

# Transient Bone Marrow Edema Syndrome of the Knee: Clinical and Magnetic Resonance Imaging Results at 5 Years After Core Decompression

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**Purpose:** We report on 24 cases of transient bone marrow edema syndrome in 18 patients who underwent core decompression of the knee. **Methods:** Diagnosis was made with the use of radiographs, magnetic resonance imaging (MRI), and core biopsy testing. Arthroscopic surgery and core decompression were carried out in all patients, and MRI was performed again, 5 years after surgery was performed. **Results:** Medial and lateral femoral condyles were affected in 15 and 7 knees, respectively. In all, 6 patients presented with bilateral involvement of the knees (migrating transient bone marrow edema syndrome). Two of these patients had affections of the medial and lateral compartments within the same knee at different times, consistent with intra-articular regional bone marrow edema syndrome. Core biopsy specimens showed areas of bone marrow edema and vital trabeculae covered by osteoblasts and osteoid seams. Resolution of symptoms and normalization of MRI findings occurred in all patients within 12 weeks after surgery. **Conclusions:** Migrating bone marrow edema was found in a high percentage (33%) of patients at 5-year follow-up; however, all patients were clinically asymptomatic, and signal alterations on MRI had resolved completely. The high incidence of migrating bone marrow edema, the lack of osteonecrotic regions in our specimens, and the fact that none of these cases progressed to spontaneous osteonecrosis seem to further support the contention that bone marrow edema syndrome of the knee is a distinct entity. **Level of Evidence:** Level II, diagnostic study; development of diagnostic criteria on the basis of consecutive patients and with universally applied reference gold standard. **Key Words:** Knee—Transient bone marrow edema—Syndrome—MRI.

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**T**ransient bone marrow edema syndrome (transient osteoporosis, algodystrophy) has been reported to occur in the knee; yet, owing to the small number of reports on this specific entity, little is known about the optimal treatment of patients with this condition.<sup>1-3</sup> In

general, the disease is self-limited; however, some authors favor the hypothesis that it represents an early, reversible form of avascular necrosis.<sup>4-6</sup> Clinically, patients present with pain during mechanical loading, combined with more or less pain at night. Its typical signal appearance on magnetic resonance imaging (MRI) (low-intensity signal on T1-weighted images corresponding to high signal intensities on fat-suppressed T2-weighted images) is a common but nonspecific signal pattern that can be found in various bony diseases.<sup>7-10</sup> As with bone marrow edema syndrome of the hip, drilling of cancellous lesions has been advocated to reduce intramedullary pressure.<sup>3,4,11</sup> Histologic findings in bone marrow edema syndrome consist of fat cell fragmentation and increased intramedullary fluid corresponding to regions of bone marrow edema seen on MRI.<sup>3,12</sup>

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Unfortunately, except for a study performed by McCarthy,<sup>3</sup> documentation of the histologic features of transient bone marrow edema of the knee has been scanty, and long-term follow-up studies that involve MRI have not been conducted. The purpose of the current study was to report on a series of patients who underwent core decompression for treatment of bone marrow edema syndrome of the knee; 5-year follow-up MRI data are presented.

