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Normal Variants and Frequent Marrow Alterations that Simulate Bone Marrow Lesions at MR Imaging

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MR imaging of the spine is routinely performed for the assessment of patients with spine-related symptoms and of patients with cancer. This article addresses normal variants and frequent alterations of the vertebral bone marrow that are encountered on MR imaging studies and can simulate lesions.

MR imaging appearance of the normal vertebral marrow

MR imaging appearance of the vertebral marrow merely depends on the relative proportion of hematopoietic cells and adipocytes within the medullary cavity of the vertebral bodies [1,2]. Most lesions and normal variants interfere with this medullary water-fat balance and are best depicted on T1-weighted spin echo (SE) MR images [2].

Normal vertebral marrow of the adult human shows intermediate signal intensity on both T1- and T2-weighted SE images (Figs. 1 and 2). As a rule, signal intensity of normal lumbar vertebral bodies on T1-weighted SE images must be higher than that of adjacent intervertebral disk in an adult patient [3]. In the thoracic spine, marrow signal intensity can be lower than that of disk because the disk can show higher signal intensity on images than in the lumbar spine. In the pelvis, marrow signal intensity should be higher than that of adjacent normal muscles on T1-weighted SE images. On T2-weighted SE images, there is no internal standard with which marrow signal intensity can be compared. It is unreliable to assess the marrow status on T2-weighted SE images. On fat-saturated T2- or intermediate-weighted fast SE images, vertebral marrow signal intensity normally ranges from intermediate to moderately elevated. After intravenous injection of gadolinium-containing contrast material, enhancement of marrow signal intensity is barely visible at visual inspection on T1-weighted SE images (see Fig. 1). Signal enhancement of the intramedullary and perivertebral veins is visible on contrast-enhanced T1-weighted SE images. Signal enhancement can be more obvious on fat-saturated T1-weighted SE images or can be quantitatively assessed by performing dynamic MR imaging studies [4,5]. Usually, normal marrow signal intensity should not increase by more than 35% in adults above 35 years of age.

It is important to keep in mind that even a normal-looking T1-weighted SE image of the spine does not enable one to exclude marrow infiltration by abnormal plasmocytes or lymphocytes, probably in situations in which the water-fat balance is not sufficiently altered to become detectable.

Important interindividual variations in vertebral marrow appearance

There are important interindividual variations in vertebral marrow appearance among normal subjects.

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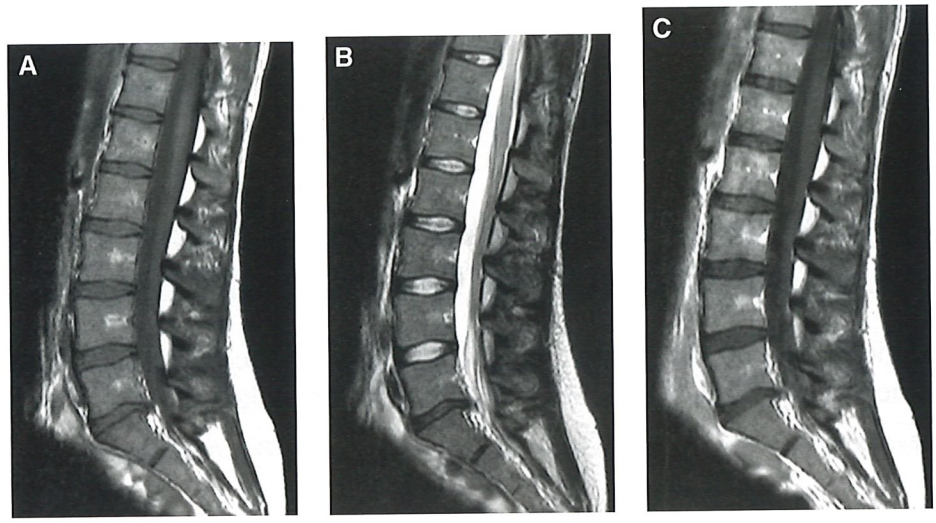

Fig. 1. Normal marrow. (*A*) Sagittal T1- and (*B*) T2-weighted spin echo (SE) of the lumbar spine of a 23-year-old woman show homogeneous marrow appearance with more fatty marrow around the vertebral veins. (*C*) On the gadolinium-enhanced sagittal T1-weighted image, moderate signal intensity enhancement can be seen, merely by noting the artifactual decrease in signal intensity of the intervertebral disk. Enhancement percentage was 70%, as determined on quantitative dynamic MR imaging study (not shown).

