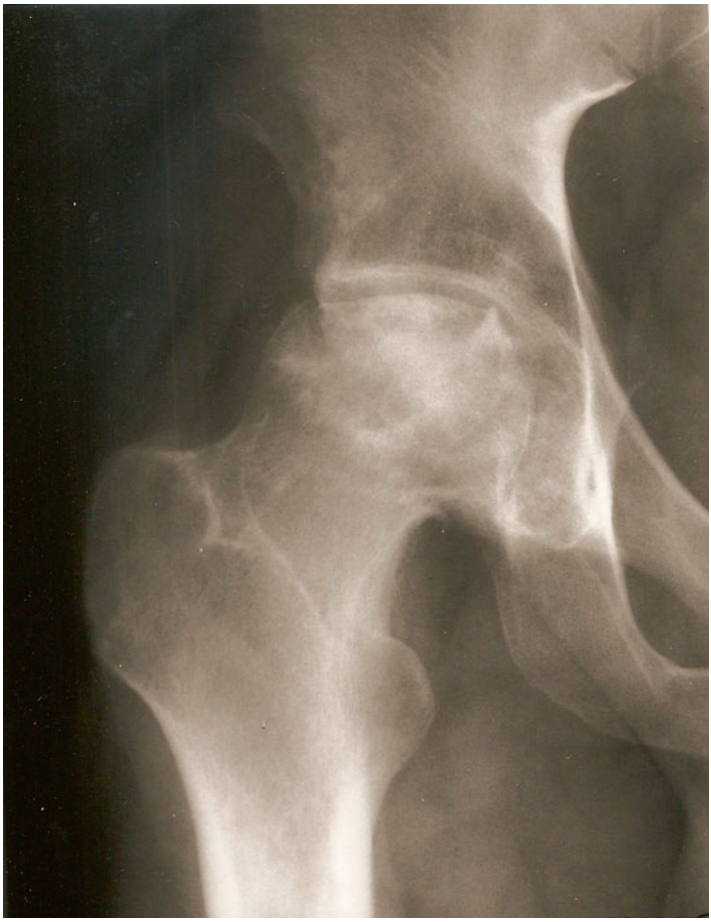

Fig. 7.7 Marked collapse and flattening of the femoral head without radiographic evidence of acetabular abnormality represents Stage IV ON

MRI as a specific modality for determining the stage, and was the first to include direct measurement of lesion size and the extent of joint involvement [19, 25, 26] (Table 7.1). In 1991 this classification was endorsed by the Association Research Circulation Osseous (ARCO), although modifications were made in 1992 and 1993 [27–29]. In 1992 it was also endorsed by the Committee on the Hip of the American Academy of Orthopedic Surgeons.

Recognizing the importance of the size of the infarct, a number of methods for measuring lesion size have been described during the past several years. However, most have relied on simple angular measurements made on plain radiographs or MRI, which are approximations rather than accurate measurements. In addition,

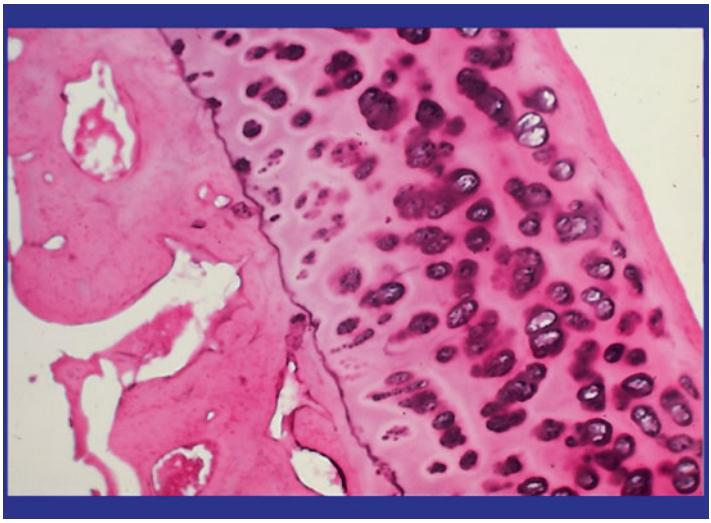

Fig. 7.8 Photomicrograph of a section of articular cartilage attached to its subchondral bony plate from a Stage IV hip. The cartilage remains viable whereas the bone is dead, as indicated by the empty osteocyte lacunae

