Osteonecrosis of the knee: a concise review of the current literature

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ABSTRACT
Osteonecrosis (ON) of the knee is a progressive disease that can lead to subchondral collapse and end-stage osteoarthritis of the knee. Originally described as a single disease, it includes three different pathologic entities: spontaneous osteonecrosis of the knee (SONK), secondary osteonecrosis of the knee, and post-arthroscopic osteonecrosis of the knee. This article reviews the current literature of these three different conditions by describing their epidemiology, etiology and pathogenesis, clinical presentations and radiographic findings. Various treatment options (e.g., core decompression, bone grafting, stem cell implantation, tibial osteotomy and arthroplasty), available for each entity, are reviewed.

KEYWORDS
Osteonecrosis, spontaneous osteonecrosis, SONK – secondary osteonecrosis, atraumatic osteonecrosis, avascular necrosis, post-arthroscopic osteonecrosis, knee.

Introduction

Osteonecrosis (ON) is the cellular elements death by ischemia of the bone and marrow. Avascular necrosis affected frequently the epiphyses of long bones: the femur is statistically the most affected bone, both in the hip (most common location) and in the knee (second in frequency). Osteonecrosis of the knee can be a devastating disease that leads to end-stage arthritis of the knee.

Ahlbäck et al. [1] first described ON of the knee in 1968. The condition was initially presented as spontaneous that typically involved the medial femoral condyle with greater prevalence in women over 60 years of age, following minor trauma.

Later studies identified patients whose characteristics and symptoms did not match these initial descriptions, which led to the recognition of three different entities: secondary ON, spontaneous ON and post-arthroscopic ON, according to Zywiel et al. and his classification [2,3].

Primary osteonecrosis or spontaneous osteonecrosis of the knee (SONK)

Epidemiology
Spontaneous osteonecrosis of the knee is most common form among the three entities. Its actual prevalence may be underestimated because many patients who present with end-stage osteoarthritis may have had unrecognized SONK [4].

Pape et al. indicated 3.4% of SONK incidence in persons aged over 50 years and a 9.4% incidence in persons older than 65 years [5].

This disease more often involved women than men, it is typically unilateral and mainly affecting the medial femoral condyle in 94% of cases. It has been also reported to affect lateral femoral condyle, tibial plateau and patella [6,7].

The medial femoral condyle predominance may be explained by local differences in blood supply between the medial and lateral condyles [8].

Etiology and pathogenesis
For many years, the pathogenesis of SONK was related to vascular origin, which would result in necrosis. Recent pathologic studies have suggested that may be secondary to subchondral insufficiency fractures in osteopenic bone associated to subsequent edema with focal ischemia, and eventual necrosis [9].

In support of this, a recent study has demonstrated the association between low bone mineral density and the onset of SONK in women over 60 years of age [10].

Moreover, meniscal tears were found to occur in 50 to 100% of patients with spontaneous osteonecrosis of the knee, it could be caused of disruption of the posterior medial meniscus root increases tibiofemoral contact pressures, altering normal knee biomechanics, which leads to the subchondral insufficiency fractures seen in SONK [11].

Berger et al. [12] prospectively assessed bone turnover in 22 patients with spontaneous ON of the knee, demonstrating that mean serum concentrations of the main biochemical markers of bone metabolism, such as bone-specific alkaline phosphatase (bone ALP), osteocalcin (OC), procollagen type I N-terminal propeptide (PINP) and C-terminal cross-linking telopeptide...
(ICTP), were not different from healthy persons and hence did not valuable in the diagnosis of spontaneous ON. Moreover, the markers elevation in samples obtained from cancellous bone signified an increased turnover either in knee ON and osteoarthritis when compared to healthy cases.