Vertebral marrow of young adults normally shows intermediate signal intensity on T1-weighted images. Other subjects of the same age range, however, can show unusual high marrow signal intensity with respect to their age. Conversely, some elderly subjects can show relatively low signal intensity marrow, instead of the expected age-related high signal intensity marrow on T1-weighted SE images. Although technical parameters may partially account for interindividual variability, interindividual variations in red marrow cellularity of the vertebral marrow probably play a role, whatever the causes.

Limited intervertebral variations in vertebral marrow appearance

There is limited variation in marrow appearance among vertebral bodies of the same subject, in contrast to marked interindividual variability in vertebral

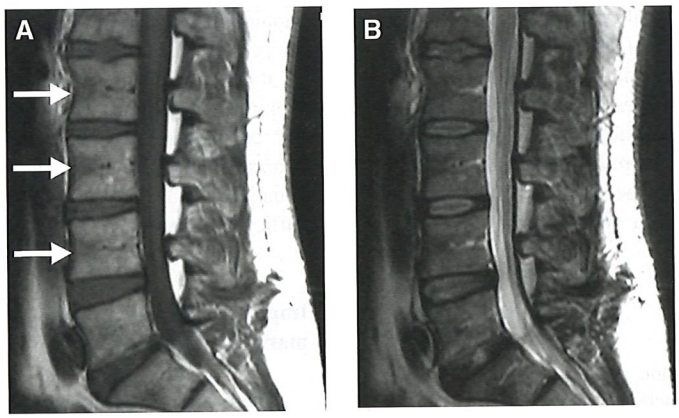

Fig. 2. Normal marrow. (*A*) Sagittal T1- and (*B*) T2-weighted SE of the lumbar spine of a 44-year-old man show moderate decrease in signal intensity in the anterior aspect of the vertebral bodies (*arrows*). Note that the same pattern of more cellular red marrow distribution is present in all vertebral bodies.

marrow appearance. Actually, several patterns of vertebral marrow appearance can be recognized that are systematically observed in all vertebral bodies of the same subject [6,7]. Red marrow is generally distributed in a homogeneous pattern within the vertebral body (see Fig. 1). Occasionally, red marrow is more cellular near the vertebral end plate, which is a metaphyseal equivalent, an area where the vasculature is generally more developed [8]. Red marrow can also be more cellular in the anterior aspects of the vertebral bodies (see Fig. 2). Finally, fatty marrow can become prominent around the vertebral basilar veins (see Figs. 1 and 2) [8]. As a rule, these variations in vertebral marrow MR imaging appearance should involve all vertebral bodies of the same subject in a similar manner (no or minor intervertebral variations).

Normal variants

Normal variants of vertebral marrow result from focal or diffuse changes in the amount of normal marrow components including fat and hematopoietic cells.

Islands of fatty marrow

At birth, vertebral marrow shows homogeneous low signal intensity. During growth, the proportion of marrow fat cells increases in a diffuse and homogeneous manner, a process called marrow conversion, which results in a progressive increase in marrow signal intensity on T1-weighted images with age [9]. During adulthood, conversion of red to yellow marrow continues at a lower pace and in a more heterogeneous manner than during growth. Foci of yellow marrow appear in the vertebral bodies (Fig. 3) [10]. Their frequency increases with age, but their number and size remain unaltered at short-term follow-up MR imaging study. As expected, these islands of fatty marrow show high signal intensity on T1-weighted SE images and low signal intensity on fat-saturated images. On non–fat-saturated intermediate or T2-weighted fast SE images, these areas show high signal intensity. They can be confused with significant marrow lesions. Analysis of the corresponding T1-weighted SE images or of fat-saturated images enables one to recognize their fatty composition, and their lack of clinical significance. CT images of these areas show normal trabecular and cortical bone. Bone scan shows normal or slightly decreased uptake in the corresponding area, if its size is large enough to enable their detection.

