Advanced hip osteoarthritis: magnetic resonance imaging aspects and histopathology correlations
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H. Leydet-Quilici†*, T. Le Corroller‡, C. Bouvier§, R. Giorgi¶, J.-N. Argenson#, P. Champsaur¶, T. Pham†, A. Maues de Paula§, P. Lafforgue†

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SUMMARY

Objectives: To correlate magnetic resonance imaging (MRI) aspects of the femoral head with histological findings in advanced hip osteoarthritis (OA), with special emphasis on bone marrow edema (BME).

Methods: MRI was performed in patients with advanced hip OA scheduled for hip arthroplasty. Coronal T1-, fat-suppressed T2-, T1 with gadolinium intravenous injection sequences were obtained on a 1.5 T MR-scanner within 1 month before surgery.

Coronal MR images corresponding to the ligamentum teres plane were analyzed by two independent readers blinded to histological data. Normal bone marrow, subchondral cyst, subchondral fracture, edema-like, necrosis-like, and necrosis MR patterns were reported on a synthesis scheme. After surgery, the femoral heads specimens were cut through the ligamentum teres plane and histologically analyzed for correlations.

Results: Twenty-three femoral heads were analyzed (female 56.5%, mean age 64.5 years). Edema-like MR pattern was correlated with histological (H) edema (Kappa (K): 0.77). Necrosis-like MR pattern was correlated with H fibrosis (K: 0.49) and with H necrosis (K: 0.24). Cyst MR pattern was correlated with H bone cysts (K: 0.58). Necrosis MR pattern corresponded to a mixture of histological lesions. Sensitivity and specificity of MRI varied from 26% to 80% and from 86% to 95% respectively.

Conclusion: In advanced hip OA, the so-called “BME” MR lesion corresponds to a combination of edema, fibrosis, and necrosis at histopathology. When the classical “BME” is more specifically separated into edema-like and necrosis-like MR patterns, MR Imaging and histological findings show substantial agreement, with edema-like MR pattern mainly corresponding to histological edema.

Introduction

Osteoarthritis (OA) is a heterogeneous and multifactorial disease characterized by progressive loss of hyaline articular cartilage and development of altered joint congruency, subchondral sclerosis, intraosseous cysts, and osteophytes. Hip OA is an incapacitating disease and a major public health problem. Today there are over 200,000 total hip replacements performed per year in the United States.

Magnetic Resonance imaging (MRI) increases the possibilities in hip and knee OA research and offers insights into the pathogenesis of the disease. Indeed, MRI is commonly used to visualize articular cartilage and other joint structures such as subchondral bone and synovium that are now recognized as parts of the disease process.

Among these lesions, the so-called “bone marrow edema” (BME) is a MRI-determined abnormality, appearing as an ill-defined area with low signal intensity on T1-weighted spin-echo (SE) sequences, and high signal intensity on T2-weighted fat-suppressed SE sequences or short TI inversion recovery (STIR) images. The prognosis role of BME has been emphasized in the recent literature, especially for knee OA, in which correlations with severity of radiographic grading and pain or OA progression have been documented.
Table I

<table>
<thead>
<tr>
<th>Lesion Description</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td>1 Ill-defined, low signal intensity on T1-weighted images and high signal intensity on T2 fat-suppressed images. Complete homogenization after gadolinium intravenous injection</td>
<td>Normal fatty marrow</td>
</tr>
<tr>
<td>2 Well defined, low signal intensity on T1-weighted images and high signal intensity on T2 fat-suppressed images. Incomplete homogenization after gadolinium intravenous injection</td>
<td>Edema-like¹¹</td>
</tr>
<tr>
<td>3 Low intensity signal on T1- and T2 fat-suppressed images. Variable after gadolinium intravenous injection</td>
<td>Necrosis-like¹¹</td>
</tr>
<tr>
<td>4 Minor deformity of the subchondral bone plate and presence of a low signal intensity line (perpendicular to the trabecular network and parallel to the subchondral bone plate) more visible on T1- and T2 fat-suppressed images, with BME in periphery</td>
<td>Sclerosis¹</td>
</tr>
<tr>
<td>5 Well defined, round, homogeneous with low signal intensity on T1-weighted images and with pronounced hyperintensity on T2 fat-suppressed images. Linear intensification in subchordal after gadolinium intravenous injection</td>
<td>Cystic bone marrow¹¹</td>
</tr>
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</table>

The term BME has been used in association with a wide spectrum of pathological conditions, including transient osteoporosis of the hip, post-traumatic contusion, insufficiency fractures, osteonecrosis of the femoral head, rapidly destructive OA, and arthritis⁶. Two studies on knee OA have suggested that areas of BME were in fact not only correlated with histological BME but also with areas of bone marrow necrosis and fibrous tissue⁵,⁶. Thus, the terms “BME pattern”, “BME-like changes”, or even “subchondral bone marrow lesions” have been proposed as more advisable⁵,¹¹. Finally, it was recently proposed that BME observed at MRI should be separated more specifically into edema-like and necrosis-like patterns¹¹.

