MED437
King Saud University

RADIOLOGY 437 TEAM

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Editting File

Radiology of hematopoietic disorders

objectives:

1. Recognize the applications and limitations of radiology for various hematologic disorders
2. Understand the appearance of common forms of anemias and possible differentiation.
3. Identify the common locations and appearance of lymphoma
4. Explain the appearance of multiple myeloma

Sources

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Same 436 lecture Slides/Team:
YES

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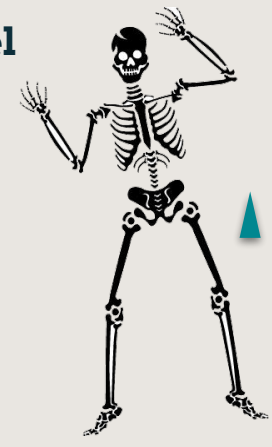
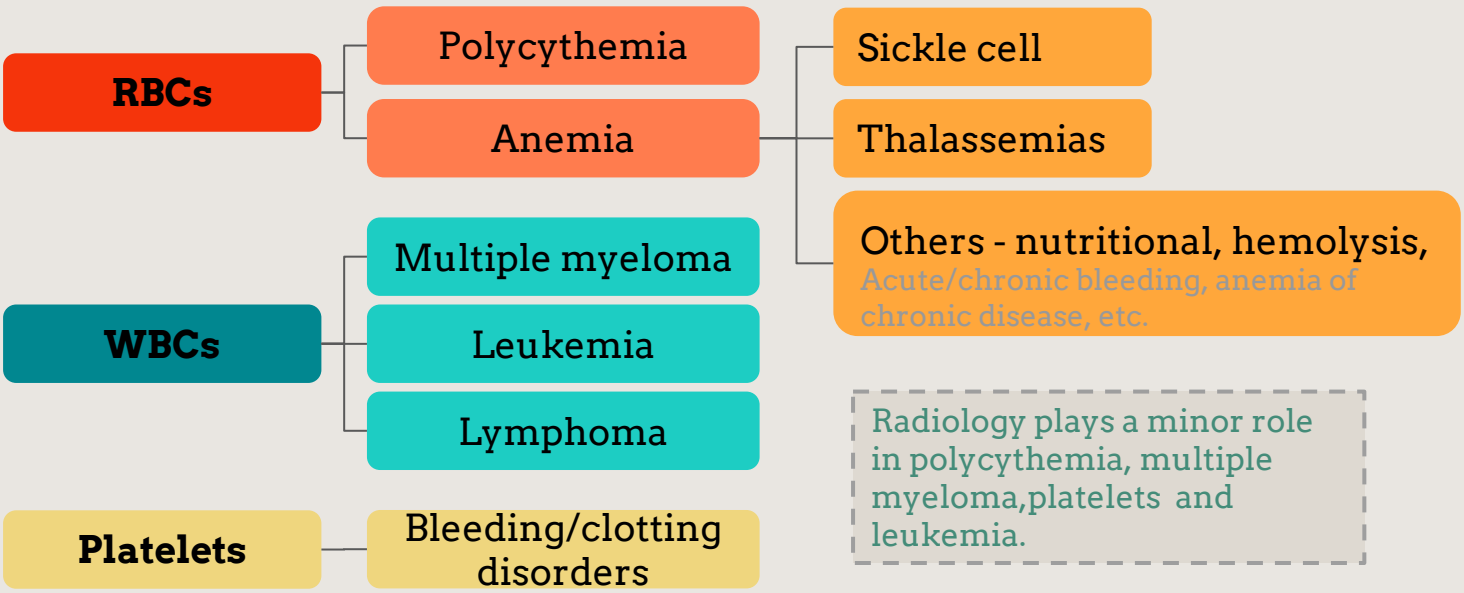


Introduction

Blood contents:

1. Cells: RBCs, WBCs, Platelets.
2. Plasma.



- Long standing/genetic anemia such as thalassemia and SCA, which are chronic (stay with the patient), will produce some signs (vs the others which are temporary types (hemolytic and nutritional).
- No Radiologic signs in polycythemia.

Anemia Features on imaging

Reactive increase in red bone marrow:

- First response: your body will increase the RBCs production in bone marrow, which is called intramedullary hematopoiesis.
- Expanded bone marrow in bones including long bones, more obvious in hands, feet, limbs, skull (seen on x-ray & CT) when the anemia has been there for sufficiently long time and SEVERE.
- Decreased T1 MRI signal in vertebral body bone marrow than adjacent discs.
- Visible on X-ray.

New marrow areas in potential organs:

- Extramedullary hematopoiesis: if the previous mechanism wasn't enough and the patient is still anemic, some other sites will try to synthesize RBCs. Or if the previous mechanism isn't working (aplastic anemia/myelofibrosis).
- But in normal adult these sites don't do hematopoiesis.
- These sites: Liver, Spleen, Lymph nodes, Thymus, Paraspinal areas with possible extension into spinal canal outside the dura, Kidneys, Meninges, Skin.

- It's rare nowadays to see extramedullary hematopoiesis in unusual sites like kidney, meninges, etc. because patients are diagnosed and treated early before they reach this severity.

Transfusions Iron overload

Not common
(Exogenous): in chronic anemia

- Some patients will develop iron overload if they have been treated with blood transfusion multiple time, because our bodies can't get rid of the iron, so it will be deposited somewhere, usually in liver and spleen brain (basal ganglia), pancreas ,etc.
- Increased CT density (brightness).
- Changes in MRI signal of liver & spleen.

Sickle Cell Anemia

doesn't go beyond the capillary

Infections:

(Common in sickle cell anemia more than other types of anemia)

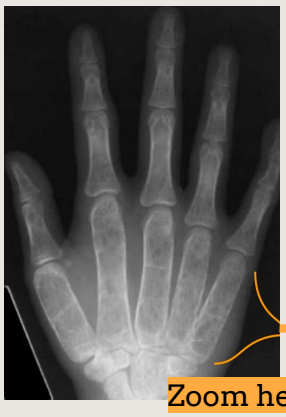
- Pneumonias, Osteomyelitis.