Islands of red marrow

Random variations in red marrow distribution occasionally do occur in addition to several patterns of vertebral red marrow distribution (see Fig. 3). Actually, cellularity of hematopoietic marrow can show spatial variations with the presence of islands

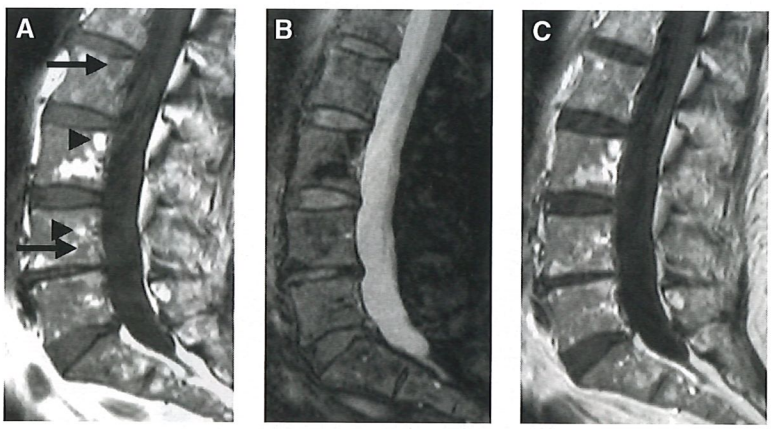

Fig. 3. Heterogeneous marrow. (*A*) Sagittal T1-weighted SE and (*B*) fat-saturated intermediate-weighted fast spin echo (FSE) of the lumbar spine of a 73-year-old woman with breast cancer show heterogeneous marrow appearance with islands of fatty marrow (*arrowheads*) and small nodules of more cellular marrow (*arrows*). Areas of more cellular marrow also show intermediate signal on fat-saturated image. (*C*) On the gadolinium-enhanced sagittal T1-weighted image, moderate signal intensity enhancement can be seen. This signal pattern remains compatible with normal heterogeneous marrow. A biopsy of the iliac crest was performed during breast surgery and showed hypercellular reactive hematopoietic marrow devoid of neoplastic cells.

of highly cellular hematopoietic marrow. These variations lead to the appearance of areas of more pronounced decrease in signal intensity than adjacent marrow on T1-weighted SE MR images. They occur in a nonpredictable manner, although they frequently involve the peripheral aspect of the vertebral bodies. Their margins are sharp if the marrow conversion process is advanced and fuzzier if the marrow conversion process is limited [11]. Occasionally, central areas of high signal intensity on T1-weighted images are present, which are an additional argument in favor of a normal variant. Presence of low-to-intermediate signal intensity on T2-weighted images, lack of evident signal enhancement on T1-weighted images after gadolinium injection, lack of trabecular bone changes on CT images, and lack of changes at follow-up MR imaging studies generally help to differentiate these benign heterogeneities from clinically relevant abnormalities [1].

Focal vertebral alterations that may simulate metastasis

Vertebral hemangioma

Vertebral hemangioma is a common vertebral lesion with a frequency of 12% in women and 9% in men (Fig. 4) [12]. Hemangiomas are multiple in about one third of cases [12]. They are generally asymptomatic. Histologically, they correspond to cavernous hemangiomas and contain dilated, blood-