## METHODS

From March 1997 to April 1999, 18 consecutive patients (13 men and 5 women; 24 knees; mean age,  $53.7 \pm 5.4$  years; range, 35 to 64 years) with bone marrow edema syndrome of the knee were treated with core decompression. (Average time between onset of symptoms and referral to our department was 4 weeks.) All patients presented with pain during mechanical loading and, to a variable degree, during the night. Characteristically, pain was present in the affected condyle when it was tapped. None of the patients presented with a history of trauma, nor was any patient taking medication that would affect bone turnover. One patient was an alcoholic with an enlarged liver and a pathologic lipid profile. Another patient from the Mediterranean suffered from thalassemia minor. MRI was performed with the use of a 1.0-T superconducting system (Magnetom "Expert"; Siemens, Erlangen, Germany) with a circular, polarized, flexible surface coil that was wrapped around the knee joint. Images were taken in the sagittal and coronal planes with a field of view of 160 mm. Sagittally, T1-weighted turbo-spin echo (TSE) (1200/12/3—TR/TE/thickness), T2-weighted TSE (5244/128/4), and gradient echo (DESS 3D 26.8/9/1.4) sequences were performed. Proton-density and T2-weighted TSE sequences (2700/15-105/4) were done in the coronal plane, followed by a coronal short T1 (150 msec) inversion recovery sequence (3975/30/4) for the depiction of marrow edema. MRI, plain radiography, and core biopsy specimens confirmed the diagnosis of bone marrow edema syndrome. All patients exhibited the characteristic pattern on MRI.<sup>2,6-9</sup> On T1-weighted images, a diffuse and homogeneous area of low signal intensity was seen corresponding to areas of high signal intensity on fat-suppressed T2-weighted images, predominantly involving the femoral head and neck. Mild to moderate joint effusion was seen in all patients.

Radiographic findings consistent with the presence of avascular necrosis were not seen in any patient;

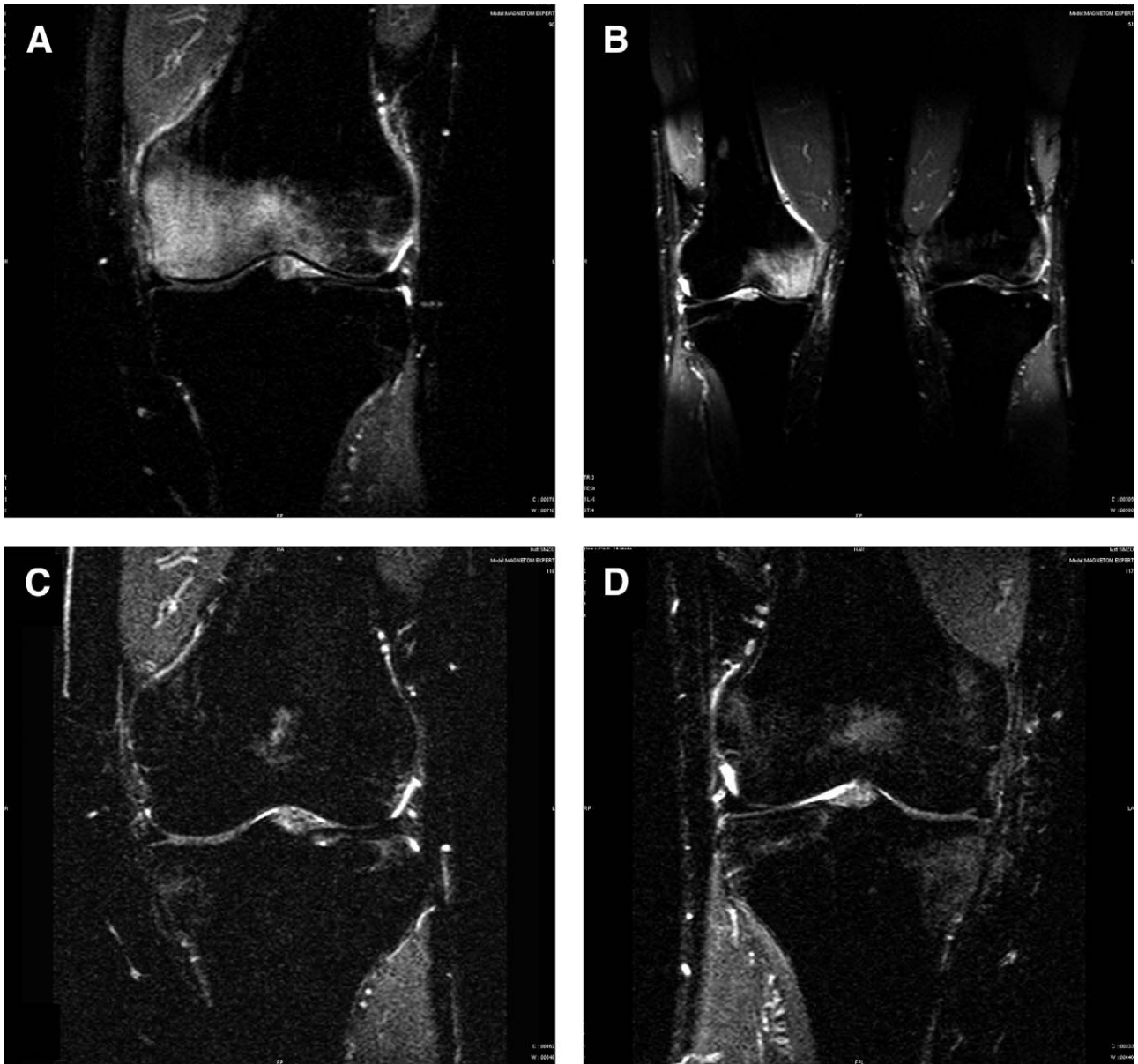
other possible causes for the presence of bone marrow edema such as neoplasm, inflammatory disease, and subchondral fracture were also excluded. Before core decompression occurred, an arthroscopy was performed in all patients. Meniscal diseases and intra-articular alterations were treated accordingly; chondromalacia of the affected compartment was not present in any knee. Core decompression of the affected femoral condyle was performed with the use of a needle (2.5-mm diameter; Ottolenghi-Set; Heintel, Vienna, Austria). Briefly, the needle was inserted into the affected condyle via an additional incision; it was then positioned in the epicenter of the edematous lesion. This procedure was done with the use of an image intensifier. Biopsy specimens from 19 knees (14 patients) were available for histopathologic evaluation.

