Hematopoietic Bone Marrow Hyperplasia: High Prevalence on MR Images of the Knee in Asymptomatic Marathon Runners

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In a prior study of marathon runners, we noticed that MR scans of the knee frequently showed hyperplasia of red (i.e., hematopoietic) bone marrow. Because the frequency of this finding in various populations is unknown, the purpose of this study was to determine the relative prevalences of hematopoietic bone marrow hyperplasia on MR examinations of the knees of healthy volunteers (n = 74), patients with symptoms of knee disorders (n = 54), and asymptomatic marathon runners (n = 23). The prevalence of hematopoietic bone marrow hyperplasia was 3% (2/74) for the healthy volunteers, 15% (8/54) for the patients, and 43% (10/23) for the marathon runners. The difference in prevalence between each of the three groups was statistically significant at p < .05. In each case with hematopoietic bone marrow hyperplasia, the distal femur was the only area affected, while the epiphysis and proximal tibia were uninvolved. This pattern of affected bone marrow with hyperplasia of the hematopoietic marrow may be useful for the differential diagnosis.

We postulate that the high prevalence of hematopoietic bone marrow hyperplasia in marathon runners may develop as a response to “sports anemia,” which is commonly found in highly conditioned, aerobically trained athletes. Furthermore, this is considered to be a normal variant when found in the pattern described here.

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In an earlier study, hematopoietic bone marrow hyperplasia was detected incidentally in the distal femurs of 10 patients during routine MR imaging of the knee [1]. This finding was considered to be a benign process, observed mostly in mildly to moderately obese women, some of whom were cigarette smokers with associated peripheral leukocytosis [1].

During a recent study of asymptomatic marathon runners [2], we noticed that the MR scans of the knee frequently showed hematopoietic bone marrow hyperplasia in these athletes. Accordingly, we compared the frequency of hyperplasia of the hematopoietic bone marrow on MR examinations of the knee in asymptomatic marathon runners, in patients with symptoms of knee disorders, and in healthy volunteers.

Materials and Methods

The knees of three different groups of subjects were evaluated by MR imaging: group 1 = 74 asymptomatic volunteer subjects who had no prior knee surgery or injuries (average age, 35 years; 33 men, 41 women); group 2 = 54 symptomatic patients who had MR imaging to assess suspected meniscal and/or ligamentous abnormalities (average age, 38 years; 26 men, 28 women); group 3 = 23 asymptomatic marathon runners who had no prior knee surgery or injuries (eight men, 15 women; average age, 40 years; average number of years training, 10; average training distance per week, 41 miles). Differences in ages and relative number of men and women among the three groups were not statistically significant (chi-square statistical analysis).

MR imaging of the knee was performed with a 1.5-T MR scanner (Signa, GE Co.,

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Milwaukee, WI) and a send/receive extremity coil. The knee was positioned in the surface coil at an external rotation of approximately 15–20°. A routine MR examination of the knee was performed as follows: coronal T1-weighted (800/20, [TR/TE]), sagittal proton density–weighted, and T2-weighted (1800, 2000/20, 25, 70, 80) images were acquired with a 4- or 5-mm slice thickness, no interslice gap, a 128 × 256 matrix, and a 16- or 20-cm field of view [1–3]. MR images were reviewed by three radiologists, each with more than 5 years experience, who evaluated the images for evidence of hematopoietic bone marrow hyperplasia, which is characterized by regions of intermediate to decreased signal intensity on T1-weighted images that replaces the normal bright signal of fatty marrow [1]. The signal intensity of these areas did not change on T2-weighted images [1]. Hematopoietic bone marrow hyperplasia was best shown by the

Fig. 1.—MR image (800/20) of knee in an asymptomatic subject shows normal bone marrow in distal femur.

Fig. 2.—MR image (800/20) of knee in a symptomatic subject shows decreased signal intensity indicative of hyperplasia of red bone marrow. Area of decreased signal intensity is less than 25% of area of distal femur.

