Pictorial review of bone marrow patterns in MRI.

Poster No.: C-1915
Congress: ECR 2016
Type: Educational Exhibit
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Keywords: Musculoskeletal bone, Musculoskeletal spine, Neuroradiology spine, MR, MR-Diffusion/Perfusion, Education, eLearning, Education and training

DOI: 10.1594/ecr2016/C-1915

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Learning objectives

The objective of this exposition is to describe the most common pathology of the bone marrow through a pictorial review of normal and pathologic patterns in MRI.
Background

MRI provides a non-invasive study of the bone marrow that defines its composition (cellularity, fat content...). The bone marrow components are: the trabeculae, the red marrow and the yellow marrow.

- The **trabeculae** is the architectural support for the marrow, which density decreases with age. The main function of trabecular bone is to be the mineral depot.
- The **red marrow** is composed of hematopoietic cellular elements, supporting stroma and vascular supply and it is characterised by containing 40% of water and its hematopoietic function.
- The **yellow marrow** is composed principally by fat cells (80%) and has a small fraction of red marrow elements and poor vascular supply.

Each component presents its own apperance on MRI pulse sequences that allows their differentiation. The red marrow is highly cellular so leads to a low signal intensity on T1-weighted sequences and high signal intensity on STIR or fat saturated T2-weighted sequences. On the other hand, the yellow marrow presents an increase signal on T1-weighted sequences and low signal intensity on STIR or fat saturated T2-weighted sequences.
Findings and procedure details

The distribution of the bone marrow components is modified with the age of the patient, physiologic stress and in the presence of pathology. The increasing age of the patient leads to a fatty conversion and low bone marrow cellularity. Moreover, it is characterised by a particular distribution pattern within the skeleton: it starts in the peripheral skeleton and progress centrally (Fig. 1). At birth all the marrow is hematopoietic (Fig. 2) and the conversion to yellow marrow begins in distal extremities (Fig. 3). The conversion finishes between 20-25 years, when the red marrow retained in axial skeleton and proximal metaphyses of long bones.

The bone marrow pathology could be classified according to common pathophysiological patterns into 5 different groups: infiltrative disorders, replacement disorders, depletion disorders, vascular disorders and others.

**INfiltrative Disorders**

The infiltrative disorders are caused by the proliferation of the native cells in the bone marrow due to benign or malignant conditions.

Marrow infiltration causes abnormal marrow signal intensity that is lower than that of muscle on T1-weighted sequences. On T2-weighted images, the signal intensity increases, although the lesions can be difficult to identify because of the poor contrast between the normal and abnormal marrow. This problem can be solved with fat-suppressed sequences. On STIR and fat-saturated T2-weighted sequences, tumor infiltration typically produces a high signal intensity that is greater than that of the red or yellow marrow. Reflecting the high water content of the neoplastic cells.

The most frequent benign process is the **marrow reconversion** or myeloid hyperplasia (Fig. 4). In cases of physiologic stress, the yellow marrow may suffer a reconversion to red marrow to supply a functional demand in order to increase the hematopoiesis. The reconversion can be caused by smoking, long distance running, obesity, middle age women, anemia, chronic diseases or after chemotherapy or radiotherapy (in non irradiated bone). Other benign conditions are myelofibrosis, polycythemia vera, mastocytosis and myelodysplastic syndrome.

Malignant diseases such as leukemia, multiple myeloma, amyloidosis and Waldenström’s macroglobulinemia are originated in the hematopoietic marrow. In **leukemia**, the
infiltration of bone marrow is typically diffuse, resulting in a diffuse decrease in marrow signal intensity on T1-weighted sequences (Fig. 5 y Fig.6).

In multiple myeloma, the infiltrative pattern on MRI is variable, ranging from normal to focal or diffuse. There are four main patterns recognised to classify the multiple myeloma: non visualized disease, micronodular ("variegated" or salt and pepper) (Fig.7), multifocal (Fig. 8) and diffuse marrow infiltration (Fig.9). Although diffuse disease may mimic the MRI appearance of extensive red marrow reversion, the signal intensity on fat suppressed T2 weighted sequences is generally considerably higher than that of muscle.

REPLACEMENT DISORDERS

The replacement disorders are due to infiltration of the bone marrow by cells that do not normally exist, for example osteomyelitis, primary bone tumours, metastasis or lymphomas. The MRI pattern is similar to the infiltrative disorders.

The osteomyelitis is characterised by the infiltration of the marrow by inflammatory cells that produce an increase in extracellular water or fluid which causes decreased signal intensity on T1-weighted sequences, an increased signal intensity on T2-weighted and fat suppressed images and contrast-enhanced (Fig. 10).

The distribution of neoplastic bone marrow involvement in patients with hematologic malignancies may be focal, multifocal or diffuse. The bone affection by lymphoma is more frequent from non Hodgkin lymphoma (NHL) than Hodgkin lymphoma (HL) (Fig. 11), meanwhile the bone primary lymphoma is rare. In patients with NHL, a focal or multifocal involvement is more common than diffuse infiltration patterns.