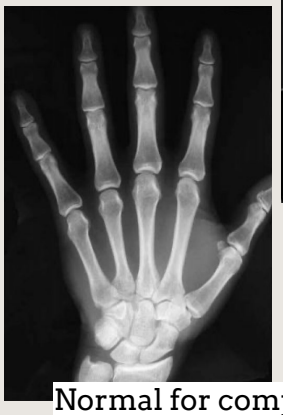
Infarcts:

- Anywhere in the body: Spleen "commonest", Kidneys (Kidney infarction is expected in sickle cell anemia), Brain, Bones.
- You can't specify which type of anemia the patient has depending on the radiologic features above (these above + previous slide), just say chronic/severe anemia.
- But if it's associated with infection/infarcts then the probability of SCA is high.
- If we correct the anemia, the extramedullary hematopoiesis will disappear.

Cases

01

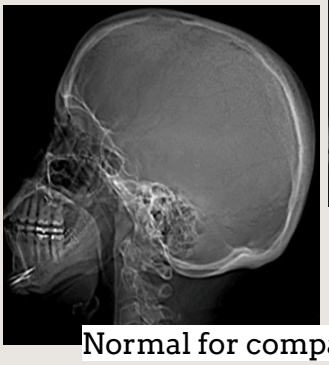



Normal for comparison

Features:

- Decreased bone density with coarse trabeculae, due to expansion in red marrow.
- Wide medullary cavity with thin cortex of metacarpal bones .
- Loss of concavity of metacarpal bones (expansion, bullet shaped, stubby bone, widening of the bones).
- Spongy bone.
- Remember that x-ray doesn't give you the diagnosis of thalassemia.
- Changes here can be seen in severe anaemia but it is classic for thalassemia.

02



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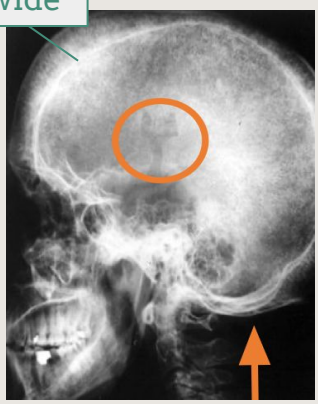
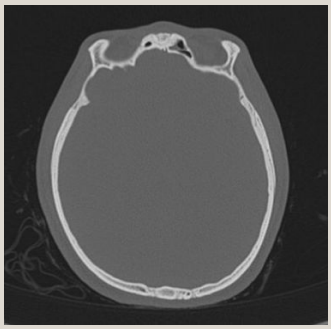
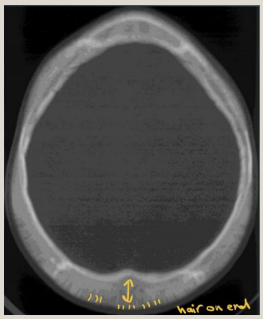


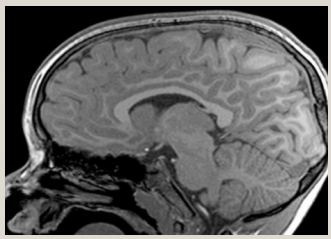
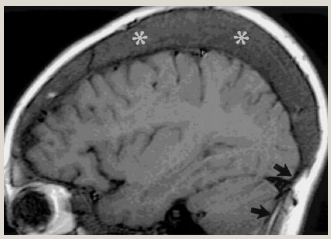
25-year-old man with **β-thalassemia**.
Lateral skull radiograph shows: Same sign as in with the hand.

- Outward expansion of diploic space with **hair-on-end** appearance.
- Widened groove for middle meningeal artery (circle)
- Spared occipital bone (arrow)

Anything seen in thalassemia can also be seen in severe anemia.

Normal for comparison	Axial CT image of upper skull
	

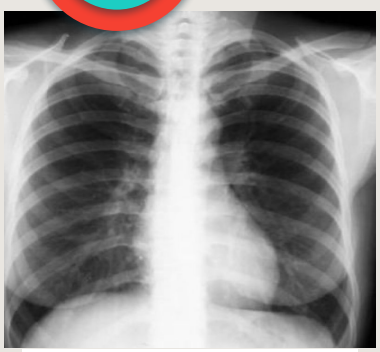
- Diploic space widening.
- Trabecular prominence.

Normal for comparison	Sagittal MRI of brain
	

- Diploic space widening representing hyperactive red marrow (*).
- Arrows → Spared occipital bone which has no marrow elements.

03

25-year-old man with β-thalassemia.
PA radiograph of chest (left).



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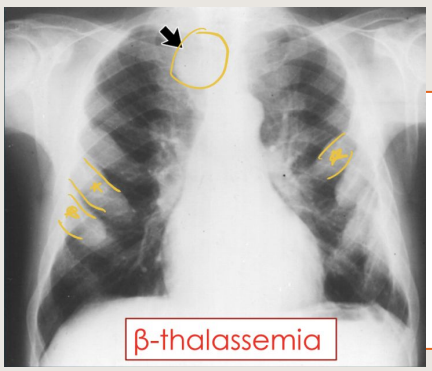
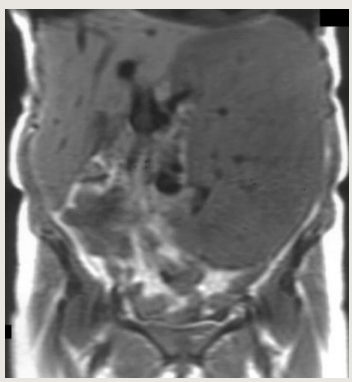


ribs are made of red marrow so expanding = hyperactivated red marrow

- ➔ Diffuse expansion of ribs.
- ➔ Arrow → right upper paraspinal thoracic mass compatible with extramedullary hematopoiesis.
- ➔ Increased brightness due to increased density of soft tissue.

04

51-year-old woman with myelofibrosis.
Coronal T1-weighted MR image:



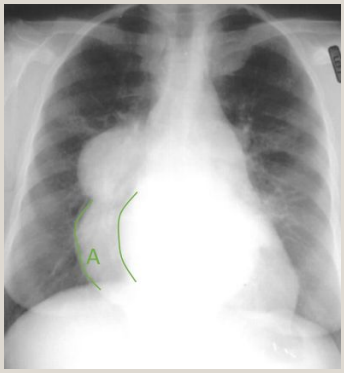
- Massively enlarged spleen 10 times bigger with a darker signal due to iron overload production.
- Splenic biopsy was followed by splenectomy.
- Pathologic examination revealed extramedullary hematopoiesis
- also common in non-functional bone marrow.