Fig. 3.—MR image (800/20) of knee in a marathon runner shows decreased signal intensity indicative of hyperplasia of red bone marrow. Area of decreased signal intensity is greater than 25% and up to 50% of area of distal femur. Epiphysis is spared, and proximal tibia is not involved.

Fig. 4.—MR image (800/20) of knee in a marathon runner shows decreased signal intensity indicative of hyperplasia of red bone marrow. Area of decreased signal intensity is greater than 50% of area of distal femur. Epiphysis and proximal tibia are uninvolved.
T1-weighted pulse sequence, so the T1-weighted coronal plane images were used for comparing the three groups.

Although hematopoietic bone marrow hyperplasia is known to occur in both the proximal tibia and distal femur [1], only changes on the distal portion of the femur were considered for the purpose of this study. The extent of hematopoietic bone marrow hyperplasia was assessed by determining the relative area of the entire distal femur with decreased signal intensity on the coronal section location with the greatest amount of involvement according to the following scheme: grade 0 = no decreased signal abnormality (Fig. 1); grade 1 = decreased signal intensity in an area less than 25% of the distal femur (Fig. 2); grade 2 = decreased signal intensity in an area greater than 25% and up to 50% of the distal femur (Fig. 3); and grade 3 = decreased signal intensity in an area greater than 50% of the distal femur (Fig. 4).

Results

The prevalence of hematopoietic bone marrow hyperplasia was 3% (2/74) in group 1, 15% (8/54) in group 2, and 43% (10/23) in group 3. The asymptomatic marathon runners had a significantly (p < .05) higher prevalence of hematopoietic bone marrow hyperplasia compared with the asymptomatic subjects and the patients. The symptomatic patients had a significantly (p < .05) higher prevalence of hematopoietic bone marrow hyperplasia compared with the asymptomatic subjects. The extent of hematopoietic bone marrow hyperplasia seen in the distal femurs of the subjects is summarized in Table 1. According to the classification scheme, the difference in the extent of marrow affected with hematopoietic bone marrow hyperplasia was not statistically significant among the three groups.

Discussion

The MR characteristics of bone marrow have been extensively described and discussed in the literature [1, 4–6]. With spin-echo pulse sequences, the fatty marrow is relatively bright on T1-weighted images [1, 5]. Cellular or hematopoietic marrow has a longer T1 relaxation time because of its lower fat content [1, 5]. On T2-weighted spin-echo sequences, the signal difference between the fatty and cellular marrow is smaller [1, 5]. Chemical-shift imaging techniques, including Dixon out-of-phase imaging, have shown additional contrast between hematopoietic and fatty bone marrow compared with conventional spin-echo imaging [5].

In the neonate, bone marrow is virtually all hematopoietic [7]. However, conversion from red (hematopoietic) to yellow (or cellular to fatty) marrow begins immediately [4, 5, 7]. This is a gradual, steady, and progressive process beginning from the distalmost points to the more proximal aspect of the long bones [4, 5, 7]. By approximately 25 years of age, the adult state of bone marrow has been realized, meaning that only the axial skeleton (pelvis, vertebrae, sternum, ribs, and skull) and the proximal shafts of the femora and humeri consist of hematopoietic marrow while the remainder of the skeleton consists of fatty marrow.

The location and extent of the relative amounts of hematopoietic and fatty components of bone marrow may be altered by the presence of disease [1, 5–7]. The numerous processes that cause this "reconversion" (i.e., increases in the amount of hematopoietic marrow present compared with the amount of fatty marrow) have been previously described and include such conditions as stress disorders or marrow replacement diseases (e.g., myelofibrosis or metastatic disease) [4, 7]. Other factors also shown to affect the reconversion of marrow are changes in oxygen tension, alterations in vascularity, and elevations in temperature [7].