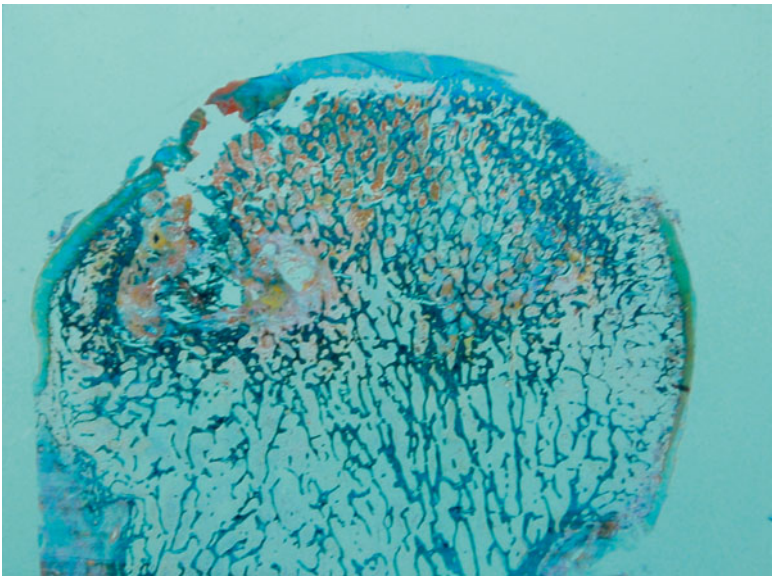

Fig. 7.9 Low power photomicrograph of a section through the femoral head shows a large lesion with elements of necrosis and attempted repair

these measurements have been used primarily to supplement non-quantitative classifications rather than as an integral part of one system [30–32].

MRI is currently the best modality for early diagnosis of ON, before changes appear on plain radiographs [33, 34]. This is important as the best results are obtained by early treatment, which in turn requires early diagnosis. The prognosis and treatment of hips with ON is also directly related to the size of the necrotic lesion and the extent of joint involvement. Accordingly, the clinical importance of using a comprehensive classification that indicates the extent of necrosis in addition to the stage is well recognized [19, 35–37]. This helps establish a prognosis, follow improvement or progression, compare different treatment options, and determine the best method of management for patients with different stages of ON. The uniform use of such a classification will help clarify the current confusion regarding both the natural history and the treatment of ON, and improve our management of patients with this perplexing disorder. A recent review of the literature shows a steady trend in this direction [36, 38].

At the present time, there are ongoing efforts to reach a consensus regarding the uniform use of a single effective classification. With advances in imaging techniques, it is now considerably easier than it was initially to measure accurately the size of the necrotic segment and the extent of joint involvement.

Management

Despite the increasing interest in osteonecrosis and the advances in understanding its etiology and pathophysiology, we still do not have an entirely satisfactory treatment. This is of particular concern because it affects most often younger adults, involves major weight bearing joints, and is usually progressive without appropriate treatment.

Prevention

A number of risk factors have been identified and these should be eliminated to the extent possible. These include alcohol ingestion, smoking, exposure to hyperbaric conditions, and corticosteroid administration. The postoperative management of organ transplantations has changed over the years, modifying the role of steroids, and accordingly the incidence of ON has diminished. When guidelines for divers and others working under hyperbaric conditions are followed, the incidence of ON decreases. During the past few years a number of genetic abnormalities have been identified which predispose patients to ON. In this group at risk, particular efforts should be exerted to minimize exposure to factors which could lead to the development of ON. Patients with hyperlipidemias might benefit from measures to control circulating lipid levels. In patients with certain coagulation abnormalities, some authorities have suggested long-term anticoagulation [4]. However, this approach

has not been generally accepted since there is little evidence that this treatment is effective in preventing ON and the dangers of routine anticoagulation most likely outweigh the theoretical benefits.

Non-operative Management

A primary goal is to diagnose ON as early as possible, before collapse of the femoral head begins. This enables us to initiate measures designed to retard or prevent progression. A number of non-operative measures have been described. Patients are often placed on limited or non-weight bearing when the hip or lower extremity is affected. Although this may help to decrease pain, there is no evidence that it will retard progression and prevent eventual joint collapse. Various physical modalities have been advocated, including ultrasound and different types of electrical stimulation. At present they are used infrequently, and further evaluation and development may be indicated [39, 40]. There was also earlier enthusiasm about the role of hyperbaric oxygen, however there is little evidence that it is effective and it is rarely used [41]. Bisphosphonates have been given to slow the progress of bone resorption and thereby delay or prevent collapse. This approach is theoretically attractive and a limited number of studies have shown early promise. However, other investigators have failed to demonstrate a positive effect in patients followed over 2 years [42] (ref). Other agents, such as vasodilators and fulleral, a powerful antioxidant, have been suggested but their effectiveness has not yet been established.