Initially, specimens were fixed in Schaffer's fluid. Sections were embedded in paraffin and were then stained with H&E. All specimens were evaluated by one of the coauthors.

Postsurgical management was done according to a standard protocol that included progressive weight bearing on the surgically treated leg, along with exercise. Partial weight bearing was started on the first day after surgery; patients typically finished partial weight bearing and went to full weight bearing within 4 to 6 weeks. MRI scans were performed in all patients at 3 months after surgery. Twelve patients (16 knees) were followed clinically for at least 60 months (range, 60 to 87 months), and MRI scans were performed at an average of 75 months (range, 60 to 87 months) postoperatively. Six patients were lost to follow-up. Two patients died of unrelated causes. Another 2 patients were untraceable because they had moved to foreign countries; 2 patients refused to undergo MRI scans because they were clinically pain-free and had resumed their normal activities of daily living. Written informed consent was obtained for follow-up examinations from each patient.

## RESULTS

In total, the medial and lateral femoral condyles were affected in 15 and 7 knees, respectively, whereas intra-articular migrating bone marrow edema was present in 2 knees (Fig 1). Six patients presented with bilateral involvement of the knees (migrating transient bone marrow edema syndrome). Two of these patients had affections of the medial and lateral compartments within the same knee at different times, consistent with intra-artic-



**FIGURE 1.** (A) MRI scans (coronal views of T2-weighted fat-suppressed images) show presence of extensive bone marrow edema of the medial femoral condyle of the left knee in a 52-year-old male patient. (B) Twelve weeks after core decompression, signal alterations have resolved in the left knee, but extensive bone marrow edema is now present in the right knee. (C and D) Six months after surgery, bone marrow edema is not detectable in both knees.

ular regional bone marrow edema syndrome. All patients clinically recovered within 6 weeks, and MRI findings normalized within 12 weeks, after surgery. Patients were thereafter free of symptoms, and none required further treatment. To date, none of the patients has developed avascular necrosis of the affected knee, and MRI scans at follow-up have been nondiagnostic in all patients (Fig 2). Core

biopsy specimens showed areas of bone marrow edema and vital trabeculae covered by osteoblasts and osteoid seams (Fig 3). Characteristically, dilated medullary sinuses adjacent to the bone surfaces and irregularly woven bone were seen. Fibrous connective tissue with sparse vessels invading the marrow cavities between residual fat cells could be seen, in addition to fibroblasts.