**Clinical presentation**

SONK can be distinguished from secondary osteonecrosis of the knee by its insidious onset and lack of identifiable etiology. The pain is severe and often is localized to the medial side of the joint with lesions of the medial femoral condyle, mimicking the pain of a medial meniscus tear. Notable history of trauma is usually absent. Pain both at rest and night, as well as pain with weight-bearing, is common and can be quite debilitating. Focal tenderness to palpation over the medial femoral condyle is the most common physical exam finding.

**Classification**

Osteonecrosis of the knee can be staged to assess the severity and to guide treatment. The Koshino classification was described in 1979, originally developed for SONK after extended for the others type, consists of four stages (Table 1). Stage I is a patient with knee symptoms but normal x-ray findings. Stage II consists of patients with flattening and subchondral radiolucency without collapse. Stage III shows a subchondral collapse. Stage IV consists of further degenerative changes with osteosclerosis and osteophyte formation.

Another classification is the modified Ficat and Arlet staging system, adapted for the knee from the original version describing osteonecrosis of the femoral head, it’s based on radiological finding (Table 2). Stage I is a patient with normal x-ray findings. In stage II there are cystic or osteosclerotic lesion with normal contour of distal part of femour, while in stage III crescent sign or subchondral bone collapse is detected. Stage IV consists of osteoarthritis changes.

**Diagnosis**

At first step evaluation, anteroposterior (AP), lateral and oblique view radiographs should be performed, although in the early course of the disease they are often negative and, in some cases, remain negative or can demonstrate radiolucency of the subchondral bone surrounded by sclerosis area or flattening of the involved condyles and collapse of the subchondral bone in later stages of the disease.

Magnetic resonance imaging (MRI) is useful in the early stages of the disease due to its high sensitivity in detecting bone edema. Initial MRI findings include bone marrow edema localized to the medial femoral condyle, and a subchondral crescent of a linear focus of low signal intensity can be seen on the T1-, and on the T2-weighted sequences, placed on the central weight-bearing aspect of the femoral condyle, moreover the overlying articular cartilage is intact. The stage of collapse is characterized by focal depressions of the epiphyseal contour for subchondral collapse and a fracture line invaded by subchondral fluid. Concurrent meniscal tears are common.

The prognosis depends of the size of the lesion: a larger lesion portending an increased risk of osteoarthritis, it was demonstrating by Jureus et al. that had indicated the development of osteoarthritis was likely when 40% or more of the joint surface was affected.

Small lesions (<3.5 centimeters squared) usually regress with non-surgical management, while large lesions (>5 centimeters squared or > 50% of femoral condyle) usually lead to condyle collapse and osteoarthritis.

**Treatment**

Non-operative management is usually reserved for smaller lesions (<3.5 centimeters squared) and consists of lateral wedge insoles, non-steroidal anti-inflammatory drugs (NSAIDs), anal-

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**Table 1** Koshino classification.

<table>
<thead>
<tr>
<th>STAGE</th>
<th>RADIOLOGICAL FINDINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal appearance</td>
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<tr>
<td>2</td>
<td>Weight-bearing area with radiolucent oval shadow in the medial femoral condyle, flattening of the condyle</td>
</tr>
<tr>
<td>3</td>
<td>Collapse of subchondral bone plate</td>
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<tr>
<td>4</td>
<td>Osteoarthritic changes such as osteosclerosis and osteophyte formation, with a shallow concave articular surface at the osteonecrotic region</td>
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**Table 2** Modified Ficat and Arlet staging system.

<table>
<thead>
<tr>
<th>STAGE</th>
<th>RADIOLOGICAL FINDINGS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal X-ray findings</td>
</tr>
<tr>
<td>II A</td>
<td>Cystic or sclerotic lesion (absence of subchondral cystic formation)</td>
</tr>
<tr>
<td>II B</td>
<td>Subchondral collapse (crescent sign) and/or subchondral aliasing</td>
</tr>
<tr>
<td>III</td>
<td>Irregular femoral contour</td>
</tr>
<tr>
<td>IV</td>
<td>Collapse of the femoral head, acetabular involvement and osteoarthritis changes</td>
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</table>
Osteonecrosis of the Knee

