Normal and Abnormal Bone Marrow

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Disclosure of Commercial Interest

Neither I or a member of my immediate family have a financial relationship with a commercial organization that may have an interest in the content of this educational activity.
Topics

- Normal Marrow Composition, Conversion, and Variants
- Marrow Hyperplasia, Reconversion, and Reconstitution
- Marrow Infiltration and Deposition Disorders
- Marrow Failure and Depletion Disorders
5-year-old, ? normal
Normal Marrow Composition, Conversion, and Variants
Composition of Bone Marrow

- Primal “brain food”
- Calorie and nutrient dense
Composition of Bone Marrow

Cancellous trabeculae
Stromal tissue
Hematopoietic cells
Fat
Red Marrow Composition

- Active in hematopoiesis
- Highly vascularized
- Color due to hemoglobin in erythroid cells
Red Marrow Composition

- Hematopoietic cellularity diminishes from near 100% at birth to 60% by adulthood
- Fat content increases with age
- By adulthood, composed of 40% fat
Yellow Marrow Composition

- Minimal hematopoiesis
- Paucity of vasculature
- Color due to carotenoids in fat droplets
Yellow Marrow Composition

- Predominantly fat in adipocytes
- 95% of cells are adipocytes
- By adulthood, composed of 80% fat
Marrow Signal Intensity on MRI

- Largely depends on the proportion of fat in the marrow
- On T1-WI, yellow marrow signal intensity similar to subcutaneous fat
Marrow Signal Intensity on MRI

- On T1-WI, red marrow signal intensity equal to or lower than skeletal muscle in infants

- On T1-WI, with aging through childhood, red marrow signal intensity becomes equal to or slightly greater than skeletal muscle and the inter-vertebral discs, but much less than subcutaneous fat
Marrow Signal Intensity on MRI

- On fat-sat T2-WI and STIR, red marrow signal intensity higher than yellow marrow and slightly higher than skeletal muscle.

- On opposed-phase GRE, red marrow signal dropout greater than yellow marrow.
Marrow Signal Intensity on MRI

- Gadolinium-enhancement greater in red marrow than in yellow marrow
- ADC values higher in red marrow than in yellow marrow
Age-Related Physiologic Pattern of Red to Yellow Marrow Conversion

- Older = fatter
Age-Related Physiologic Pattern of Red to Yellow Marrow Conversion

- Appendicular to axial
- Distal to proximal
- Diaphyseal to metaphyseal
- Central to subendosteal
Age-Related Physiologic Pattern of Red to Yellow Marrow Conversion

- Soon after ossification in the epiphyses and apophyses
Age-Related Physiologic Pattern of Red to Yellow Marrow Conversion

- No sex difference, except boys get fat heads quicker
Red to Yellow Marrow Conversion
T1-Weighted MRI

3-month-old

10-month-old
Red to Yellow Marrow Conversion
T1-Weighted MRI

6-year-old

16-year-old
Adult Distribution of Red Marrow

- Residual red marrow in primarily in the axial skeleton
Physiologic Red Marrow Residua in the Appendicular Skeleton

- Spotty or flame-shaped with base near physis
Physiologic Red Marrow Residua in the Appendicular Skeleton

- Slightly higher signal intensity than skeletal muscle
Tarsal Marrow Edema-Like Signal

- Seen in 60% of asymptomatic children and adolescents
- Talus, calcaneus > navicular, cuneiform > cuboid, MTs
- Patchy, sub-endosteal, bilateral and mostly symmetric
Tarsal Marrow Edema-Like Signal

- Microtrauma repair phenomenon with fibrovascular tissue and high bone turnover but no edema
Marrow Hyperplasia, Reconversion, and Reconstitution
7-year-old girl with sickle cell disease
Marrow Hyperplasia and Reconversion

- Replacement of yellow marrow by red marrow

- Conditions with increased hematopoiesis
  - Chronic hemolytic anemia (sickle cell, thalassemia)
  - Treatment with hematopoietic growth factors (G-CSF, GM-CSF, erythropoietin)
  - Increased oxygen demands or impaired oxygen delivery (smoking, high altitude residence, endurance athletics, cyanotic congenital heart disease)
  - Menorrhagia
  - Obesity
11-year-old girl with obesity and anemia
12-year-old girl with sickle cell disease