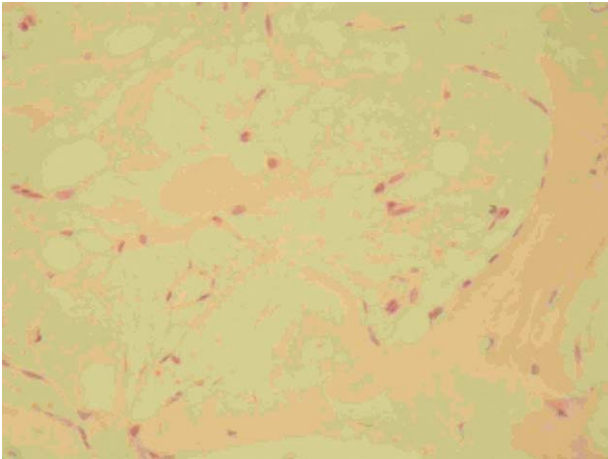


**FIGURE 2.** MRI scans (A) coronal view of T2-weighted fat-suppressed images and (B) sagittal view of T1-weighted images show the presence of bone marrow edema in the left medial condyle of a 49-year-old male patient. (C) Five years after surgery, signal alterations consistent with bone marrow edema are not detectable on coronal T2-weighted fat-suppressed images.

## DISCUSSION

To date, significant confusion exists concerning the pathophysiology and nomenclature of bone marrow edema syndrome.<sup>2,11</sup> Although the disorder was initially described as transient osteoporosis—osteopenia is a late finding on plain radiographs—the term *bone marrow edema syndrome* was suggested as more appropriate, on the basis of early MRI findings and histologic features.<sup>2,12</sup> Furthermore, the relationship of bone marrow edema syndrome and avascular necrosis remains open to controversial debate.<sup>5,13</sup> Con-

siderable overlapping of these syndromes favors the hypothesis that bone marrow edema syndrome is regarded as a prodrome to classic avascular necrosis. In the initial stages of avascular necrosis, only focal subchondral areas of bone marrow edema are seen.<sup>2,8</sup> Frequently, however, the location is not confined to the loading zone; thus, the observed pattern may be nonspecific. Yet, in the irreversible early stage, a subchondral osteonecrotic area is characteristically surrounded by a reactive interface.<sup>2,8</sup> On the other hand, the diffuse pattern of bone marrow edema syndrome on MRI, which is distinct from the usual focal



**FIGURE 3.** A biopsy specimen from a 52-year-old patient (H&E, original magnification  $\times 40$ ) shows fat cell fragmentation and the presence of intramedullary fluid, indicative of bone marrow edema.

pattern of avascular necrosis, and the histologic finding of new bone formation—vital bone trabeculae are covered with osteoid seams and lining cells—indicate that bone marrow edema syndrome is a distinct entity.<sup>3,12,13</sup> In line with previous studies,<sup>3,12</sup> we were able to demonstrate in our specimens major histologic features, including osteoid seams, irregularly woven bone, dilated sinuses, and the presence of intramedullary fluid. The extent of fat cell fragmentation varied considerably, but findings consistent with areas of osteonecrosis were not seen in trabecular or bone marrow tissue regions. McCarthy<sup>3</sup> has demonstrated in his specimens reactive bone formation and osteoclastic resorption, both of which are indicative of high bone turnover. Pathogenetically, this high turnover rate was considered suggestive of a vasomotor response, similar to that seen in classic reflex sympathetic dystrophy,<sup>3</sup> and is in good accordance with increased bone turnover seen in bone marrow edema syndrome of the hip.<sup>13</sup>

