Early Irreversible Osteonecrosis Versus Transient Lesions of the Femoral Condyles: Prognostic Value of Subchondral Bone and Marrow Changes on MR Imaging


OBJECTIVE. The purpose of this study was to determine the MR imaging features that enable differentiation between early irreversible osteonecrosis and transient lesions in nontraumatic lesions of the femoral condyle having the "bone marrow edema" pattern on MR imaging.

MATERIALS AND METHODS. We reviewed 23 nontraumatic painful lesions of the femoral condyle in 23 patients (12 men and 11 women; mean age, 62 years). All patients had undergone radiography of the knee with findings that were normal or inconclusive. Also, all patients underwent MR imaging that revealed the bone marrow edema pattern in a condyle. Lesions observed after trauma, surgery, or glucocorticoid medication, or with epiphyseal collapse or degenerative joint disease on initial plain radiographs, were excluded from this study.

CONCLUSION. Careful assessment of MR imaging changes occurring in the subchondral area can enable confident differentiation between transient epiphyseal lesions and early irreversible osteonecrosis of the femoral condyle.

The "bone marrow edema" pattern is characterized by an ill-defined marrow area of low signal intensity on T1-weighted MR images and of intermediate to high signal intensity on T2-weighted images. When the bone marrow edema pattern is seen in an epiphysis on MR imaging, several diagnoses must be considered, including posttraumatic or stress fractures, osteonecrosis, transient osteoporosis, reactive changes underlying degenerative articular disease, and a poorly understood self-resolving condition referred to as the "transient bone marrow edema syndrome" [1-14].

Spontaneous osteonecrosis of the femoral condyle is a peculiar clinical entity that occurs in elderly patients and generally involves the medial femoral condyle [15-19]. On MR imaging, spontaneous knee osteonecrosis shows the bone marrow edema pattern and subtle subchondral bone changes in the affected condyle [20-23]. This MR imaging appearance differs from that of typical avascular osteonecrosis because it lacks the cardinal MR feature of epiphyseal osteonecrosis—that is, the demarcation rim or reactive interface that separates necrotic bone and marrow from adjacent viable tissue and shows a low signal intensity on T1-weighted images and a "double line" appearance on T2-weighted images [20-23].

The importance of early distinguishing of spontaneous osteonecrosis from transient epiphyseal lesions is based on the considerable difference in clinical prognosis and treatment of these entities [10-14]. This differential diagnosis is difficult in lesions without subchondral bone fracture—the pathognomonic sign of osteonecrosis—on plain radiographs.
and with the bone marrow edema pattern on MR imaging.

We reviewed the initial MR examinations of 23 patients who presented with femoral condyle bone marrow edema lesions for which prospective radiographic and MR imaging follow-up studies showed either complete resolution (n = 14) or evolution to collapsed osteonecrosis (n = 9). Our aims were to compare the initial subchondral bone and marrow changes observed at MR imaging in both categories of lesions and to determine the most reliable features that enable differentiation between these conditions.

Materials and Methods

Patients

The study population consisted of 23 patients (12 men and 11 women; mean age, 62 years; range, 38–85 years) in whom signal intensity changes consistent with marrow edema were revealed at MR imaging in the subchondral region of one femoral condyle. These patients had undergone radiography of the knee with findings that were normal or inconclusive and had been referred between January 1990 and January 1995 for MR imaging evaluation of spontaneous knee pain. Patients with a history of trauma, meniscectomy, or glucocorticoid intake were excluded. Lesions that showed radiographic or MR imaging evidence of degenerative disease or collapsed osteonecrosis on plain films by the time of the first MR examination were also excluded.

The lesions involved the medial femoral condyle in 18 patients and the lateral condyle in five patients. Conventional radiographs, including lateral, postero-anterior, and transcondylar views of the femorotibial joint, showed either no abnormality (n = 18) or nonspecific findings described as discrete subchondral sclerosis (n = 3) or subtle subchondral bone rarefaction (n = 2) within the involved condyle. Seventeen patients had undergone technetium-99m bone scans that consistently showed increased isotope uptake in the femoral condyle revealing the bone marrow edema pattern on MR imaging.

MR Imaging Studies

MR imaging of the knee was performed at a median interval of 4 weeks (range, 2–20 weeks) after the onset of symptoms using a 0.5- or 1.5-T superconducting magnet (Gyroscan; Philips Medical Systems, Best, The Netherlands). Initial MR imaging examinations included coronal T1-weighted spin-echo and sagittal intermediate- and T2-weighted spin-echo images, with respective TR/TE of 415/20 msec, 2000/20, and 2000/80. Sections 3.5–5.0 mm thick were obtained with a field of view of 140 mm in the coronal plane and 180 mm in the sagittal plane and with an acquisition matrix of 204 × 256.