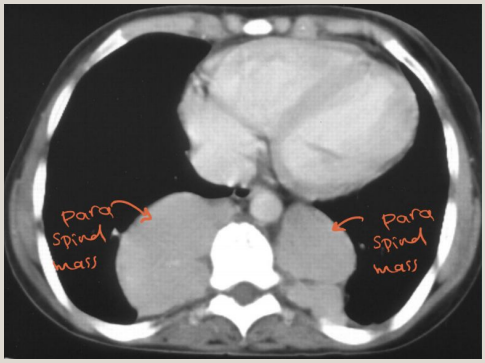
Extramedullary hematopoiesis = new area of hematopoiesis OUTSIDE of bone marrow. Myelofibrosis = Red marrow replaced by fibrous scar tissue. Which is why the body starts looking for new areas to make RBC.

05

23-year-old woman with history of thalassemia and known extramedullary hematopoiesis . Paraspinal area is one of commonest site of extramedullary hematopoiesis.

PA chest film (left) & Axial contrast-enhanced CT (right)



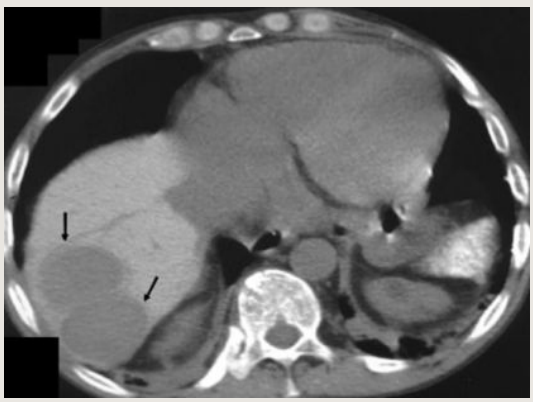


Well-marginated, bilateral, paraspinal masses compatible with extramedullary hematopoietic tissue.
No bone erosions means it's not an aggressive mass.
Click here to see the original picture

Uniformly enhancing bilateral paraspinal hemopoietic masses with NO bony erosion.
This is why it's not a sarcoma.
(A) Double density sign confirms mass in mediastinum. seen in Lymphoma, infection, TB, but if in thalassemia patient it means extramedullary hematopoiesis.

06

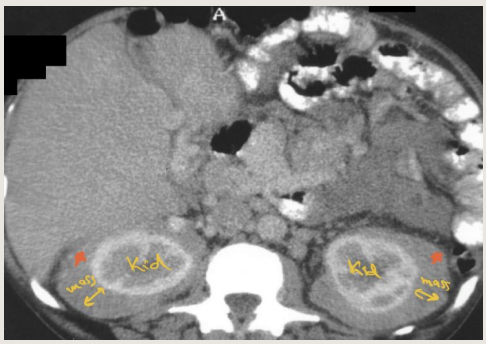
40-year-old man with sickle cell disease. Axial unenhanced CT scan at thoracoabdominal level. severe chronic anemia



- Arrows → two uniformly low-attenuation (compared with liver parenchyma), well circumscribed lesions.
- Percutaneous biopsy showed extramedullary hematopoiesis.
- Hyperdense liver due to iron overload because of multiple blood transfusions.

07

56-year-old man with myelofibrosis. Axial contrast-enhanced CT scan through kidneys:

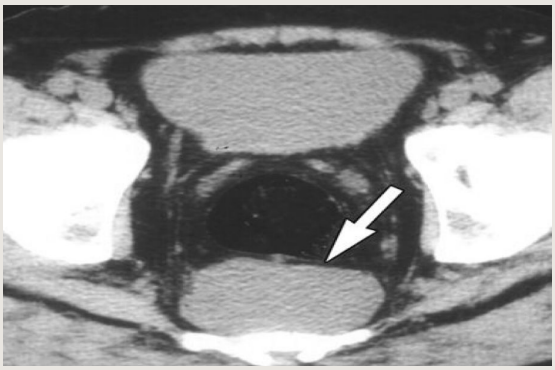


*soft tissue density

- Bilaterally symmetric enhancing perinephric masses.
- Biopsy showed extramedullary hematopoiesis.
- If we don't have a history and we won't be sure; it will be doubtful and may be mistaken by tumor and further investigation is needed.
- Severe chronic anemia with extramedullary hematopoiesis.

08

48-year-old man with hemolytic anemia and myelofibrosis.
Axial CT scan through pelvis shows:

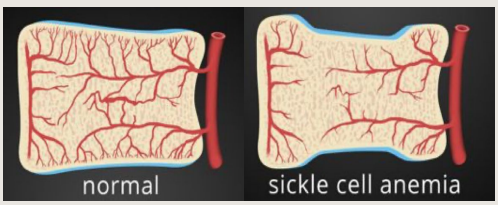


- Arrow → well-marginated presacral soft-tissue mass (typical sign).
- Any soft tissue mass below the rectum and sacrum is abnormal
- No bony erosion
- Biopsy (not often needed) showed extramedullary hematopoiesis.

Sickle Cell Disease

Click here to see the normal picture

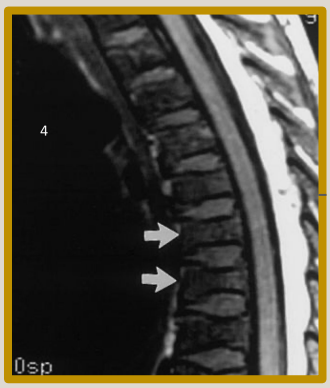
May be manifested as:



- Anemia:
  - Growth failure.
  - Hyperkinetic heart failure.
  - Expanded intramedullary hematopoiesis.
  - Presence of extramedullary hematopoiesis.
- Vaso-occlusive due to sickling:
  - Infarcts in spleen*, bone marrow*, kidney, bowel, brain*, muscles etc. *most common
- Superimposed infection due to splenic malfunction:
  - Pneumonia (Pneumococcus, H. influenzae, Staph. aureus, Chlamydia, and Salmonella).
  - Osteomyelitis (Salmonella) Very common.
  - Resistance against malaria.