Etiology and Pathogenesis
Secondary osteonecrosis (SON) is the second most common type in the knee and usually affects patients younger than 45 years and frequently involves multiple lesions in several joints concurrently [2,33]. Some evidence has shown that alcohol and corticosteroid abuse cause bone marrow adipose cell enlargement, which increases intra-osseous pressure leading to bone ischemia [34]. This theory has been extended to other conditions, such as Gaucher’s disease, dysbaric disorders, and some myeloproliferative disorders. Other risk factors, tobacco and sickle cell disease, may cause SON due to their vaso-occlusive effects [35].

Clinical Presentation
Patients usually describe a gradual onset of pain over the affected area. The pain is often focused over either the medial or lateral femoral condyle or involves also tibial condyle. The pain may complain in other joints, because secondary osteonecrosis frequently involves multiple joints [41].

Diagnosis
Similar to SONK, radiographs and MRI are main diagnostic tools for secondary osteonecrosis.

Instead of SONK, multiple lesions may be observed in SON and in 80% of cases will have bilateral involvement. Furthermore, while SONK lesions are isolated to the epiphysis, lesions of SON may be seen in the epiphysis, metaphysis, and/ or diaphysis of the femur [2,33].

Additionally, there is often a hypointense serpentine line in T1 with a well-defined border and a rim or double halo sign, adjacent to the proximal border of the osteonecrotic bone [36,37].

As for SONK, the same two-stage classification systems (Koshino and Modified Ficat and Arlet staging system) are utilized for secondary osteonecrosis of the knee.

Treatment
Nonsurgical management is recommended for those patients who are asymptomatic, the therapeutic options are similar of...
SONK treatment. Therefore, symptomatic patients will need surgery [3].

There are several joint-preserving methods that have had increasing interest in recent years, primarily to delay the necessity of TKA in a patient group who are often young and active, and are more likely to be immunocompromised secondary to a concurrent disease process. If the cartilage surface is not depressed or arthritic, joint-preserving techniques such as core decompression and bone grafting are available.

Subchondral autologous bone marrow concentrate was an effective procedure for treating young patients with SON of the knee with a lower complication rate and a quicker recovery as compared with TKA [38]. The authors avoided the use of osteochondral grafts in patients with SON because the lesions usually involve multiple condyles, which do not lend themselves to a single osteochondral graft. Neither UKA is recommended for secondary osteonecrosis due to the frequent involvement of multiple condyles [27,28].

**Differential diagnosis**

A careful history and physical exam can help differentiate between ON and similar clinical entities, including osteochondritis dissecans, osteochondral lesions, bone marrow edema, bone contusion, meniscal lesions, osteoarthritis, tumor and infection.

An infection or tumor can simulate avascular necrosis, it is important consider systemic signs.

Osteochondritis dissecans (OCD) is often a difficult differential diagnosis with osteonecrosis of the knee. The OCD is an idiopathic, focal anomaly in the formation of the subchondral bone that may cause instability or detachment of a bone fragment and cartilage, with progression towards arthrosis. This condition affected male teenagers, and in 50% of cases is post-traumatic. The patients may have mechanical pain during sport or sub-continuous pain with swelling and joint lock. The differences with respect to ON is the target of age and the onset and the correlation to the trauma, moreover, the place which is the lateral surface of medial condyle.

**Conclusion**

Osteonecrosis of the knee collects differential entities united by similar clinical presentation and imaging findings. Treatment is guided by corroborated classifications. Recently, the techniques already consolidated over time have been accompanied by treatments with stem cells and osteochondral autograft transplantation to delay joint replacement, showing promising outcomes.

**References**

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Authors' Notes: No part of this study has been submitted or duplicated elsewhere. This study has been read and approved by all authors and each author believes that the manuscript is valid and represents honest work.

Declaration of Conflicting Interests: The authors declare that they have no competing interests.

Funding sources: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.