Deutsch et al. [1] first described hematopoietic bone marrow hyperplasia seen incidentally in the peripheral marrow of healthy subjects during routine MR studies of their knees. Those study subjects were mostly women who were mildly to moderately obese, some of whom also had leukocytosis, presumably related to cigarette smoking [1]. The relationship between these two factors is unknown [1]. The higher prevalence of hematopoietic bone marrow hyperplasia found in the patients in the present study compared with the asymptomatic subjects is, likewise, unknown.

We suspect that the high prevalence of hematopoietic hyperplasia seen in the marrow of the asymptomatic marathon runners is the result of "sports anemia" in these subjects. Sports anemia is commonly found in physically active persons, particularly aerobically trained athletes, such as long-distance runners [8–11]. These otherwise healthy persons typically have chronically low or low-normal RBC, hematocrit, and/or hemoglobin levels [8]. This occurs especially in athletes whose training is rigorous [8]. Proposed causes of sports anemia include hemolysis, hematuria, gastrointestinal bleeding, excessive sweat loss, and/or an increase in plasma volume. The exact mechanism that produces this condition is unknown; it may be specific to an activity or result from a combination of factors [8–11]. For marathon runners, the conversion of fatty marrow to hematopoietic bone marrow may be a response to the anemia, similar to the hyperplasia of hematopoietic bone marrow seen with other forms of anemia [5].

Similar to the findings of Deutsch et al. [1], the MR findings in each of the subjects in our three groups showed epiphyseal sparing with respect to hematopoietic bone marrow hyperplasia.

Table 1: The Relative Extent of Marrow of the Distal Femur Affected by Hematopoietic Bone Marrow Hyperplasia

<table>
<thead>
<tr>
<th>Grade</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
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<tr>
<td>0</td>
<td>72 (97)</td>
<td>46 (85)</td>
<td>13 (5)</td>
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<tr>
<td>1</td>
<td>0 (0)</td>
<td>3 (6)</td>
<td>2 (9)</td>
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<tr>
<td>2</td>
<td>1 (1)</td>
<td>2 (4)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>3</td>
<td>1 (1)</td>
<td>3 (6)</td>
<td>4 (17)</td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td>54</td>
<td>23</td>
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Note.—Group 1 = asymptomatic subjects, group 2 = symptomatic subjects, group 3 = asymptomatic marathon runners. Grade 0 = no decreased signal abnormality, grade 1 = decreased signal intensity in an area less than 25% of distal femur, grade 2 = decreased signal intensity in an area greater than 25% and up to 50% of the distal femur, grade 3 = decreased signal intensity in an area greater than 50% of the distal femur.
sia. Of note is the fact that, in asymptomatic persons, the epiphyses and apophyses are not involved in hematopoiesis and contain fatty marrow as soon as ossification develops [5]. Reconversion of fatty to hematopoietic marrow occurs in the epiphyses and apophyses only under extreme conditions [5]. Therefore, this pattern of affected marrow may be useful for the differential diagnosis, indicating a less serious problem. The relative extent of marrow affected with hematopoietic bone marrow hyperplasia was variable among the subjects in this study and, therefore, the changes were assessed only semiquantitatively. Apparently, as the requirements for increased hematopoiesis develop, the response is graded such that the amount of marrow that reconverts from fatty to hematopoietic marrow is contingent on the needs of the subject [5].

While one limitation of this study is that there was no analysis of peripheral blood and/or bone biopsy performed on the marathon runners, it is unlikely that these extremely healthy persons had any of the reported conditions that may cause marrow reconversion (e.g., sickle cell anemia, osteomyelitis, chronic granulocytic anemia, Gaucher disease) [1, 5, 6], considering the extent of their training and the levels of athletic performance. Because MR imaging is routinely used for the examination of the musculoskeletal system of injured athletes [3], it is important to note that hematopoietic bone marrow hyperplasia in the pattern described in this study may be a normal finding in these cases.

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