Analysis of Initial MR Images

Initial MR images were reviewed independently by two musculoskeletal radiologists who were unaware of patient name, age, sex, and outcome. Radiographs and follow-up MR imaging studies were not available.

All lesions had bone marrow edema as a common MR imaging feature in association with several subtle changes in the subchondral bone and marrow; none of these lesions presented the demarcation rim or reactive interface typical of avascular osteonecrosis.

Fig. 1.—Schematic view of sagittal T2-weighted MR image of femoral condyle shows, within ill-defined area of intermediate to high signal intensity suggestive of edema, subchondral area of low signal intensity (A), thin line of low signal intensity (B), and focal epiphyseal contour deformity (C).

Subchondral bone and marrow changes.—The presence, length, and thickness of subchondral areas of low signal intensity immediately adjacent to the subchondral bone were determined and measured on sagittal T2-weighted images. Subtle focal contour deformities of the subchondral bone plate were graded on a scale of 0–3, as follows: 0 = absent, 1 = possible flattening, 2 = possible depression, 3 = depression. The presence, length, and distance from subchondral bone of thin lines of low signal intensity, running in the vicinity of and approximately parallel to the articular surface, were determined and measured on the T2-weighted images. These subchondral changes are schematized in Figure 1 and illustrated in Figures 2 and 3.

Extent of edema.—The cranial and lateral extent of the ill-defined area of low signal intensity was measured on the coronal T1-weighted images. Sagittal extent was deduced from the number of coronal slices that showed the lesions.

Fig. 2.—65-year-old man with 4-week history of spontaneous knee pain. Sagittal T2-weighted MR image (2000/80 [TR/TE]) of medial femoral condyle shows subchondral area of low signal intensity (arrowheads) and subtle focal epiphyseal contour depression (grade 3 deformity) (arrow). At 12-month follow-up, this lesion had evolved to epiphyseal collapse typical of osteonecrosis.

Fig. 3.—59-year-old woman with 5-week history of spontaneous knee pain. Sagittal T2-weighted MR image (2000/80 [TR/TE]) of medial femoral condyle shows line of low signal intensity (arrow) within more diffuse area of increased signal intensity, suggestive of edema. This lesion showed complete resolution at 6-month follow-up.
TABLE 1  Clinical Data for Patients with Early Irreversible Osteonecrosis and Patients with Transient Epiphyseal Lesions

<table>
<thead>
<tr>
<th>Patients</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Duration of Symptoms (wk)</th>
<th>Involved Condyle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early irreversible osteonecrosis</td>
<td>9</td>
<td>5</td>
<td>Mean ± SD</td>
<td>Median</td>
</tr>
<tr>
<td>Transient lesions</td>
<td>14</td>
<td>7</td>
<td>Mean ± SD</td>
<td>Median</td>
</tr>
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</table>

Comparison: Not significant; p = 0.003; Not significant

Patient Follow-Up and Lesion Outcome

All patients were treated conservatively with a functional discharge and nonsteroid analgesics. To determine the lesion outcome, follow-up imaging was performed regardless of whether symptoms persisted. Conventional radiographic studies (n = 45) and MR imaging studies (n = 39), including coronal T1-weighted spin-echo and sagittal T2-weighted spin-echo images, were obtained at short-term (2–6 months for 20 MR studies) and at long-term (9 months–4 years for 19 MR studies) follow-up. MR imaging follow-up was pursued unless either plain radiographs showed occurrence of obvious epiphyseal collapse of the involved condyle or MR images showed complete resolution of marrow abnormalities.

Nine lesions showed epiphyseal collapse and subchondral fracture with a “radiolucent crescent sign” typical of knee osteonecrosis on follow-up radiographs. MR imaging follow-up showed persistent abnormalities, but none of these lesions presented the demarcation rim or reactive interface typical of avascular osteonecrosis. These nine irreversible lesions all involved the medial femoral condyle.

Fourteen lesions showed complete healing, with resolution on follow-up MR imaging studies of the initial abnormalities seen on MR imaging. The initial radiographic studies showed normal findings in all but two cases that showed the presence of discrete subchondral bone sclerosis (n = 1) or rarefaction (n = 1). Two other lesions showed the appearance of regional osteoporosis on follow-up radiographs. These subtle subchondral bone changes all resolved within 1 year. Nine of these transient lesions involved the medial condyle and five, the lateral condyle.