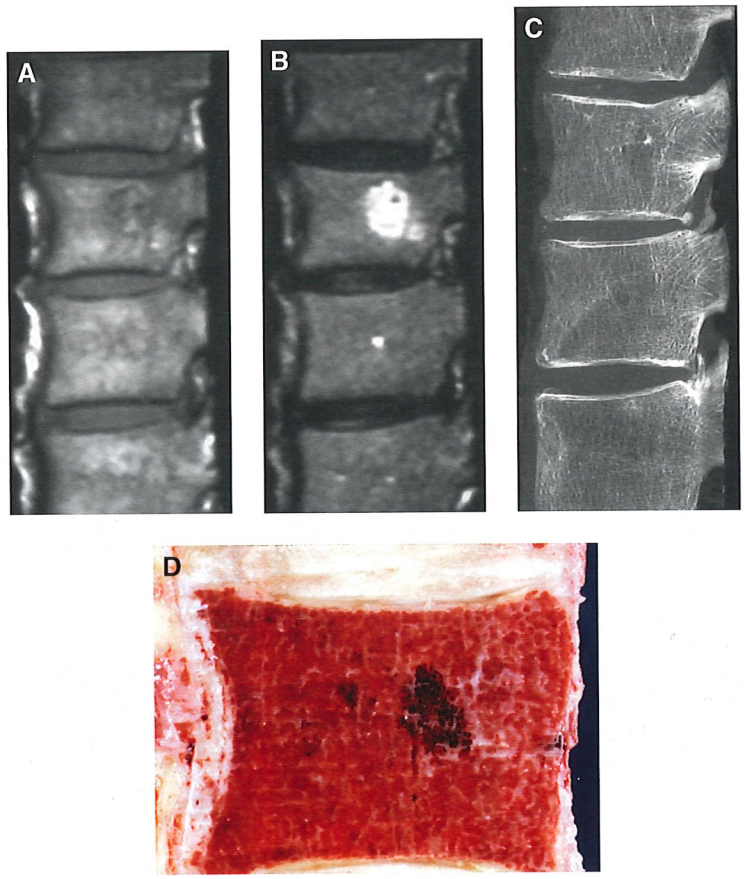

Fig. 4. Vertebral hemangioma. (*A*) Sagittal T1-weighted SE and (*B*) T2-weighted FSE of the lumbar spine of a cadaver specimen show an area of high signal intensity on T2-weighted image that shows almost normal signal intensity on T1-weighted SE image. There is a small punctate area of low signal within the lesion. (*C*) Radiograph of the specimen shows almost normal trabecular bone pattern with a small sclerotic island. (*D*) Photograph of the corresponding anatomic section shows a vertebral hemangioma with small punctuated area that corresponds to dilated vessels.

filled, vascular spaces lined by flat endothelial cells, set in a stroma containing large amounts of adipose tissue and no hematopoietic cells [13,14]. On T1-weighted SE images, signal intensity of asymptomatic vertebral hemangioma is higher to that of adjacent marrow (see Fig. 4) [15], although it can also be equivalent and not visible on T1-weighted images (Fig. 5). On T2-weighted SE images, its signal is consistently high (see Fig. 4). Presence of fat cells and dilated vessels with interstitial edema most likely accounts for its high signal intensity on T1- and T2-weighted images, respectively [16]. Frequently, punctuated or linear areas of low signal intensity are also seen on T1- and T2-weighted images, probably caused by the presence of thickened trabeculae. Signal enhancement of hemangioma after gadolinium injection is variable, depending on its appearance on T1-weighted images and the type of sequence that is obtained after contrast injection. Enhancement pattern can be homogeneous or peripheral.

Occasionally, asymptomatic vertebral hemangioma shows low signal intensity on T1-weighted images, with marked enhancement on postcontrast T1-weighted SE images (Fig. 6). These hemangiomas can be confused with significant marrow lesions. CT images generally show a rather specific trabecular