Contrasting with knee OA, very few data are available on bone marrow MR features in hip OA and on the histopathological significance of BME in this particular joint. One recent study only found that the BME pattern corresponds to a mixture of histological lesions including edema, necrosis, and fibrosis lesions¹². The aim of this study was to correlate MRI patterns and histological findings in hip OA, with special emphasis on BME.

Methods

From September to December 2007, a prospective study was designed to evaluate MRI findings and their correlations with histology in hip OA. Because pathological specimens can be obtained only at the time of joint replacement, the study concerned only the femoral heads of advanced hip OA.

Patient selection

All patients with advanced hip OA scheduled to undergo surgical hip replacements in our Orthopedic Department were eligible. Exclusion criteria were declining participation to the study, contraindications for MRI, rapidly destructive hip OA¹³, and OA secondary to specific diseases (Paget’s disease, avascular necrosis or rheumatoid arthritis) or severe dysplasia¹⁴. Informed consent was obtained.

MRI

All patients underwent hip MRI within 1 month before surgery. The MRI exams were performed with a 1.5 T MR scanner (Philips Intera). Images were obtained in the coronal plane using T1 SE (time to echo (TE)/time to repetition (TR) 18/500 ms); fast spin-echo (FSE) T2-weighted with fat saturation (TR range/TE range, 3000–6000/60–75, echo-train length (ETL) of 8); T1 SE with gadolinium injection sequences, (slice thickness 3 mm, and matrix 512 × 204). The femoral heads only were analyzed because it was not possible to obtain suitable material for histopathology from acetabulum. In addition, the study focused on the coronal slice corresponding to the femoral head fovea, which allowed direct topographic correlation with the corresponding sample at histopathology.

MRI examinations were analyzed independently by two readers (two staff radiologists with 5 years and more than 15 of experience in musculoskeletal MR imaging) blinded to histopathological data. Eight different elemental MR lesions were described in keeping with published MR descriptions (Table I). For categorization, we used the distinction of BME changes between edema-like and necrosis-like¹¹. An edema-like pattern corresponded to an ill-defined area, with low signal intensity on T1-weighted images, high signal intensity on T2 fat-suppressed images, and complete homogenization after gadolinium intravenous injection. A necrosis-like pattern corresponded to a well-defined area, with low signal intensity on T1-weighted images, high signal intensity on T2 fat-suppressed images, and incomplete and inhomogeneous enhancement after gadolinium intravenous injection.

Discrepancies between the two radiologists were resolved by consensus.

The tight ball and socket constitution of the hip joint made it difficult to distinguish, without prior intra-articular contrast injection, the acetabular cartilage from the adjacent femoral cartilage under limited image resolution. So, cartilage abnormalities were not analyzed.

For each femoral head, MRI lesions observed on the ligamentum teres section were drawn on a synthesis scheme (Fig. 1)⁹.

Histopathology

After total hip arthroplasty the femoral heads were instantly fixed in a 4% neutral buffered formalin solution and then cut into 1-mm-thick coronal slices. The slices were photographed and then decalcified with a rapid decalcifier (RDO, prepared in our laboratory). After decalcification, the slices were cut into five or six samples, depending on the femoral head size, and the location of the samples was recorded on a scheme (Fig. 1). Each sample was processed into paraffin wax, cut into 4-μm-thick slices and stained with hematoxylin and eosin. Finally, the analyzed area corresponded to a 4 μm coronal section crossing the ligamentum teres plane.

Histopathological analysis was performed by a pathologist experienced with bone diseases and OA who was blinded to MRI data. Every anatomical zone was precisely described according to the classification in Table II. The lesions on each slide were rated according to a semi-quantitative method. For each slide, the pathologist selected the predominant histological lesion(s) (Table II).