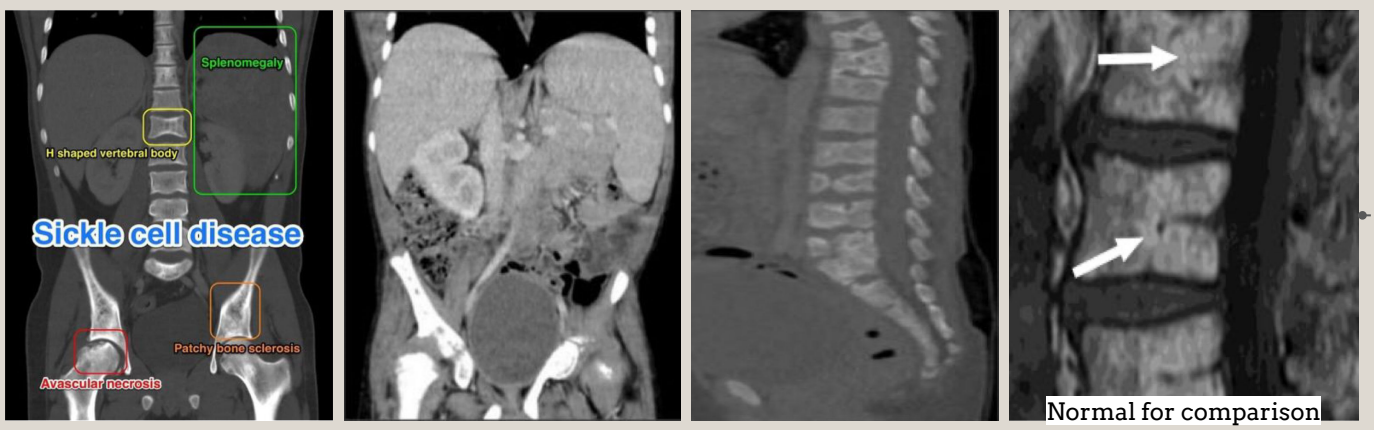
Cases

Red marrow in vertebral bodies in a 7-year-old girl with Sickle Cell Anemia.



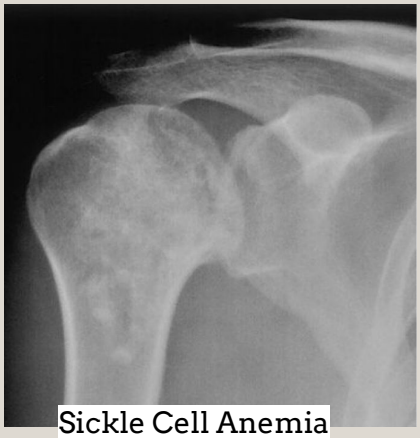
Sagittal T1-weighted MRI of spine shows:

- Low signal intensity in vertebral bodies compared to discs.
- H-shaped vertebrae (arrows in Pic 4) due to osteonecrosis of vertebral endplates. Can be seen in any kind of anemia not just sickle cell.
- H shaped vertebrae is characteristic of sickle cell due to central depression of end plate.
- depressed center due to avascular necrosis.
- if you see infarction with signs of anemia then it's highly suggestive of SCD.
- Other causes of infarction include idiopathic avascular necrosis , steroids ..etc.
- Bone infarcts typically occur in the medullary cavities and epiphyses.
- Epiphyseal infarcts are frequently seen in the femoral and humeral heads and more often bilateral than avascular necrosis due to other diseases.

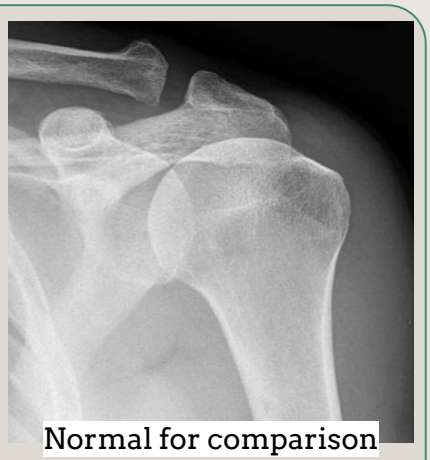


Frontal radiograph of right shoulder in a 22-year-old patient:

- Medullary bone infarcts in SCA.
- Area of patchy sclerosis and radiolucency.
- Infarcts usually seen in humours head / femoral head (big long bone) mostly bilateral.



Sickle Cell Anemia

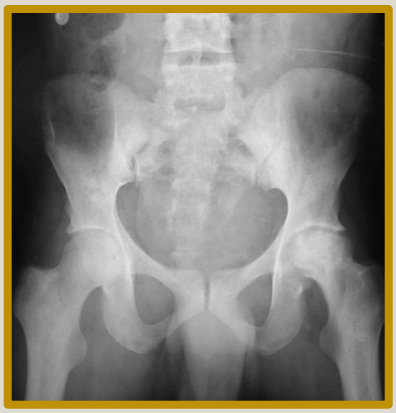


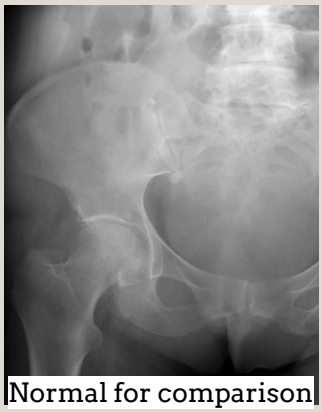
Normal for comparison

avascular necrosis heterogeneous bone infarction like an island.

AP radiograph in a 44-year-old man shows:

- Left hip → Advanced avascular necrosis. more sclerosis and intermittent area of lucency.
- Right hip → Normal.
- He also has secondary osteoarthritis.