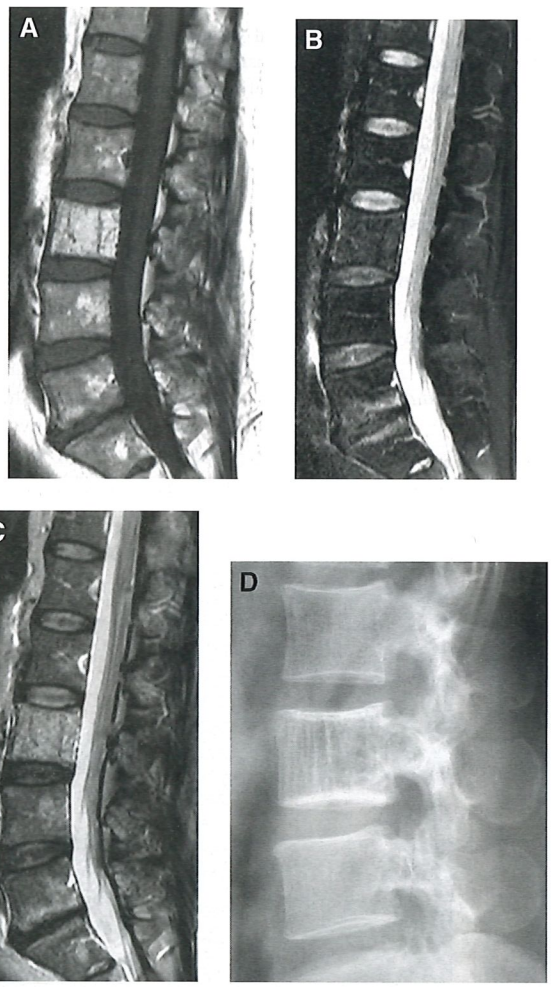

Fig. 5. Typical vertebral hemangioma. (*A*) Sagittal T1-weighted SE, (*B*) T2-weighted FSE, and (*C*) fat-saturated intermediate-weighted FSE images of the lumbar spine of a 54-year-old woman shows marrow change in the L3 vertebral body with high signal on T1, intermediate signal on T2, and subtle increased signal on fat-saturated intermediate-weighted FSE images suggestive of a vertebral hemangioma. (*D*) Lateral radiograph of the spine shows thickened vertical trabeculae without vertebral hypertrophy suggestive of vertebral hemangioma.

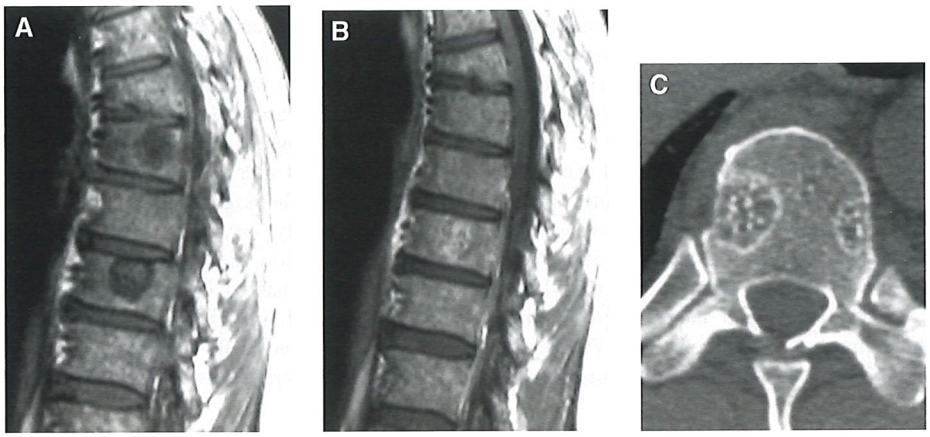

Fig. 6. Atypical vertebral hemangioma. (*A, B*) Precontrast and postcontrast sagittal T1-weighted SE images of the thoracic spine of a 69-year-old man show two areas of low signal intensity that enhance after contrast injection. (*C*) Axial CT image shows the typical appearance of a vertebral hemangioma. Rarely, hemangioma can show a nonspecific pattern of decreased signal on T1-weighted SE images.

bone pattern suggestive of vertebral hemangioma (see Fig. 6) [14,17], although small hemangiomas can remain occult of CT images.

The symptomatic vertebral hemangioma generally demonstrates low signal intensity on T1-weighted images with extraosseous component [14,17].