Correlation MRI/histology

Histopathological and imaging analyses were performed independently and in a blinded manner. Comparison between the
Fig. 1. Coronal T1 SE-weighted (A) and FS T2 FSE-weighted (B) MR images through the femoral head fovea showing the edema-like (stars) and necrosis-like (arrowheads) MR patterns. Coronal T1 SE-weighted MR section after gadolinium intravenous injection (C) exhibiting the incomplete enhancement of the necrosis-like lesion (arrowheads) and the homogenization of the edema-like lesion. The necrosis MR pattern displays no enhancement (arrows). Schematic drawing obtained (D) showing the edema-like pattern (EL), the necrosis-like pattern (NL) and the necrosis pattern (arrows). (E) The photographed slice of the femoral head.
Statistical tests were two-tailed, and predictive values (PPV and NPV) with their 95% CI. All analyses were performed with R software (version 2.7).

Demographics and clinical parameters of included and excluded patients did not differ (Table III).

**MRI findings (Table IV)**

The inter-rater agreement for MRI was good ($K: 0.97$). The lesions most frequently observed were edema-like and necrosis-like, found in 100% (23/23) and 73.9% (17/23) of patients respectively. Cystic lesions and necrosis were present in 56.5% (13/23) and 34.8% (8/23) of the femoral heads, respectively. We found no subchondral fractures in our population.

Edema-like and necrosis-like lesions presented a close topographic relation, with an edema-like lesion consistently found at the periphery of necrosis-like lesions. Isolated necrosis-like patterns, i.e., not associated with edema-like, were not observed.

**Correlation between MRI and histological findings (Tables V–VII)**

The best correlations were between edema-like at MRI and histological BME ($K: 0.77$; CI 95%: 0.61–0.89). Necrosis-like was correlated with histological bone marrow fibrosis ($K: 0.49$; CI 95%: 0.28–0.69) and to a lesser degree with bone marrow necrosis ($K: 0.24$; CI 95%: 0.01–0.47). MRI cystic bone marrow was correlated with histological pseudocysts ($K: 0.58$; CI 95%: 0.32–0.78). MRI necrosis was weakly correlated with histological bone marrow necrosis ($K: 0.28$; CI 95%: 0.03–0.52) and corresponded mainly to a mix of histological lesions. Normal hematopoietic and fatty marrow at MRI corresponded to histological normal bone tissue ($K: 0.9$; CI 95%: 0.73–1). MRI specificity was much better than sensitivity for any elemental bone marrow lesion. Sensitivity and specificity of MRI varied from 26% to 80% and from 86% to 95%, respectively.

**Discussion**

Hip OA is an incapacitating disease and a major public health problem. The aim of this study was to correlate MR patterns and histological findings found in hip OA, with special emphasis on BME. Interestingly, our data showed a substantial agreement between MRI and histological findings for edema-like pattern and histological BME.

Other diseases and OA in other body parts seem to behave somewhat differently. For example, in rheumatoid arthritis, BME changes would correspond to regions of inflammation, being variously associated with invading pannus, lymphocytic aggregations, and increased vascularity. In avascular necrosis, BME change would correspond essentially to zones of necrosis, reorganization, or scar tissue fibrosis of the subchondral bone. For knee OA, MRI BME seemed to correspond to a mix of histological lesions except edema. Two studies compared MRI patterns and histopathology in tibial plates of knees with severe OA undergoing total joint replacement. Zanetti et al. described six MRI patterns; marrow edema found at histology represented a small percentage of tissue and was present in equal proportions in each of the MRI zones. The MRI edema-like pattern was composed mainly of normal tissue (fatty bone marrow, normal trabeculae, and blood vessels). Yet, in hip OA our results show that the edema-like MR pattern mainly corresponds to histological edema and to a lesser degree to vascular fibrosis, and that the necrosis-like MR pattern corresponded mainly to marrow necrosis combined with fibrosis. If we had included both edema-like and necrosis-like lesions together, we would probably have obtained a histological mixture of fibrosis, edema, and necrosis, as reported in previously published studies.