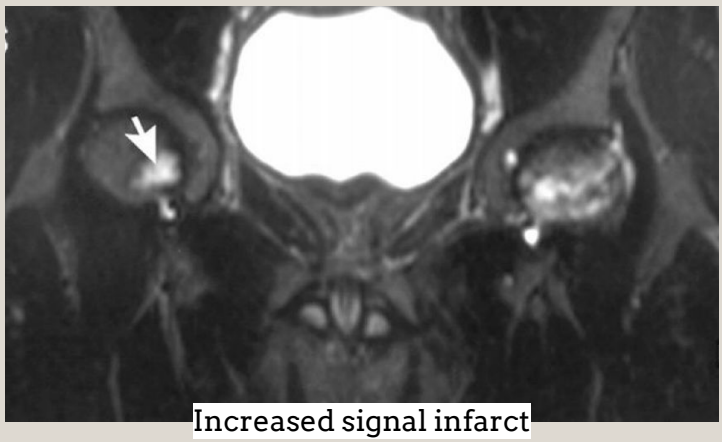




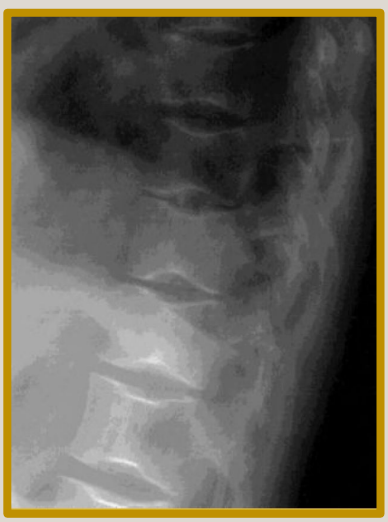
Normal for comparison

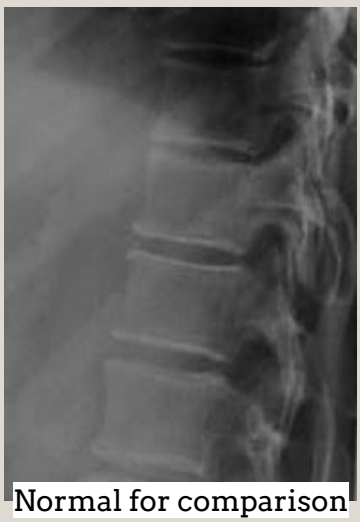
Coronal STIR MRI image in the same patient:

- Right hip → Stage 1 avascular necrosis
- Left femoral head → Advanced changes of avascular necrosis.
- It's important to keep in mind that X-ray modality is not sensitive to early stages of bone necrosis!! In this 44-year old case, x-ray only was able to detect the necrosis in its late stages, while MRI detected it even the early changes in the right hip!
- Bone marrow edema (white arrow) appears as an increased signal due to early bone infarction. Increased signal infarct
- Avascular necrosis = Bone infarction.



Increased signal infarct

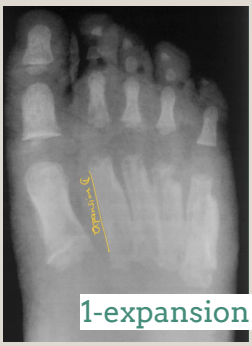




Normal for comparison

Lateral radiograph of spine shows: H-shaped vertebrae in a 15-year-old patient with SCA.

- Classic boxlike endplate depressions in middle portion (see the lowest vertebra shown) due to osteonecrosis (bone infarction) of the vertebral endplates.
- Here we can say he has sickle cell disease.

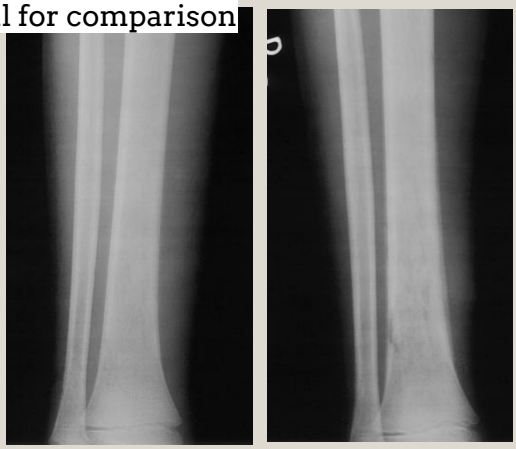


Hand-foot syndrome (Dactylitis) (infection of metatarsal bone) in SCA.

- Frontal radiograph of right foot in a 3-year-old girl.
- Thick periostitis and subperiosteal new bone along the metatarsal shafts. And metacarpal phalanges. Inflammation of the bone.

1-expansion 2-supposed to be concave 3-new bone formation

Normal for comparison

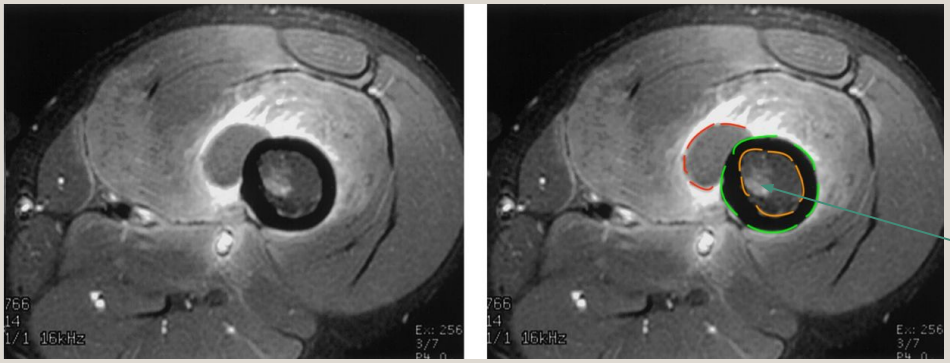


They have opportunistic infections:
Salmonella osteomyelitis in a 10-year-old boy with SCA.

- Left → Initial film at onset of lower shin pain and fever is normal.
- Right → Film 7 days later shows mottled lower tibial shaft and diffuse periostitis of the lower diaphysis.
- Moth-eaten appearance.
- Bone infections need 6 weeks to 6 months to heal.
- Bone infarcts and osteomyelitis are difficult to differentiate on history (pain + anemia), clinical examination and plain x-ray images but are very important to avoid
- complications of osteomyelitis.
- **The treatment will be different in both, so we need an accurate Diagnose, how?** Additional imaging (**best by MRI**, can be done by US) because in X-ray they are similar, If you see fluid/abscess collection → Infection , NO → Infarction.
- Infarction → Conservative and observation. While Infection → Antibiotic.
- **MRI findings that highly suggest infection:**
  - Cortical defects in bone.
  - Adjacent fluid collections (abscess) in soft tissue.
  - Bone marrow enhancement. All 3 = infection
- Ultrasound guided aspiration of fluid collection around the involved bone can be confirmatory.
- MRI is gold standard in differentiating between bone infarcts and osteomyelitis.

Osteomyelitis of femur in a 24-year-old patient with SCA.
Axial T1-weighted MRI after contrast shows:

- Heterogeneous enhancement of marrow cavity.
- Rounded low-signal-intensity area adjacent to the shaft that is non-enhancing (fluid collection).
- Enhancement of the soft tissues around the shaft and of the adjacent musculature.
- Areas of enhancement are likely infected.