Vertebral enostosis: compact bone island

A compact bone island consists of lamellar cortical bone embedded within the trabecular network of the medullary cavity [18]. In a radiologic study of cadaver spine, their frequency was 14% and their size varied between 2 and 10 mm [19]. They frequently involve the periphery of the vertebral bodies and spare the central area [20]. Their signal intensity is very low on all sequences and adjacent marrow generally has a normal appearance (Fig. 7) [18]. Rarely, a peripheral high signal intensity rim surrounding a central low signal intensity area has been reported on STIR images of compact bone islands (Fig. 8) [21]. This pattern must be considered to be

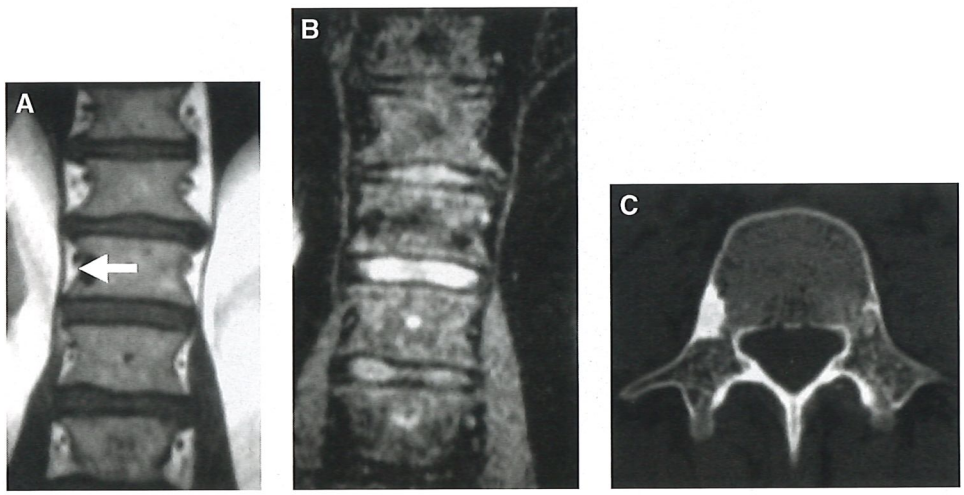

Fig. 7. Typical vertebral enostosis. (*A*) Coronal T1-weighted and (*B*) STIR images show an area of very low signal intensity in the right aspect of the vertebral body (*arrow*). (*C*) Axial CT image of that vertebral body shows a typical bone island, adjacent to the vertebral wall.

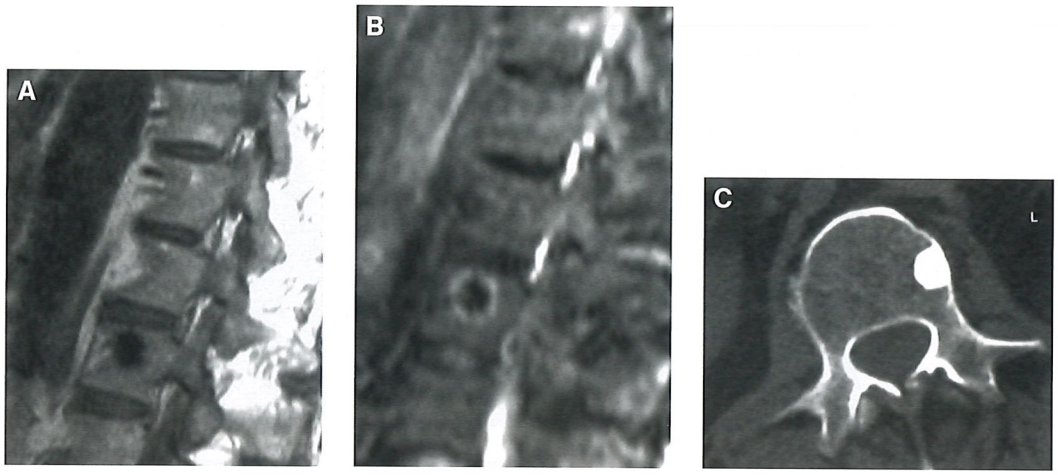

Fig. 8. Atypical enostosis. (*A*) Sagittal T1-weighted image of the lumbar spine shows an area of decreased signal intensity. (*B*) On the sagittal fat-saturated intermediate-weighted FSE image, the lesion shows a central area of low signal intensity and a peripheral rim of high signal intensity. (*C*) Axial CT image shows a vertebral enostosis. Bone scintigraphy (not shown) was normal. Rarely, vertebral enostosis may show a peripheral rim of high signal intensity on fat-saturated intermediate-weighted FSE images.

exceedingly rare and is more frequently suggestive of sclerotic metastases than an uncommon bone island.