Pathologic Correlation

A medial femoral condyle was obtained from a patient of the current series who had shown typical knee osteonecrosis at follow-up and who underwent total knee arthroplasty 8 months after initial MR examination. The specimen was cut into 5-mm-thick sagittal sections and photographed and radiographed. After fixation and stain, subchondral marrow composition was assessed by a pathologist.

Statistical Analysis

Statistical analysis was performed by a statistician from our institution. Numeric variables were compared using the Wilcoxon rank sum test. Fisher’s exact test was used to compare categoric variables. P values of less than .05 were considered statistically significant.

The performance of the statistically significant parameters to differentiate transient epiphyseal lesions from early irreversible osteonecrosis was assessed by sensitivity, specificity, and positive and negative predictive values for qualitative parameters, and by receiver operating characteristic curves for quantitative measurements. Receiver operating characteristic curves were constructed and the areas under the curves were computed by maximum likelihood estimation using the LABROC 1 program (C. Metz, Chicago, IL), except for the ordinal classification of epiphyseal contour deformities, for which the method of Hanley and McNeil was used [24].

Reproducibility of findings between both observers was assessed by kappa coefficient and intraclass correlation coefficient for categoric and numeric variables, respectively.

Results

Comparison of Clinical Data Between Patients with Early Irreversible Osteonecrosis and Those with Transient Lesions

Gender and age of the patients with early irreversible osteonecrosis were not significantly different from those of patients with transient lesions (Table 1). The interval between the onset of symptoms and the initial MR study was significantly shorter in the patients with transient lesions (mean, 4 weeks) than in those with early osteonecrosis (mean, 10 weeks).
Comparison of Initial MR Findings Between Early Irreversible Osteonecrosis and Transient Lesions

Subchondral areas of low signal intensity on T2-weighted images were significantly more frequent in early irreversible osteonecrosis than in transient epiphyseal lesions \( (p = .048) \) (Tables 2 and 3). When present, they were significantly longer \( (p = .002) \) and thicker \( (p = .006) \) in early irreversible osteonecrosis than in transient epiphyseal lesions (Figs. 4 and 5).

Subtle focal deformities of the epiphyseal cortex were significantly more frequent \( (p = .012) \) and more severe \( (p < .001) \) in early irreversible osteonecrosis than in transient epiphyseal lesions.

The frequency and length of thin lines of low signal intensity were not different between the two categories of lesions. The maximal distance separating these lines from the epiphyseal cortex was significantly higher in early osteonecrosis than in transient epiphyseal lesions \( (p = .005) \).

The extent of the edemalike changes was not different between categories of lesions.

Prognostic Value of the MR Imaging Findings

The presence of subchondral low-signal-intensity areas on T2-weighted images and of contour deformities had a perfect sensitivity to recognize early irreversible osteonecrosis (Table 4).

The thickness and length of the subchondral areas of low signal intensity on T2-weighted images, the severity of subtle epiphyseal contour deformities, and the distance separating low-signal-intensity lines from the epiphysial surface were relevant for differentiating early osteonecrosis from transient epiphyseal lesions. Receiver operating characteristic curves obtained for the length and the thickness of the subchondral low-signal-intensity component on T2-weighted images were constructed for both observers (Fig. 6). To discriminate early osteonecrosis from transient lesions, acceptable cut-off levels for the length and thickness of the subchondral low-signal-intensity component were, respectively,
Fig. 5.—63-year-old man with 5-week history of spontaneous knee pain.
A, Initial plain radiograph of left knee does not show evident bone abnormality.
B, Coronal T1-weighted MR image (415/20 TR/TE) shows ill-defined region of decreased signal intensity in medial femoral condyle (arrowheads) with better-defined subchondral low-signal-intensity area (arrows).
C, Sagittal T2-weighted MR image (2000/80) through medial compartment shows 5-mm-thick, 22-mm-long subchondral area of low signal intensity (asterisk) and a line of low signal intensity (arrows).
D, Plain radiograph of knee obtained at 5-month follow-up shows appearance of subchondral bone fracture typical of osteonecrosis of medial femoral condyle.
E and F, Photograph (E) and radiograph (F) of sagittal section from resected medial condyle show subchondral bone fracture (arrows).
G, Photomicrograph shows thickened and fragmented necrotic bone and abnormal marrow with amorphous cellular debris in anterior (a) aspect of condyle, adjacent to subchondral bone fracture. Note normal appearance of subchondral bone and marrow in posterior (p) aspect of condyle. (H and E, ×10)

more than 14 mm (sensitivity, 89% and 88%; specificity, 93% and 87%, for the two observers) and more than 4 mm (sensitivity, 100% and 100%; specificity, 82% and 74%, for the two observers). The severity of epiphyseal contour deformities (area under the curve = 952 ± 0.43 for both observers) and the distance separating the low-signal-intensity lines from the epiphyseal surface (area
under the curve = 0.962 ± 0.055 and 0.891 ± 0.098 for the two observers) were also valuable to identify early osteonecrosis.