Treatment Before Femoral Head Collapse

When osteonecrosis is diagnosed before femoral head collapse has taken place, a number of surgical procedures have been employed to delay or halt progression and promote healing. Technically, they vary considerably from one another, but essentially all are based upon physiologic principles, which address one or more aspects of the pathology involved. The results and complications reported have varied widely from one series to another. This section gives only a very brief overview of some of these procedures, and the reader is urged to look elsewhere if more information is required. Some surgeons have been reluctant to treat asymptomatic lesions, especially when complicated techniques are being considered. However, prior to trabecular collapse there is little correlation between the degree of pain per se and the outcome, and the majority of asymptomatic lesions do eventually become painful. Therefore, treatment designed to preserve the femoral head should not be withheld or delayed solely because the osteonecrotic lesion is asymptomatic or minimally painful [2, 43–45].

Core Decompression

One of the earliest and most often used methods of treating ON of the femoral head is "core decompression" [46, 47]. During the 1960s Arlet and Ficat, as part of their study of ON, removed diagnostic cores of bone from the femoral head and neck [20]. Patients noted prompt relief of pain following this procedure, which was felt to be due to relieving the high intraosseous pressure found to be present. This procedure became known as "core decompression" and was widely used to treat early cases of ON. Subsequently it has undergone several modifications including the use of several small perforations into the lesion rather than a single large core track. It has also been supplemented with electrical stimulation [40, 48] and by the addition of bone grafts and various agents to stimulate vascular ingrowth and bone formation, such as VEGF, bone morphogenetic protein (BMP), demineralized bone matrix (DBM), and mesenchymal stem cells, which will be discussed later.

The results reported following conventional core decompression have varied widely, but a review of the literature found a very low incidence of complications and a satisfactory result in 65–70 % of patients treated early [49–51]. Core decompression is now the most widely used joint preserving procedure in the United States. It can act through several mechanisms including decreasing elevated intraosseous pressure, removing areas of necrotic bone, stimulating the ingrowth of new vessels, and possibly as a channel for the introduction of materials that can stimulate vascular and bone growth. It is a relatively simple procedure with a very low rate of complications, when performed properly. Results with smaller lesions are better than with larger lesions, and it has been suggested that lesions which occupy less than 15 % of the femoral head, especially if located medially in a region of minimal weight bearing, may heal spontaneously and do not necessarily require treatment. In the cases that fail core decompression, later conversion to hip arthroplasty is not compromised.

Osteotomy

Various types of intertrochanteric osteotomies have been used. The rationale for these procedures is the ability to shift the necrotic segment out of the major weight bearing region of the femoral head, and replace it with normal cartilage and bone. Only a limited amount of displacement is possible with varus/valgus or flexion/extension osteotomies [52], but considerably more displacement can be obtained by anterior or posterior transtrochanteric rotational osteotomies. These have been described by Sugioka [24] and Atsumi et al. [53]. These procedures have also been used after a certain amount of femoral head collapse has occurred and seem effective, so long as it is possible to shift a relatively normal segment of joint surface into

the weight bearing region. It is necessary to study X-rays carefully prior to determining whether the procedure is indicated, and if so, the type and extent of the osteotomy. Satisfactory results have been attained at selected centers familiar with these procedures, but they are technically difficult and have not attained widespread popularity.

Bone Grafting

A number of bone grafting procedures have been described using cancellous and cortical bone, bone substitutes, and vascularized grafts. Grafts can be inserted into the necrotic region through a channel made in the lateral femoral cortex, through the femoral neck, and directly through a trap door in the articular surface of the head [54–56].

Phemister [57] and later Bonfiglio and Bardenstein [58] created a channel extending from the lateral femoral cortex into the necrotic region of the head. Dead bone was removed and a cortical graft, usually composed of a nonvascularized fibula, was inserted. More recently, vascularized fibular grafts have been used. Rosenwasser et al. [59] made a window in the anterior femoral neck through which they removed most of the necrotic material and filled the cavity with autogenous bone from the ilium. In a small series they found intermediate term results to be quite satisfactory. In order to restore the circulation to the necrotic region more quickly, a number of techniques have been employed which insert a segment of bone with its attached muscle-pedicle directly into the region [12, 54, 55]. Satisfactory short and intermediate term results have been observed in a small number of studies, but long-term success with most of these techniques has not been confirmed and they are now used infrequently.