Focal nodular hyperplasia of red marrow

Focal nodular hyperplasia of red marrow is the most extreme pattern of focal hypertrophy of the red marrow component (Fig. 9). It causes the presence of one or multiple nodules of decreased signal on T1-weighted images. It occurs relatively rarely in normal individuals but it is frequent in patients with regenerating hematopoietic marrow after marrow aplasia or in response to the administration of hematopoietic growth factors. Typically, the signal of these areas remains compatible with that of normal red marrow including moderate decrease in signal intensity on T1-weighted SE images, intermediate to low signal intensity of T2 fast SE images, moderate increase in signal intensity on fat-saturated intermediate- or T2-weighted fast SE images, and no or moderate enhancement after gadolinium injection. Most frequently, the nodule signal intensity is similar or slightly lower than that of the adjacent intervertebral disk [22]. Short-term follow-up MR imaging

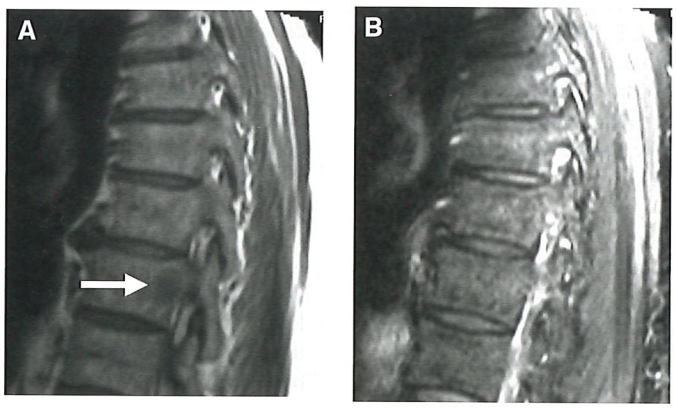

Fig. 9. Nodule of red marrow. (*A*) Sagittal T1-weighted and (*B*) fat-saturated intermediate-weighted FSE images of the thoracic spine of a 73-year-old man with lung cancer show an area of slight decrease in signal intensity (*arrow*). The signal of the lesion is similar to that of the intervertebral disk. Biopsy of another similar (larger) lesion in the same patient demonstrated normal but hypercellular marrow.