Primary bone tumours are a wide group of diseases that includes the osteosarcomas (Fig.12), enchondroma, osteochondroma, chondroblastoma, chondromyxoid fibroma, plasmocitoma, fibrosarcoma, giant cell tumor and many others. The MR study is indicated for the lesion characterisation, local staging and surgical planning. It can evaluate the intramedullary extension and invasion of the adjacent physeal plates, joints, muscle compartments and neurovascular bundles.

Metastasis localize in the red marrow because it has a richer blood supply than fatty marrow (Fig. 13). In adults, the common sites for metastatic lesions are the vertebrae, pelvis, proximal femoral metaphysis and skull. The metastases use to enhance after the administration of intravenous gadolinium, except the sclerotic metastases.
DEPLETION DISORDERS

The myeloid depletion is due to the loss of normal red marrow that could be in a regional or diffuse fashion. It is most commonly caused by chemotherapy, radiotherapy or aplastic anemia, but in many instances the cause is unknown. Aplastic or hypoplastic marrow shows diffusely high signal intensity on T1 and T2 - weighted sequences and decreased signal intensity on fat-suppressed sequences.

An effect of radiation therapy is marrow suppression which affectation depends on the radiation dose, volume of marrow treated and the treatment frequency. In the acute phase (day 1 to 3 of irradiation), the bone marrow develops an oedema, which appears hypointense on T1- weighted sequences and hyperintense on fat-saturated T2 - weighted and STIR sequences. After the gadolinium administration it presents a transiently increased enhancement on T1- weighted sequences. Later, on day 4-10, focal areas of haemorrhage can be detected (hyperintense on T1 and hypointense on T2/STIR). The pattern of increased signal on STIR images decreases over time between the third and sixth week after treatment. At this point marrow signal on T1- weighted sequences increases, corresponding to fatty marrow. After the sixth week, the majority of affected patients will have hyperintense T1 signal (fatty marrow) that can last up to 2 years (Fig.14). These marrow changes depend directly on the radiation dose. Local irradiation with doses in the range of 3-45Gy result in rapid bone marrow alteration which may persist up to 2 years. Regeneration of bone marrow is expected with local radiation doses below 30Gy, while doses above 50Gy will result in marrow ablation.

Chemotherapy in oncologic patients induces changes in the cellular composition and vascularity of the bone marrow that is reflected as oedematous marrow. During the first week of treatment, the bone marrow shows low signal intensity on plain T1-weighted sequences and high signal intensity on T2 - weighted and STIR sequences. Over time, with destruction of the myeloid elements and increasing fatty deposition, the marrow will show hyperintense T1 signal.

Aplastic anemia is a relatively rare condition characterized by anemia with pancytopenia on peripheral smear and hypocellularity of the bone marrow. A lot of cases are idiopathic, but it can be inherited (Fanconi anemia) or acquired (toxins, medications, infection...). On MRI, it tends to have diffusely hyperintense T1 signal but occasionally it can appear heterogeneous on T1 - weighted sequences with areas of patchy low signal corresponding to foci of fibrosis (Fig.15).
VASCULAR DISORDERS

The vascular disorders are due to oedema or ischemia.

The **bone marrow oedema** is the most frequent affectation of the bone marrow. It is caused by a nonspecific increase in water content that produces decreased signal intensity on T1-weighted sequences and an increased signal on fat-saturated T2-weighted and STIR sequences. The bone marrow oedema can be found in trauma (bone contusions and stress fractures), migratory osteoporosis, bone marrow oedema syndrome (Fig.16), tumours, sympathetic reflex dystrophy (Fig. 17), infections, early osteonecrosis (fig. 18) and articular affections.

**Bone marrow ischemia** favours fatty marrow over hematopoietic marrow, due to the limited vascular supply of yellow marrow relative to the red marrow. The ischemia can be caused by trauma, steroids treatment, sickle cell disease… (Fig 19)

OTHER DISORDERS:

**Paget disease** (osteitis deformans) is characterized by a disturbance in bone remodelling due to an increase in osteoblastic and osteoclastic activity. The result is a trabecular disorganization, fatty marrow and vertebral body expansion. It can present three phases:

- Hypervascular phase that presents signal decreased on T1-weighted sequences and mild high signal on T2-weighted sequences.
- Blastic or sclerotic phase shows low signal on T1-weighted and T2 weighted due to marrow fibrosis.
- On later stage can suffer a fatty transformation, with high signal on T1-weighted and T2-weighted sequences.

**Osteoporosis** can have a heterogeneous appearance due to decreased cellular marrow and increased fat component. On MRI sequences, it has heterogeneously hyperintense signal on T1-weighted, while signal can be variable on T2 weighted. There are several findings that range from accentuation of vertical and horizontal marrow lines, presence of subchondral lobules of fat, prominent bone vascularization or dotted foci of high signal intensity on T2-weighted fat-suppressed sequences.

**Serous atrophy** is attributed to the gelatinous transformation of bone marrow. It is characterized by fat cell atrophy, loss of hematopoietic cells and deposition of extracellular gelatinous substances. This pattern can be visualized in patients with anorexia nervosa, alcoholism, malignancies, chronic heart failure and HIV/AIDS.
Fig. 1: Normal developmental transformation of marrow in the skeleton. At birth, there is global red marrow (A). At childhood, there is fatty conversion of distal extremities (B). Finally, adults presents red marrow in axial skeleton and may have it at proximal metaphyses of femora and humeri.