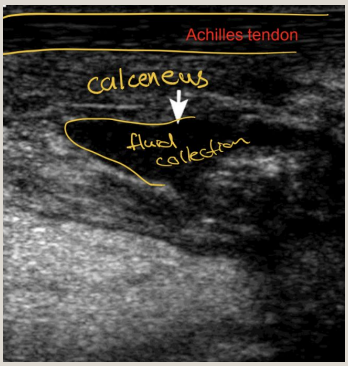


Red: Abscess.
Orange: Bone marrow.
Green: Cortex.

Enhanced bone marrow

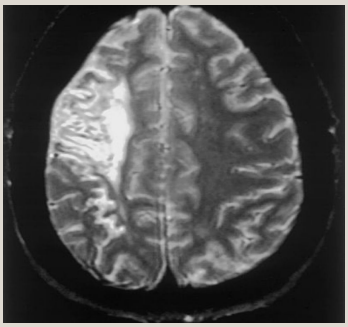
Soft-tissue infection in a 52-year-old man with homozygous sickle cell disease.
Longitudinal high-resolution ultrasound image of L. ankle shows:

- Arrow → hypoechoic (dark) fluid collection deep to Achilles Tendon.
- Thick pus was aspirated from this area under ultrasound guidance



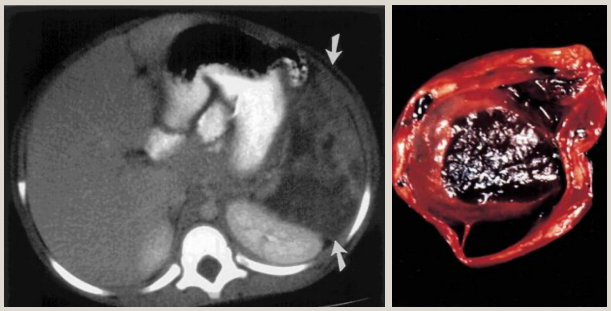
Chronic infarct in a 19-year-old patient with SCA and longstanding mild left sided weakness.
Axial T2-weighted MRI shows:

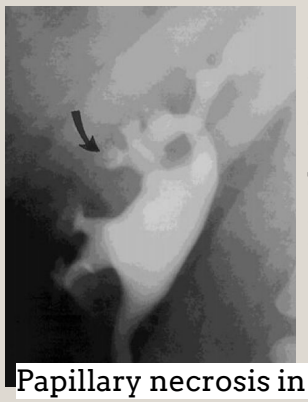
- Area of high signal intensity and enlargement of overlying CSF spaces, compatible with chronic infarction and atrophy.
- Infarction in right parietal lobe, unusual in normal person, but expected in SCA patient.



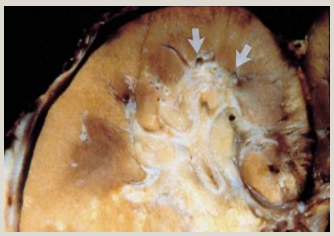
Sequestration syndrome with splenic infarction in SCA.
Axial CT after contrast shows:

- ➢ Enlarged spleen that enhances heterogeneously and minimally with large non-enhancing areas (arrows). Areas of infarction
- ➢ Photograph of spleen in a different patient shows areas of congestion and central necrosis.
- ➢ In Acute setting, splenectomy has to be done to prevent perforation & internal bleeding! because of high chance of rupture.
- ➢ Sequestration = infarction.




Papillary necrosis in SCA

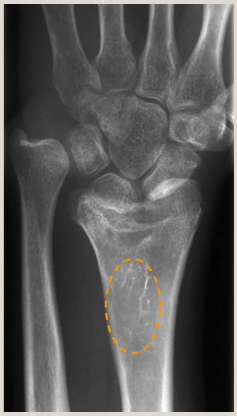
Frontal view of kidney during excretory urography in a 32-year-old man with SCA shows a small, round collection of contrast material in a missing **papillary** tip (arrow). contrast is leaking out
Papillary necrosis has a lot of causes, like pain killers (commonest), alcohol and SCA.



Photograph of a kidney from a different patient shows loss of papillary tips in some upper pole pyramids (arrows). Papillary necrosis and retrograde reflux of contrast. (typical sign).

Growth disturbance in distal radius in a 12-year-old girl.

- Anteroposterior (AP) radiograph of left wrist shows epiphyseal shortening and a cup deformity of adjacent metaphysis.
- Also changes of old bone infarct in distal radius.
- Early closure of growth plate.



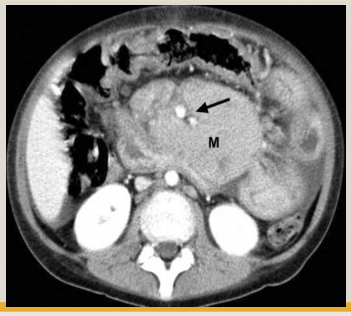
Lymphoma

- It's neoplastic proliferation of the lymphocytes.
- Again, radiology has no role in diagnosing the subtypes of lymphoma, but we can identify the disease extent because sometimes it's hard to do physical examination of these masses especially if it is in a deep location ex: near the aorta.
- Most of the time we do CT ,,, MRI takes long time.
- Imaging has two role: Staging and guiding the biopsy if no other accessible lymph node is available.

Hodgkin's Disease (Classical)	Non Hodgkin's Lymphoma
❑ Lymphocytic predominance. ❑ Mixed cellularity. ❑ Lymphocytic depletion. ❑ Nodular sclerosis - the most common. ❑ Most common in cervical and mediastinal.	❑ Burkitt lymphoma (jaw and abdomen) due to viruses like EBV virus. ❑ Burkitt-like lymphoma (abdomen and nodes). ❑ Large B-cell lymphomas (abdomen and nodes) most common seen type DLBC. ❑ Lymphoblastic lymphoma (Mediastinum, nodes, bone marrow). ❑ Anaplastic large cell lymphoma (Nodes, skin, soft tissue, bone). ❑ Other peripheral T-cell lymphomas. ❑ MALT lymphoma. ❑ Seen in everywhere.