Free Vascularized Fibular Grafts

The use of free vascularized fibular grafting (FVFG) deserves particular attention. Since its introduction in 1979, it has been performed at a limited number of specialized centers in the United States, Asia, and Europe [60–64]. Similar to a conventional core decompression, a large channel is prepared extending from the lateral femoral cortex into the head, ending close to the articular surface. After debriding the necrotic material and inserting cancellous bone, a segment of the patient's ipsilateral fibula together with arteries and veins is placed within this channel. A micro-vascular anastomosis to local vessels is then performed. In addition to providing decompression and removal of necrotic material, the revascularized fibula brings an immediate vascular supply to the region and provides support

to the articular surface to retard or prevent collapse. The procedure is technically demanding and requires the participation of a well-trained micro-vascular surgeon. It is performed ideally by two teams operating simultaneously and has a steep learning curve. The complication rate is not insignificant and later conversion to total hip replacement may be difficult. However, gratifying results have been reported from those centers experienced with FVFG. The 2-year survival rate has been reported as high as 60–98 %, and the survival for hips operated upon before collapse is between 78 and 100 % [64] (ref). Results with small lesions are better than with large lesions, and patients treated prior to collapse have better results than those treated after a limited amount of collapse. Relatively few patients with Stage I lesions have undergone FVFG. The procedure remains controversial and many feel that the disadvantages outweigh the possibility of obtaining results that are better than with simpler procedures, such as core decompression. If it is to be performed, it should be done primarily at selected centers. The specific indications and contraindications have not yet been established, and further studies are required to determine them.

Mesenchymal Stem Cell Introduction

The use of mesenchymal stem cells derived from autologous bone marrow to treat osteonecrosis was pioneered by Hernigou in 1989 [65]. Various modifications of the original technique have been described. Over 2000 patients have been treated during the past 20 years and the results reported by Hernigou, Gangji, and others were superior to those achieved by core decompression alone. This is perhaps the most promising of the newer techniques for the early treatment of ON. In addition to the biological effects of core decompression alone, this technique adds the active role played by these mesenchymal stem cells in promoting bone and vascular regeneration. It has been utilized to date at relatively few centers, but if the results obtained by additional investigators continue to be promising, it may enjoy much wider use in the future [65–67].

Treatment After Femoral Head Collapse

Most of the techniques described above for treating hips before femoral head collapse can also be used after a limited amount of collapse has occurred. Results in general are not as good as when they are employed earlier, prior to collapse, but most series have recorded better outcomes than for hips managed non-operatively. The indications and contraindications should be considered carefully.

Subchondral Collapse: Stage III

A small number of patients will be seen with the presence of a crescent sign, indicating collapse of subchondral bone, but without gross flattening of the articular surface. For simplicity some classifications have grouped these together with hips in which flattening of the femoral head has already taken place. In view of the known pathophysiology of ON, it would seem possible that so long as the articular surface remains anatomically round, healing of the underlying cancellous bone, either spontaneously or assisted by grafts or other surgical techniques, could result in a relatively anatomical joint. There are few reports regarding treatment of hips at this stage. However, they indicate that the outcome following various methods of management was better than for hips in Stage IV where femoral head flattening was present [65–68]. This underscores the value of using a classification system which clearly identifies this stage as separate from hips with gross collapse. In Stage III we would therefore favor treatment methods designed to preserve the joint.

Collapse of the Articular Surface: Stages IV–VI

Once irreversible collapse of the articular surface has taken place, attempts to preserve the femoral head will be less successful. However, where the amount of collapse is small and is not accompanied by significant pain, disability, or radiographic involvement of the acetabulum, it is often reasonable to consider one of the joint preserving procedures described earlier. Although the results in general are not as good as when these are performed earlier, it is often possible to retard progression, relieve discomfort, and buy time before hip arthroplasty is required. For example, FVFG has been advocated by some in cases of early collapse. Those experienced with rotational osteotomies have obtained satisfactory results even after femoral head collapse, as long as it was possible to rotate the collapsed area out of the region of major weight bearing.

However, if the pathology has progressed beyond the point of early collapse, joint preserving procedures may no longer be indicated. Previously, hips in Stage IV without radiographic evidence of acetabular involvement were considered candidates for femoral endoprosthetic replacement or hemi surface replacement arthroplasty (SRA) by some surgeons. Although early results were usually satisfactory, these procedures did not do well with longer follow-up. Even a normal acetabulum cannot for long withstand the presence of a metallic prosthesis, and subsequent studies showed that by the time arthroplasty was indicated clinically, the acetabular cartilage had already undergone degenerative changes [18]. Hemi-arthroplasty is therefore seldom used today.