Our current understanding of the pathogenesis of bone marrow edema syndrome involves diffuse subacute ischemia, which completely heals in most cases because of a sufficient repair mechanism.<sup>2,14</sup> Koo et al.<sup>15</sup> hypothesized that the major determinant of the potential for spontaneous repair is the magnitude of the ischemic stimulus, suggesting that a 3-graded bone reaction in ischemia is the result of bone cell variability and sensitivity to various hypoxic stimuli. Hence, capillary stasis related to a local circulatory disturbance and subsequent impaired venous outflow are consistent not only with histologic findings of dilated

sinuses, but also with MRI and investigations of coagulation disorders.<sup>16</sup> In line with these observations, we were previously able to point to a possible involvement of hypofibrinolysis on the basis of elevated levels of plasminogen activator inhibitor and/or lipoprotein(a) as a cause of this condition.<sup>17</sup> Accordingly, elevated levels of plasminogen activator inhibitor, which are induced by a single administration of low-dose lipopolysaccharide, have been shown to cause osteonecrosis of the medial femoral condyle in rabbits.<sup>18</sup> Recent reports on the efficacy of conservative approaches that use the prostacyclin analogue iloprost also seem to underline the importance of coagulation disorders in this disease.<sup>19</sup>

In a series of 10 patients (12 knees) with bone marrow edema syndrome, Vardi et al.<sup>20</sup> showed affection of the medial and lateral femoral condyles in 8 and 4 knees, respectively. In line with this observation, the medial femoral condyle was more prone to bone marrow edema in our patients (15 knees were affected), whereas bone marrow edema syndrome was seen in 7 knees at the lateral femoral compartment. When evaluating intraosseous and extraosseous blood supply to the distal femoral condyles, Reddy et al.<sup>21</sup> were able to show that, in contrast to the lateral femoral condyle, the intraosseous supply to the medial femoral condyle appears to consist only of a single nutrient vessel that supplies the subchondral bone with an apparent watershed area of limited supply. Thus, it can be hypothesized, given the current understanding of a basic involvement of subacute ischemia in the pathogenesis of bone marrow edema syndrome, that the observed preponderance of affection of the medial femoral condyle further corroborates this hypothesis. The incidence of contralateral migration of bone marrow edema was higher in our patients when compared with previous studies.<sup>22</sup> Migration of bone marrow edema within different compartments of the same knee has been reported in only a few cases.<sup>23-25</sup> Nevertheless, this phenomenon was observed in 2 of our patients. It is interesting to note that both patients also showed affection of the contralateral knee at different times, along with 4 other patients who exhibited migration of bone marrow edema syndrome to the contralateral knee. These observations and the diffuse pattern on MRI—signal alterations were not restricted to subchondral areas but extended inhomogeneously to epiphyseal regions—seem to distinguish bone marrow edema syndrome from avascular necrosis.<sup>14</sup>

In bone marrow edema syndrome of the hip, core decompression has demonstrated immediate relief of pain and shortening of the spontaneous course.<sup>4,13</sup>

Yet, only a few cases of bone marrow edema syndrome of the knee in which patients were treated by core decompression have been reported so far.<sup>2,3,11</sup> Nonsurgical therapeutic strategies include application of analgesia,<sup>2</sup> calcitonin,<sup>2,26</sup> prostacyclin analogues,<sup>19</sup> and bisphosphonates.<sup>27,28</sup>

## CONCLUSIONS

Our results suggest that core decompression is a safe and effective procedure in the treatment of patients with bone marrow edema syndrome of the knee. At 5 years after surgery, signal alterations consistent with bone marrow edema were not present in any case on MRI, and patients were free of symptoms without recurrence of bone marrow edema syndrome or progression to avascular necrosis. The high incidence of migrating bone marrow edema, the diffuse pattern on MRI, and the lack of osteonecrotic regions in our specimens seem to further support the contention that bone marrow edema syndrome of the knee is a distinct entity.

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