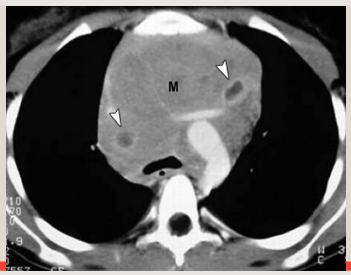
Lymphoma can present as mass anywhere in the body

Cases

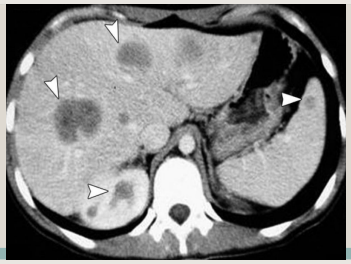


Non Hodgkin's Lymphoma (NHL) in an 11-year-old boy.
Axial CT scan with contrast shows:
- Large lymphomatous mass (M)* encasing the mesenteric vessels (arrow).
- Lymphoma mass does not compress or invade, it encases it respects other surrounding structures. (very typical)

*fluffy mass & it's not compressing on the vessels but encasing them instead



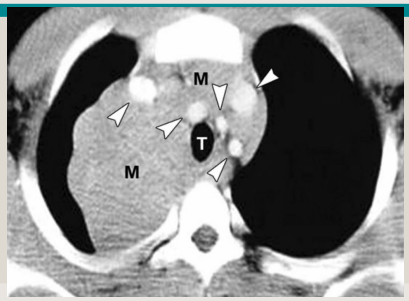
NHL in a 14-year-old boy.
Contrast-enhanced CT scan shows:
- Large anterior mediastinal mass (M) that originates from thymus.
- A few cysts with central low attenuation and a peripheral enhancing ring are present (arrowheads).
- Decreased blood supply in the center.

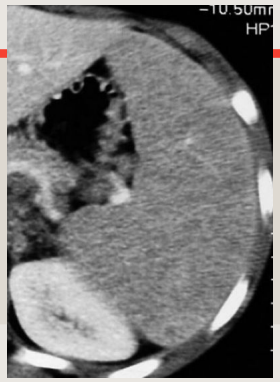


NHL in a 16-year-old girl.
Contrast-enhanced CT scan shows:
- Low-density lesions (arrowheads) in both hepatic lobes, with small nodules in spleen and right kidney.

HD in a 17-year-old boy.
Contrast-enhanced CT scan shows:

- Large mediastinal mass (M). Trachea (T) is compressed, and great vessels (arrowheads) are displaced.
- Fluffy mass is lymphoma until proven otherwise



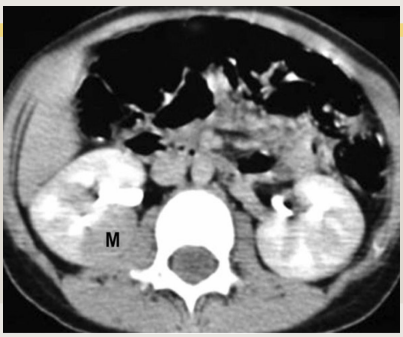


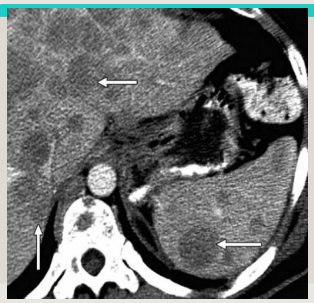
HD in a 12-year-old girl.
Contrast-enhanced CT scan shows:

- Enlarged spleen with a diffusely inhomogeneous appearance hypodensity of spleen. common to have splenic involvement (kidney & liver is rare)

NHL in a 14-year-old boy.
Contrast-enhanced CT scan shows:

- Single well-defined, low density mass (M) in right kidney.
- Primary renal lymphoma (very rare to find organ involvement without lymph node involvement).
- RCC is first diagnosed when you see a kidney mass but could also be caused by the lymphoma



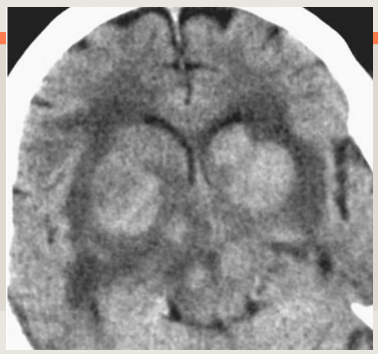


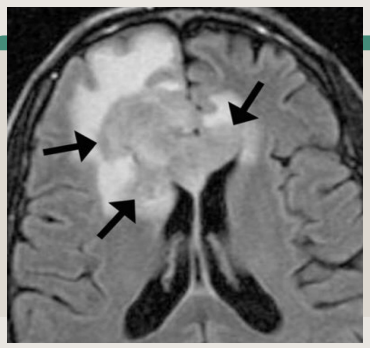
Axial CT scan shows:

- Diffuse hepatosplenic involvement in lymphoma.
- Multiple round, homogeneous, low density nodules (arrows) in liver and spleen.

72-year-old immunocompetent woman with primary CNS non-Hodgkin's B-cell lymphoma.
Unenhanced CT image shows:

- Classic hyperdense masses involving deep white and gray matter.
- Hyperdense basal ganglia.



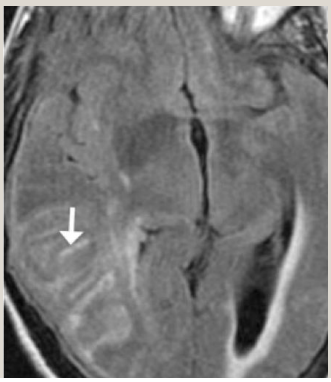


44-year-old HIV-positive woman with primary CNS non-Hodgkin's B-cell lymphoma.
Axial FLAIR MRI shows:

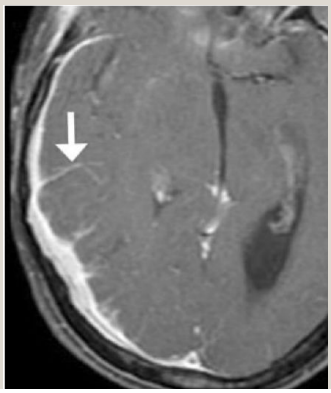
- Lesion isointense to gray matter (arrows).
- Expansion of white matter.

63-year-old woman with primary meningeal lymphoma.

- MRI shows hyperintensity and enhancement (arrows) involving sulci and leptomeninges.
- First differential diagnosis is infection (meningitis).