When the pathologic changes have progressed to the point where unequivocal acetabular degeneration is present, Stages V through VI, hemi-arthroplasty is rarely considered and some type of total hip replacement is the procedure of choice when

clinically indicated. When THR was initially introduced there was serious concern about performing this procedure in the young, active patient with ON because of the high incidence of failure and the short survivorship as compared to the older patient with degenerative joint disease (DJD) [69, 70]. However, since that time there have been considerable improvements in surgical techniques and design and manufacture of THR prostheses. The outcomes and survivorships reported in more recent studies approach those of older patients with other conditions. Although it is still preferable to preserve the normal hip where possible, there is no longer the urgency to do so at all costs and perhaps embark on a complicated procedure with a questionable chance of success. Where clinically indicated, standard THR for the patient with advanced stages of ON is now usually the preferred procedure. Results are generally excellent, complications are limited, and mean survivorship of 25 or more years may be anticipated [46, 47, 71–73].

An alternative to conventional THR is SRA. The rationale for this procedure is that it is less invasive and more physiologic than THR since only the diseased portion of the femoral head is sacrificed and the normal neck and shaft are not violated. In the 1970s the reluctance to perform standard THR on younger patients with ON led to interest in SRA. However, an increasing incidence of failure with these early designs led to their virtual abandonment by 1982 [74]. However, it was felt by some that the problem was due to failure of the acetabular component which required a thin shell of polyethylene cemented into place with a thin layer of methacrylate to accommodate the large femoral head. This led to a basic change in component design which now employs a biologic ingrowth metal rather than a plastic acetabular component, articulating with the metal femoral cap. The early and intermediate results with these components were quite good and many felt that the basic problem had been solved. These metal-on-metal SRAs gained a significant degree of popularity and were preferred by many for the young, active, male patient with ON and other conditions [75, 76].

Unfortunately, a different set of problems began to develop which were related specifically to the metal on metal articulations of both SRAs and standard THRs. By 2008 there were reports of local soft tissue reactions and pseudo-tumor formation around some of these components, which caused pain, component loosening, and revision surgery [77, 78]. There was also increasing concern regarding possible long-term systemic effects of metallic ions. As a result, there has been a dramatic shift away from these components, although a limited number of surgeons continue to use SRA for selected patients, such as the young active male with ON.

Future Goals

Although we have made reasonable progress in understanding and treating osteonecrosis during the past several years, there is considerably more to be accomplished. We must continue to learn more about the etiology, pathogenesis, and treatment of ON. This will be aided by the development of an effective experimental model, which is currently not available.

It is important that orthopedists and radiologists continue to increase their awareness regarding the need for earlier diagnosis and evaluation of the patient with ON using modern, comprehensive methods of staging and classification which indicate both the stage and the extent of involvement. This in turn will lead to a more accurate evaluation and comparison of the various methods of treatment, and will enable us to improve our management of patients with osteonecrosis.

A number of joint preserving procedures have been described, some of which have been mentioned here. In most instances, the authors who have devised and used these techniques have reported good results. However, many of these reports have involved small numbers of patients, short follow-up and use by a limited number of investigators. It is important to have the more promising techniques evaluated independently by others using well-designed studies. This will provide objective and accurate information regarding the effectiveness of these techniques which in turn should lead to increased use of those found to give the best results. In addition, a number of newer approaches to the treatment of ON have been suggested during the past few years. These include the use of mesenchymal stem cells, bisphosphonates, and various bone and vascular growth enhancing factors. Genetic studies have already yielded important information which could improve treatment and possibly lead to gene therapy in selected cases. We will await with interest the further development and evaluation of these techniques to determine their potential clinical role.

And finally, significant improvements in arthroplasty have taken place since its introduction. Total hip replacement now plays an important role in the treatment of patients with advanced stages of ON, and is the most frequently employed procedure once it is determined that joint preserving surgery is no longer indicated. Improvements in surgical technique, and in the design and manufacture of components will continue and will lead to increasing survivorship of these prostheses. Although we will still seek to prevent the development of ON and to preserve rather than replace the normal joint whenever possible, these advances will provide a practical solution to the management of the young active patient with ON in whom progression and severe joint damage cannot be prevented.

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