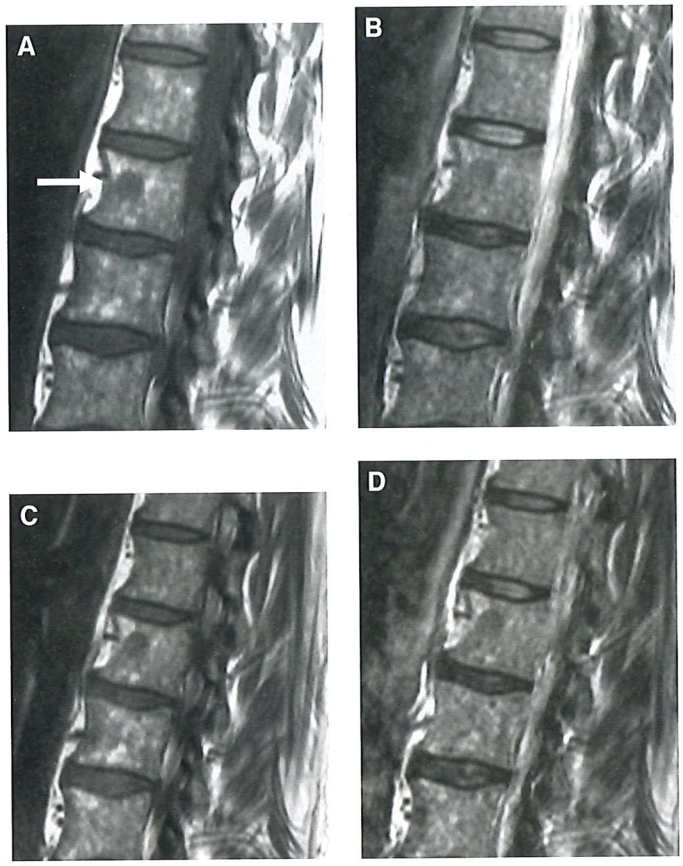

Fig. 10. (*A, B*) Sagittal T1- and T2-weighted SE images of the spine of a 56-year-old woman show an area of slight decrease in signal intensity (*arrow*). The signal intensity of the lesion is intermediate on T1- and T2-weighted SE images, and the lesion is compatible with an area of red marrow. Bone scintigraphy and CT scan were normal. (*C, D*) Corresponding images obtained 3 years later show no change in MR imaging appearance, increasing the likelihood of a nonsignificant marrow alteration.

study demonstrates no change in MR imaging appearance (Fig. 10). CT images and bone scan images should be normal. Experience with G6 PD fluorodeoxyglucose–positron emission tomography imaging is limited but these areas may show slight increased hypermetabolic uptake in comparison with adjacent red marrow [22].

Diffuse hematopoietic marrow hyperplasia

Diffuse hematopoietic marrow hyperplasia is defined by the presence of hypercellular hematopoietic marrow in the axial skeleton and by expansion of hematopoietic marrow in the appendicular skeleton (marrow reconversion). It occurs in response to numerous stimuli that trigger production of red marrow cells. Administration of hematopoietic growth factors during chemotherapy typically causes transient increase in marrow cellularity [23]. Several chronic disorders that are associated with anemia including hereditary hemoglobinopathies and chronic infection also cause red marrow expansion [24]. Diffuse red marrow hyperplasia is also observed in middle-aged obese women; in heavy smokers; and in subjects with intensive sports activities, such as long-distance running [25,26].

On T1-weighted SE images, hematopoietic marrow hyperplasia is associated with a marked decrease in signal intensity of vertebral marrow that becomes lower than that of adjacent disk (or gluteus muscles in the pelvis). Occasionally, hematopoietic marrow hyperplasia is heterogeneous because of the presence of residual fatty marrow and foci of red marrow. On T2-weighted SE images, vertebral signal intensity is low probably because red marrow hyperplasia is associated with an increase in the intracellular amount of iron. Intermediate signal intensity is observed on

fat-saturated intermediate-weighted images. After intravenous gadolinium injection, signal intensity enhancement is moderate but can increase up to 80% on dynamic T1-weighted SE images. In the appendicular skeleton, expansion of red marrow in distal limbs can be observed along with nodules of regenerating red marrow that can simulate bone metastasis.

Diffuse hematopoietic marrow hyperplasia can be confused with diffuse marrow infiltration in the spine and with focal metastases in the limbs [27]. As a rule, marrow hyperplasia shows a signal similar to that of red marrow. The signal intensity pattern of diffuse marrow infiltration by neoplastic cells can be different to that of red marrow. There are cases, however, in which confusion is possible. Several techniques can be used to differentiate red marrow hyperplasia from red marrow infiltration by neoplastic cells. In- and out-phase gradient echo images, T1 relaxation time determination, hydrogen proton spectroscopy, dynamic contrast MR imaging studies, and diffusion-weighted images have all shown to be of some help but none has demonstrated definite conclusive results. Fluorodeoxyglucose positron emission tomography imaging has also shown limitation in this setting because diffuse increased uptake can be observed in red marrow hyperplasia as in neoplastic medullary infiltration [28,29]. Obtaining a blind iliac crest biopsy may remain the more accurate technique to address this occasionally difficult problem.

Summary

MR imaging appearance of normal marrow shows important variations among individuals because of focal or diffuse alteration in the amount of yellow and red marrow. Nodules of hematopoietic marrow remain difficult to characterize, mainly because no single noninvasive imaging modality is able to demonstrate specific features. Diffuse red marrow hyperplasia remains a diagnostic challenge but is easily accessible to blind iliac crest biopsy, if necessary. Vertebral enostosis and hemangioma show a spectrum of changes on MR images but other imaging modalities may contribute to their characterization.

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