- Reconversion occurs in reverse order of normal marrow conversion
17-year-old with right femoral Ewing sarcoma on chemotherapy
Hematopoietic Growth Factor Therapy (G-CSF, GM-CSF, Erythropoietin)

- Low signal intensity on T1-WI can simulate or obscure neoplastic infiltration of the marrow
Transient Marrow Hyperplasia Induced by G-CSF

- Resolves 4-6 weeks after discontinuation of therapy

On G-CSF

Off G-CSF for 3 months
8-year-old with thalassemia, 75 days after bone marrow transplant

- Engraftment ensues 2-4 weeks after transplant, starting in the vertebral column.
8-year-old with thalassemia, 75 days after bone marrow transplant

- Engraftment complete by 3 months after transplant, but may not get full reconstitution of hematopoietic marrow
Marrow Infiltration and Deposition Disorders
5-year-old with shoulder pain, anemia and leukopenia
Acute Leukemia

- Diffuse low marrow signal intensity on T1-WI and high signal intensity on fat-suppressed T2-WI and STIR
- Bilateral symmetry may be misinterpreted as normal
- Marrow may appear normal if < 20% neoplastic cells
- ALL and AML cannot be reliably distinguished by MRI
6-year-old with fever, knee pain, and normal CBC
“Aleukemic” or “Subleukemic” Leukemia

- Can masquerades as an infectious, rheumatologic or orthopedic disorder
“Aleukemic” or “Subleukemic” Leukemia

- MRI can suggest the diagnosis before leukocytosis or blasts appear in the peripheral blood
5-year-old with ALL

Pre-Therapy

Post-Induction Chemotherapy
Marrow fat fraction increases in patients responding to chemotherapy
Regenerating red marrow can be indistinguishable from residual or recurrent leukemia
Leukemia Therapy Response Evaluation

Pre-Therapy

Post-Induction Chemotherapy

- No routine role for MRI
Marrow infiltration by malignant cells decreases the extracellular water fraction and restricts diffusion.

Marrow ADC values increase with effective leukemia therapy related to cell membrane compromise and an increased ratio of extracellular to intracellular water.
Diffusion MRI for Leukemia

- Diffusion values in normal marrow are widely variable in childhood.
- ADC values in untreated leukemia do not differ significantly from those in hyperplastic red marrow.
8-year-old with history of treated ALL
Relapsed Leukemia

- Suggested by finding well-defined marrow lesions
Leukemia Relapse Detection by MRI

- Can be detected by MRI several weeks before diagnosis by iliac bone marrow aspirate or biopsy, due to marrow sampling bias

- Must differentiate from marrow hyperplasia from G-CSF, osteonecrosis and stress injury related to osteopenia
3-year-old with constipation
Metastatic Neuroblastoma
Metastatic Infiltration of the Marrow

- Usually multifocal, but can be diffuse, most commonly in neuroblastoma, rhabdomyosarcoma or Ewing sarcoma

- MRI and FDG-PET are comparable in diagnostic efficacy

- Easier to detect in yellow than in red marrow
1-month-old with right foot sarcoma, marrow metastases
Metastatic Infiltration of the Marrow

- Difficult to discern from hematopoietic marrow

- Since tumor infiltration tends to replace marrow fat, loss of red marrow signal intensity on opposed-phase GRE suggests the absence of tumor infiltration

- Gadolinium-enhanced sequences increase specificity but not sensitivity

- Due to the effects of tumor treatment on the marrow, MRI is of limited utility in assessing for residual metastatic disease in the marrow
18-year-old with elevated ferritin and history of AML
Iron Overload

- Most commonly a consequence of numerous blood transfusions
Iron Overload

- Reduces marrow signal intensity, particularly on GRE T2*-W images, and on SE T1-W images at high iron concentrations.