Axial FLAIR MR images



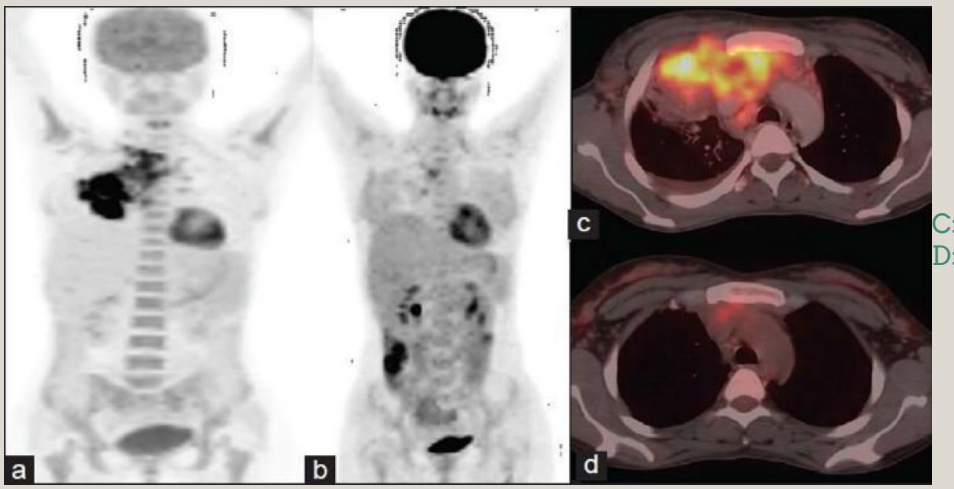
Post contrast T1 weighted MR images

Leptomeningeal enhancement

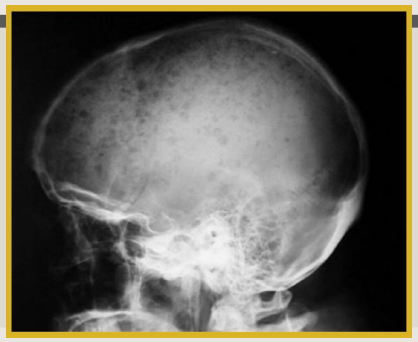
Diagnosis of lymphoma:

- If accessible area, then open-surgery-Biopsy is often performed (e.g. Axilla and groin).
- If not accessible, CT guided biopsy is done to reach final diagnosis.
- MRI is not commonly used unless you suspect a lymphomatous lesion in a specific area (e.g.brain)!! (forget about MRI, it's NOT used to assess lymphoma (patient can't wait for 3-4 hours for you to visualize his body, while you have an excellent modality (CT scan) that takes only 2-3 mins!!!).

PET-CT IS GOLD STANDARD TO DIAGNOSE AND FOLLOW UP THERAPY.



C: Active disease.
D: After chemotherapy.



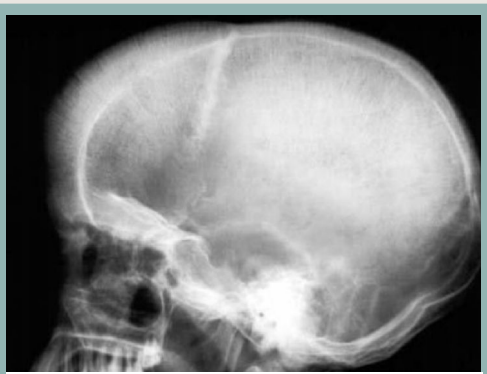
Lateral skull radiograph shows:

- Multiple very sharply outlined (punched out) lytic lesions of multiple myeloma.
- This sign appears late in advanced stage and we don't see it because we usually diagnose it early.

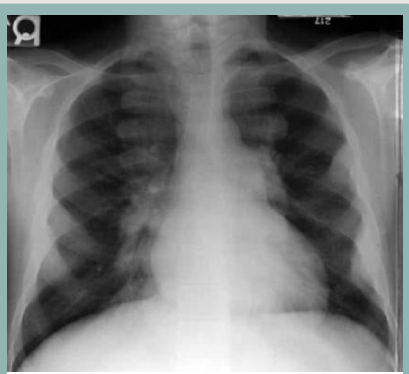
Questions by Dr. Alhawas:

Q1/ Findings shown here can be seen in:
1. Any severe chronic anemia.
2. Thalassemia.
3. Sickle cell anemia.
4. Lymphoma.

Findings:



Hair on end, Normal occipital bone & Expansion of diploic space



Widening of ribs = hyperactive red marrow

SUMMARY

- **Intra**medullary hyperplasia can be seen in Thalassemia, Sickle cell anemia, Iron deficiency anemia, Any severe chronic anemia except bone marrow failure.

  Signs of INTRA medullary hyperplasia include:

1. Expanded bone marrow in bones including long bones of hands, feet, limbs, skull.
2. Decreased T1 MRI bone marrow signal than adjacent discs.

- **Extra**medullary hematopoiesis can be seen in ALL SEVERE CHRONIC ANEMIAS. Sites of extramedullary hematopoiesis include Liver, Spleen, Paraspinal areas with possible extension into spinal canal outside the Dura, Kidneys, Meninges, Skin, Lymph nodes, Thymus.

  Extramedullary hematopoiesis appears as homogeneous soft tissue masses on imaging.
- INFARCTS and INFECTIONS are additional findings in Sickle cell anemia.
- Bone infarct vs infection it is important to diagnose early so that antibiotics can be started early to prevent complications. MRI with contrast and ultrasound/CT guided aspiration of fluid collections are very helpful if imaging is unable to differentiate these two.
- Multiple myeloma produces punched out lytic lesions in bones with background bone appearing normal. Opposite to bony metastases, myeloma more often involves intervertebral discs and mandible, and less often involves pedicles.
- Lymphoma can produce a mass anywhere in the body. CT is often used to scan whole body to evaluate the disease extent (staging), and to do CT-guided biopsy to make tissue diagnosis if not already diagnosed. Rest is all by laboratory and clinical based.

QUESTIONS

1. What is the classical sign in sickle cell anemia?

a) Moth-eaten appearance.

b) H-vertebrae.

c) Bilateral perinephric mass.

d) Anterior mediastinal masS.

2. All signs seen in thalassemia can also be seen in chronic severe anemia?

a) true

b) false

3. What is the first sign we can appreciate in response to reduction of RBCs?

a) New marrow areas in potential organs.
b) Reactive increase in red bone marrow.
c) Transfusion iron overload.
d) Punched out lytic lesions.

4. What is the gold standard for diagnosis and follow up of lymphoma?

a) MRI

b) CT without contrast.

c) CT with contrast.

d) PET-CT scan.

5. which one these MRI findings is suggestive of infection :

a) Adjacent fluid collections in soft tissue.
b) Cortical defects in bone.
c) Bone marrow enhancement
d) all of the above

1-b
2-a
3-b
4-d
5-d

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