Bone Marrow

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BONE MARROW: CHALLENGES FOR THE RADIOLOGIST

Far from being inert, the bone marrow is a dynamic organ. While composed primarily of water, protein (within cells), and fat, the relative amounts of each are variable not only from person to person depending on their physiologic requirements for the oxygen carrying capacities of hemoglobin but also in the same person over time. As one passes from infancy through childhood and into adulthood, the make-up of bone marrow changes. Just as there are normal variants in every aspect of anatomy, there are normal variants in bone marrow. However, the bone marrow is not immune to disease processes that alter its constituents and often replace them. Radiologists should understand the normal progression of the appearances of bone marrow as one ages, recognize normal variants and normal patterns, and then identify pathologic processes that are manifested by certain disease processes. Although the detection of bone marrow abnormalities is vital for early detection and treatment of disease, false-positive reports of marrow abnormalities can lead to unwanted procedures and the risk of unnecessary treatments. This article explains bone marrow contents and the normal progression of bone marrow changes as they occur throughout the aging process, and provides examples of pitfalls and variants that may simulate disease.

Much has been written in the literature regarding the pathologic changes in bone marrow with disease. Metastatic lesions in bone are approximately 30 times more common than primary bone tumors. The ability to detect these lesions has changed dramatically since the early 1970s when Damadian, Lauterbur and Mansfield began experimenting with magnetic resonance (MR) imaging. The increase in levels of water-bound proteins in metastatic deposits cause these lesions to exhibit signal characteristics that are different from the normal surrounding marrow. However, these lesions are often discrete foci of abnormal signal intensity and are therefore not difficult to detect on T1-weighted sequences, especially against the background high signal intensity of yellow marrow in adults and older children.

Far more challenging to the novice radiologist is the diffuse replacement of marrow in which the signal characteristics of the entire visualized marrow compartment are abnormal or there are symmetric changes. These abnormalities or changes can occur in physiologic and pathologic states, including in smokers, in people living at altitude, and in those with hematologic malignancies, and often as a result of therapeutic effects, including chemotherapeutic and radiotherapeutic effects. Challenges also arise in the pediatric population because of the highly cellular content of their bone marrow. Isolated marrow lesions can appear similar to red marrow on T1-weighted images, and diffuse marrow infiltration can be difficult to distinguish from diffuse hematopoietic marrow, particularly in the acute leukemias.

In these populations, other MR imaging sequences, such as dynamic contrast enhancement and quantitative serial assessments of the fat fraction of bone marrow, are often used to distinguish normal from abnormal bone marrow.

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BONE MARROW CONTENTS AND PHYSIOLOGY

From an imaging point of view, the main constituents of the medullary cavity of bone are osseous matrix and bone marrow, of which the latter is divided into red and yellow marrow. Osseous matrix is the cancellous bone that provides the architectural structure for the red and yellow marrow components. It is too simplistic to think of red marrow as being simply made up of cells and yellow marrow as being simply made up of fat; in reality it is more complex, with relative amounts of both present in all marrow (Fig. 1).

Bone marrow is made up of fat, water, and protein. The relative amounts of these components vary. In infants and children, red marrow is made up of approximately 40% fat, 40% water, and 20% protein. As one gets older, the relative amount of the fatty elements increase, and by the age of 70 years, red marrow consists of approximately 60% fat, 30% water, and 10% protein. This approximates the relative amounts of the contents of the yellow marrow, which is approximately 80% fat, 15% water, and 5% protein, irrespective of age.

Approximately 95% of yellow marrow is composed of adipocytes, and under the influence of a magnetic field and magnetic gradients, the protons within adipose cells behave differently from those within water; hence the difference in signal intensity.[1]

BONE MARROW SIGNAL INTENSITY

In newborns and infants, red marrow contains little if any fat, having very low signal intensity on both T1- and T2-weighted sequences. This signal is often equal to or lower than that of the adjacent muscle (Fig. 2). As the skeleton matures it contains an increasing amount of fat, which leads to increased signal intensity on both T1- and T2-weighted images (Fig. 3). On T1-weighted sequences of the lumbar spine in adults, for example, a useful internal reference is that the signal intensity of normal marrow is higher than the signal intensity of the adjacent intervertebral disk.[2] In general, the signal intensity of red marrow is usually higher than that of muscle on T1-weighted images. The exact signal intensity depends on several factors including the cellularity, lipid content, water content, surrounding trabecular bone, iron content of marrow and hematologic components contained within it, and of course the imaging sequence chosen.

On T2-weighted imaging, red marrow also tends be slightly brighter than muscle; however, the signal intensity can approximate that of fatty marrow, hence the need to perform T1-weighted imaging in which the contrast between the two is more pronounced. Fatty marrow, which as discussed contains approximately 95% adipocytes, tends to follow subcutaneous fat signal on both T1- and T2-weighted sequences, due to the short T1 relaxation times (spin-lattice relaxation times) and long T2 relaxation times (spin-spin relaxation times) of the fat protons within the hydrophobic groups contained in relatively heavy molecules.

Bone marrow abnormalities are clearly seen on short-tau inversion recovery (STIR) sequences, which are extensively used in the evaluation of bone marrow and its lesions. Normal fatty marrow has low signal intensity; however, the signal intensity of red marrow is intermediate, similar to that of muscle. STIR sequences are of great value in the evaluation of bone marrow pathologic conditions because of their increased detection of focal lesions in red and yellow marrow, and because they provide reduced motion artefact with fast imaging times.

Trabecular bone has little inherent signal because of its relatively low proton content, but contributes to T2 shortening because of the production of local magnetic field gradients. This effect of trabecular bone becomes even more

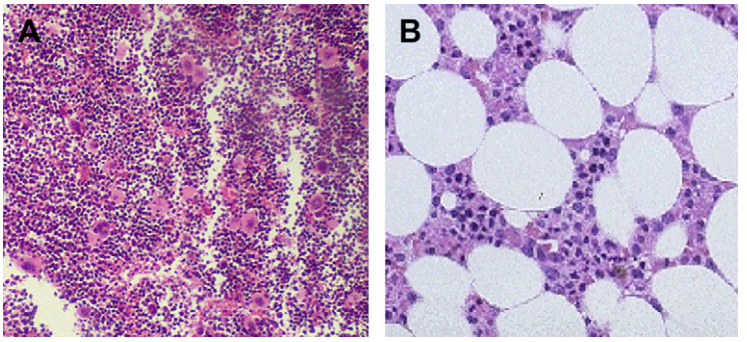

Fig. 1. Histologic specimens of bone marrow demonstrating highly cellular marrow (*A*) and fatty marrow (*B*) (hematoxylin and eosin, original magnification ×200).