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Fig. 2: Sagittal T1- weighted sequences (A), T2- weighted sequences (B) and STIR sequences that show the normal red marrow distribution in 2 years old child.

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Fig. 3: Normal developmental transformation of red marrow into fatty marrow in the long bones. It begins in epiphyses and apophysis (left), followed by diaphyseal conversion (middle). Residual red marrow may persist in proximal metaphyses (right).

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Fig. 4: Bone marrow reconversion in a woman with obesity and osteochondral injury on medial femoral condyle. Coronal T1-weighted sequence (A) in which there are patchy areas of hypercellular, hypointense marrow in the femoral diaphysis. These areas appear hyperintense on FS-PD-weighted sequence (B).

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Fig. 5: Leukemia: (A) Coronal T1 - weighted sequence shows an heterogeneous hypointense area at diaphysis and metaphysis of femur. (B) Coronal FS-PD-weighted image shows the corresponding area as hyperintense.

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**Fig. 6:** Chronic myeloid leukemia. (A&B) Axial and coronal T1-weighted sequences show heterogeneous hypointense areas at femoral head, neck and diaphysis. (C) Coronal T1-FS-PD-weighted image shows the corresponding hyperintense areas.

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**Fig. 7:** Variegated pattern: Coronal T1-weighted whole body sequence (A), sagittal T1-weighted (B) and STIR-weighted sequences show bone marrow micronodular hypointense infiltrates on T1-weighted and hyperintense on STIR.

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**Fig. 8:** Multifocal pattern: Coronal T1-weighted (A) and STIR-weighted whole body sequences (B) show multiple focal lesions (>5mm) on femurs, humerus, iliac bones, left clavicle and lumbar vertebrae. These lesions present low signal on T1-weighted and high signal on STIR sequences.

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Fig. 9: Diffuse pattern: Coronal T1-weighted (A) and STIR-weighted whole body sequences (B) show a diffuse decreased marrow signal on T1-weighted and high signal on STIR.

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Fig. 10: 11 years children with osteomyelitis in right hip. (A) Coronal T1-weighted sequence shows a focal lesion on femoral head that presents low signal intensity. The lesion presents high signal intensity on T2 GRE sequence (B) and enhancement on T1-weighted with iv contrast (C).

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Fig. 11: 11 years children with Hodgkin lymphoma (HL): (A) Focal low signal lesion in T1-weighted sequence located in the right anterior superior iliac spine. (B) In STIR sequences is characterised by its high signal intensity. This lesion is due to the infiltration of the lymphomatous disease.

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Fig. 12: (A and B) Axial T1-weighted sequences and (C) sagittal DP-SPAIR sequences that show an ossified mass on the iddorsal aspect of lateral femoral condyle of the left knee. There is irregularity of the posterior cortex of the femur and invasion of the medullary component. The findings are consistent with paraostal osteosarcoma.

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**Fig. 13:** 58 years man with pulmonary adenocarcinoma. Axial T1-weighted sequence (A) shows an hypointense lesion on lesser trochanter of the right femur with increased signal after contrast administration (B).

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Fig. 14: Patient with high-grade sarcoma on femoral biceps muscle, treated with surgery and radiotherapy. Coronal (A) and sagittal FS PD-SPAIR-weighted sequences show postradiotherapy changes in soft tissues and in femoral bone marrow. There are patchy areas of hyperintense signal.

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**Fig. 15:** Aplastic anemia secondary to azathioprine treatment: Coronal (A) and sagittal (B) T1-weighted sequences that show patchy areas of high signal due to fatty infiltration of the marrow.

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**Fig. 16:** 39 years pregnant woman with pain in groin. MRI sequences are acquired after birth and are consistent with bone marrow oedema syndrome. T1-weighted sequence (A) shows low signal intensity areas on both femoral heads and necks. FS-PD weighted (B) and T2-weighted sequence shows the respective hyperintense areas.

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**Fig. 17:** Patient with chondrosarcoma of the 5th metatarsal bone that has undergone surgery. During post-operative period, he develops sympathetic reflex dystrophy. Sagittal (A) and coronal (B) FS - PD weighted sequences show hyperintense patchy areas on bone marrow and soft tissue oedema.

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**Fig. 18:** Patient with right groin pain for 18 months. MRI study shows an advanced avascular osteonecrosis. Coronal (A) and axial (B) T1-weighted sequences shows the fracture line surrounded by hypointense areas that spread to the femoral head. Axial PD-weighted sequence (C) shows the respective hyperintense areas.
**Fig. 19:** Bone infarcts: two lesions in the femoral diaphysis and medial tibial plateau. They are characterized by irregular serpiginous margins with low signal intensity in T1 (a) and T2 (b) sequences, and intermediate to high fat signal in the centre.
Conclusion

MRI is the imaging modality of choice for the studio of bone marrow disorders, due to the identification of different patterns that allow to make the diagnosis of different pathologies.
References