This distinction is crucial for elucidating the pathophysiology of “BME”. These two MR lesions were the most frequently encountered in our study. Furthermore there was a very close topographic
Table III
Characteristics of the population

<table>
<thead>
<tr>
<th>Population</th>
<th>Included patients</th>
<th>Excluded patients</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men n (%)</td>
<td>10 (43.5)</td>
<td>2 (25)</td>
<td>0.43</td>
</tr>
<tr>
<td>Women n (%)</td>
<td>13 (56.5)</td>
<td>6 (75)</td>
<td>0.43</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>64.5</td>
<td>62.4</td>
<td>0.84</td>
</tr>
<tr>
<td>Symptoms evolution (months)</td>
<td>28</td>
<td>22.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Delay MRI/surgery (days)</td>
<td>6.9</td>
<td>10.2</td>
<td>0.25</td>
</tr>
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</table>

Table IV
MRI observation

<table>
<thead>
<tr>
<th>MRI observation</th>
<th>Number of patients (total = 23)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal H. marrow</td>
<td>12</td>
<td>52.2</td>
</tr>
<tr>
<td>Normal F. marrow</td>
<td>23</td>
<td>100</td>
</tr>
<tr>
<td>Edema-like</td>
<td>23</td>
<td>100</td>
</tr>
<tr>
<td>Necrosis-like</td>
<td>17</td>
<td>73.9</td>
</tr>
<tr>
<td>Sclerosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Necrosis</td>
<td>8</td>
<td>34.8</td>
</tr>
<tr>
<td>Subchondral fracture</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cystic bone marrow</td>
<td>13</td>
<td>56.5</td>
</tr>
</tbody>
</table>

Fig. 2. (A) BME in the intertrabecular space below normal hematopoietic marrow (HES ×10); (B) BME: faint eosinophilic material between adipocytes and around a vessel (HES ×20); (C) fibrous replacement of fatty marrow (HES ×10); (D) subchondral fibrous intertrabecular spaces with pseudocysts and numerous ectatic vessels (HES ×10); (E) pseudocysts with central basophilic material and necrotic bone trabecula at higher magnification (HES ×20); (F) eosinophilic necrotic material in the intertrabecular space (HES ×20).
some cases they are also found in apparently normal subjects and can reverse. Nevertheless, very few data are available on OA to indicate which MRI findings are the result of true disease and which are the result of normal variations. Therefore, it is challenging to prove that a bone marrow lesion is a truly abnormal finding. However, differentiation from normal variations is crucial to avoid unnecessary treatment in patients with OA.

In our study, MRI specificity was better than sensitivity to detect any histological elemental lesion. This suggests a threshold phenomenon for MRI detection of BME-like changes, i.e., histological changes must be substantial to be depicted by MRI. This has already been pointed out in other processes such as rheumatoid arthritis or ankylosing spondylitis.

Some limitations inherent to the materials and methods used in this study should be discussed. First, because of the need to obtain gross anatomical material, our study was limited to hip OA advanced enough to justify total hip replacement. For the same reason, it was limited to femoral heads, because en bloc resection of the acetabulum is not technically feasible. However, the MRI lesions we observed on acetabuli were not significantly different from those observed on femoral heads (data not shown). This study concerned a limited number of cases, but it is in the range found in the literature on this topic. Finally, distinguishing edema-like and necrosis-like patterns are not always easy and require sometimes a complete MRI protocol including gadolinium injection. So it is probably not realistic to apply this in routine clinical practice.

The strengths of our study are as follows. Femoral heads can be properly resected as a whole and provide much better anatomical material than knee pieces. Also, a major difficulty in MRI–histological correlations is to ensure that the areas analyzed by both methods are actually the same. Otherwise, the observed associations remain too crude to allow suitable conclusions. We believe this goal was achieved in this study.

Evidence is mounting that MRI patterns corresponding to so-called BME have great importance whatever the pathology, mechanical or inflammatory, and may be considered as crucial prognosis factors. In knee OA, such MRI patterns are generally associated with clinically and radiologically poor prognosis, but in some cases they are also found in apparently normal subjects and can reverse. Nevertheless, very few data are available on OA to characterize the underlying histological processes. We chose to specifically separate “bone marrow edema pattern” into edema-like and necrosis-like lesions, the former corresponding to histological BME, and the latter to bone marrow fibrosis and necrosis. Our data showed a good correlation between edema-like MRI patterns and histopathological BME. We hypothesize that the edema-like lesion represents a potentially reversible stage preceding the more advanced and pejorative necrosis-like lesion. Our conclusions need to be confirmed by further histological and clinical studies.

Contributions

All authors have made substantial contributions to this work, especially for the conception and design, drafting and final approval. Jean-Noël Argenson provided femoral heads, Corinne Bouvier and André Maues de Paula performed Histopathological analysis and Roch Giorgi did the statistical analysis. Hélène Leydet-Quilici (helene.leydet@mail.ap-hm.fr) takes responsibility for the integrity of the work as a whole, from inception to finished article.
Conflict of interest
All authors have no conflict of interest.

Acknowledgments

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