**Pathologic Findings**

Histologic analysis of the subchondral area of the resected femoral condyle showed necrotic, thickened, and fragmented bone that contained amorphous marrow debris surrounded by fibrovascular tissue (Fig. 5G).

**Interobserver Reproducibility**

Interobserver agreement was perfect (κ = 1) for the detection of subchondral low-signal-intensity areas and of the low-signal-intensity lines. Measurements of the low-signal-intensity areas on T2-weighted images and of the maximal distance separating the low-signal-intensity lines from the epiphyseal surface, and appreciation of epiphyseal contour deformity, were satisfactorily reproducible (intraobserver correlation coefficient > 0.81). Quantification of the extent of edema and of the size of the low-signal-intensity lines was poorly reproducible (intraobserver correlation coefficient < 0.71).

**Discussion**

The current study of nontraumatic femoral condyle lesions showing the bone marrow edema pattern on MR imaging demonstrates that precise analysis of the bone and marrow changes observed in the subchondral area enables the detection of features of prognostic value. Actually, three features observed in the subchondral area appeared of value to differentiate early irreversible osteonecrosis from transient epiphyseal lesions.

First, low-signal-intensity subchondral areas detected on T2-weighted MR images were of the utmost importance. Actually, their absence was always indicative of complete reversibility at follow-up. Lesions that showed such low-signal-intensity subchondral areas could be either transient or irreversible, but a length of more than 14 mm or a thickness of more than 4 mm were indicative of evolution to collapsed osteonecrosis. The exact significance of these subchondral areas remains unknown. Of interest, similar changes have been observed in established spontaneous osteonecrosis of the femoral condyle in elderly patients and in osteonecrosis of the femoral head and were shown to correspond at histology to necrotic bone, cellular debris, and thickened collapsed trabeculae [3, 8, 10, 20–22, 25–27]. Our pathologic findings in a resected necrotic condyle parallel this description. The main thrust of our study was to demonstrate that low-signal-intensity subchondral areas were observed in both transient lesions and early irreversible osteonecrosis, but that quantitative assessment of these changes enabled confident differentiation between these conditions.

Second, the presence of subtle focal deformity of the epiphyseal contour was observed in all knees with early irreversible osteonecrosis, whereas the absence of any deformity was indicative of a complete reversibility. Finally, the location of thin low-signal-intensity lines with respect to the subchondral bone differed between both categories of lesions, deeply located lines indicating early irreversible osteonecrosis. However, the frequency, length, and width of these lines lacked significance. The exact pathologic nature of these two findings remains hypothetical. Epiphyseal cortex deformities point toward the hypothesis of subchondral bone fracture, whereas low-signal-intensity lines could represent impacted trabeculae. Actually, these two MR imaging features are commonly observed in the setting of occult posttraumatic and stress fractures [5, 9, 28–31].

Irreversible lesions from this series consistently demonstrated at follow-up radiologic features pathognomonic for spontaneous osteonecrosis of the medial femoral condyle, including epiphyseal collapse and subchondral bone fracture [15–19]. Spontaneous osteonecrosis of the knee typically involves the medial femoral condyle of elderly patients, although exceptional cases of lateral femoral condyle or medial tibial plateau involvement have been reported [19, 21, 32, 33]. Our study is in agreement with the literature series in that all irreversible osteonecrosis lesions involved medial femoral condyles. On the contrary, transient lesions were observed in five lateral condyles and in nine medial condyles. Definite designation of the transient epiphyseal lesions remained delicate and was beyond the scope of this paper. Transient osteoporosis, epiphyseal stress fractures, or even self-resolving osteonecrosis must be considered as possible diagnostic hypotheses [5, 8, 11, 13, 14]. Most of all, the commonality of several MR features—which, however, differ in frequency and magnitude—between early irreversible osteonecrosis and
MR Imaging of Femoral Condyles

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