- May also manifest with a reduction in signal intensity in other components of the reticuloendothelial system, such as the liver and spleen.
Marrow Depletion and Failure
17-year-old girl with pancytopenia

T1-W

Gad T1-W
Aplastic Anemia from Parvovirus B19 Infection

- Parvovirus B19 is cytotoxic to marrow progenitor cells
Aplastic Anemia from Parvovirus B19 Infection

- Parvovirus B19 infection is particularly detrimental in conditions with shortened erythrocyte lifespan
  - Sickle cell
  - Thalassemia
  - Spherocytosis
  - HIV
Aplastic Anemia

- Can be idiopathic or due to infection or drug reaction

- Abnormal extent of high marrow signal intensity on T1-W images reflects diminished hematopoietic marrow

- Loss of high marrow signal intensity on T1-W images
  - Transfusional hemosiderosis
  - Regenerative hematopoietic marrow
  - Development of clonal disease (myelodysplastic syndrome or leukemia)
9-year-old with ALL in remission and knee pain
Osteonecrosis (Avascular Necrosis, Bone Infarction)

- Geographic shape with “double line” sign of outer sclerotic rim and inner rim of vascularized granulation tissue or chondroid metaplasia
Osteonecrosis

- Sequence of hemorrhage, edema, liquefactive necrosis, granulation, fibrosis and sclerosis

- Associated conditions marked by adipogenesis, impaired perfusion, or osteocyte apoptosis
  - Sickle cell disease
  - Gaucher disease
  - Chronic renal failure
  - Bone marrow transplantation
  - Steroid therapy
  - Antiretroviral therapy for HIV infection

- Unusual in hematopoietic marrow, except in patients with hemoglobinopathies
ALL patient with bone pain and fever
Bone Marrow Necrosis

- Geographic lesions with peripheral enhancement and variable central signal intensity
Bone Marrow Necrosis

- Necrosis of myeloid elements, marrow fat and medullary stroma but preservation of bony trabeculae

- Distinct from osteonecrosis (less axial, less extensive)

- Associated with malignancy (especially ALL), sickle cell disease, infection

- Due to microvascular occlusion
19-year-old with sickle cell disease, acute leg pain and fever
Sequestered packed rbc’s increase T1 relaxivity leading to high signal intensity on fat sat T1-W images
15-year-old with sickle cell disease and acute bone marrow infarction

- Rim enhancement develops after several days and thickness of rim increases over time
Sickle Cell Acute Bone Marrow Infarction

- Detectable by MRI in 1/3 of acute pain crises

- Sickle cell disease predisposes to Staphylococcus and Salmonella bone infection

- Acute infarction and acute osteomyelitis can present identically with pain, swelling, fever, and leukocytosis

- Marrow edema and extra-osseous fluid collections commonly seen on MRI in both infarction and infection
Sickle Cell Acute Bone Marrow Infarction

- Bright marrow signal intensity on fat sat T1-W images may favor infarction over infection

- Infarction 50X more common than infection
Teenager with wrist pain and erythematous subcutaneous nodules
Pancreatitis-Associated Marrow Fat Necrosis

- Intra-osseous fat necrosis, polyarthritis and panniculitis
Pancreatitis-Associated Marrow Fat Necrosis

- Most commonly involves ankles, knees, and wrists
- Occurs in 2-3% of cases of pancreatitis
- 2/3 of cases with mild or no abdominal symptoms
- ? Due to lipolysis by pancreatic enzymes
15-year-old, post-XRT for extraosseous supraclavicular Ewing sarcoma
Radiation Therapy Effect on Marrow

- Sharply delimited by the radiation therapy portal
Radiation Therapy Effect on Marrow

- Edema and hemorrhage in the acute phase
- Replacement of hematopoietic marrow by fat and fibrosis in the chronic phase
- In young patients and at doses < 30-40 Gy, hematopoietic marrow may regenerate and fatty replacement may be incomplete
21-year-old with Pallister-Killian syndrome, knee cellulitis, ? osteomyelitis
Severe malnutrition
Gelatinous Transformation (Serous Atrophy) of the Marrow

- Focal loss of hematopoietic cells, fat cell atrophy, and deposition of gelatinous mucopolysaccharides

- Associated with scurvy, radiation therapy and cachexia (anorexia nervosa, cancer, AIDS)

- “Starvation marrow”

- Can be misinterpreted as technical error leading to unnecessary repeat imaging

- May mask stress fractures or osteomyelitis
Summary

- Awareness of deviations from the normal age-related process of hematopoietic to fatty marrow conversion is essential for recognizing many marrow pathologies on MRI in children.

- While a specific diagnosis may not be possible, recognition of patterns of marrow signal abnormality on MRI can refine the differential diagnosis.