Radiology of Hematopoietic Diseases and Anemia

Lecture 26

Objectives

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

Color index:

Black: Main text

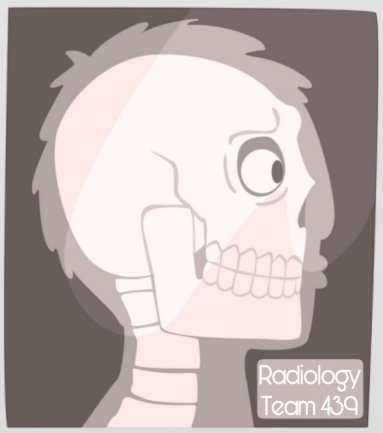
Red: Important

Yellow: Golden notes

Green : Drs notes 439

Dark green : Drs notes 438

Gray: Extra



Introduction

Blood Contents:

- Cells: RBCs, WBCs, Platelets.
- Plasma: Water, Electrolytes, Proteins…

Blood disorders:

RBCS	WBCs	Platelets

• Polycythemia
• Anemia
  ○ Sickle cell
  ○ Thalassemia
  ○ Other: Nutritional (Iron or folate Deficiency) or Hemolytics (G6PD…)
	• Lymphoma
	• Multiple myeloma
	• Leukemia (usually radiology has no role).
		Bleeding/coagulation disorders

General features of anemia on imaging:

1 Reactive increase in red bone marrow

- First response: your body will increase the RBCs production in the red bone marrow - which is present in the axial skeleton and the flat bones, like the scapula and sternum -. This is called intramedullary hematopoiesis.
- Expanded bone marrow in bones including long bones (which contain yellow marrow, not red). it is more obvious in hands, feet, limbs, skull
- Decreased T1 MRI signal in vertebral body bone marrow than adjacent discs. (سواد)

2 New marrow areas in potential organs

- If the previous mechanism wasn't enough and the patient is still anemic, or if the previous mechanism isn't working (aplastic anemia/myelofibrosis), some other sites will try to synthesize RBCs (extramedullary hematopoiesis), but in normal adult these sites don't do hematopoiesis.
- Such as: 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.

3 Transfusions iron overload (Hemochromatosis)

- Exogenous; in chronic anemia, due to transfusion.
- 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.

1: Sickle cell Anemia

Clinical features:

Sickle cell disease may be manifested as:

1. **Anemia** → Growth failure, Hyperkinetic heart failure, Expanded intramedullary hematopoiesis, presence of extramedullary hematopoiesis.
2. **Vaso-occlusion** → Infarcts in spleen (splenic sequestration, autosplenism), bone marrow, kidney, bowel, brain, muscles etc.
3. **Superimposed infections:**
   a. Pneumonia (Pneumococcus, H. influenzae, Staph. aureus, Chlamydia, and Salmonella).
   b. Osteomyelitis (Salmonella)

Note:

- You can't specify which type of anemia the patient has depending on the radiologic features above.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.

- Sickle cell anemia has a very specific appearance in the vertebrae. Other types of anemia do not have such appearance. This specific sign is called H-shaped vertebrae, it happen due to the occlusion of small capillaries at the end plates of the vertebrae. this will lead to microinfarcts. Microinfarcts will accumulate over time weakening the vertebrae. when the vertebrae bears the weight, they will become compressed, leading to H-shaped vertebrae, as illustrated in figure 1

- Figures 2-4 are showing features of sickle cell disease on imaging

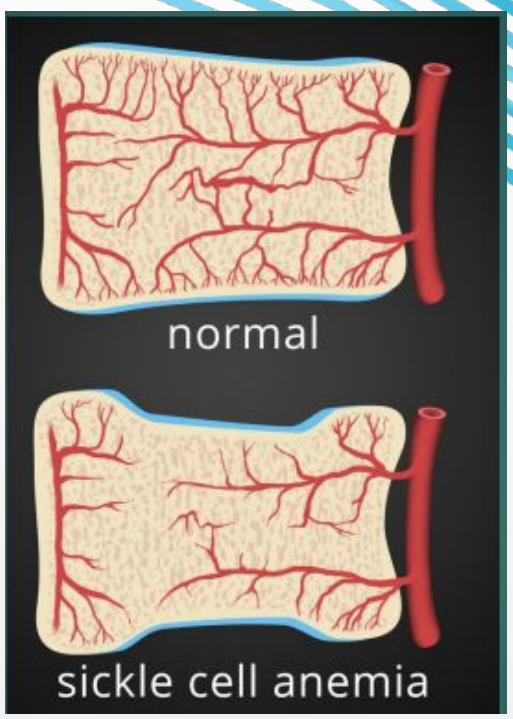


Figure 1

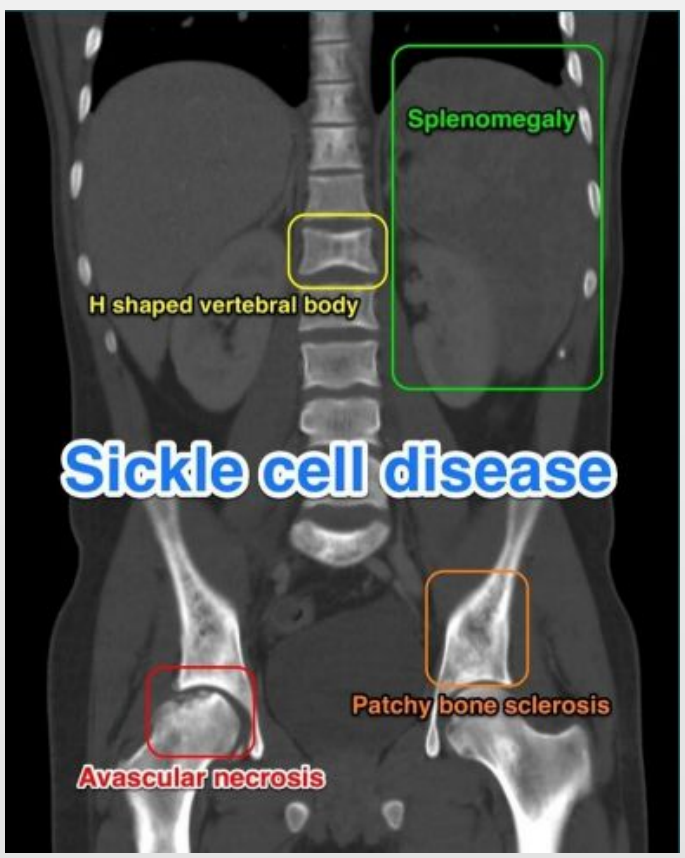


Figure 2

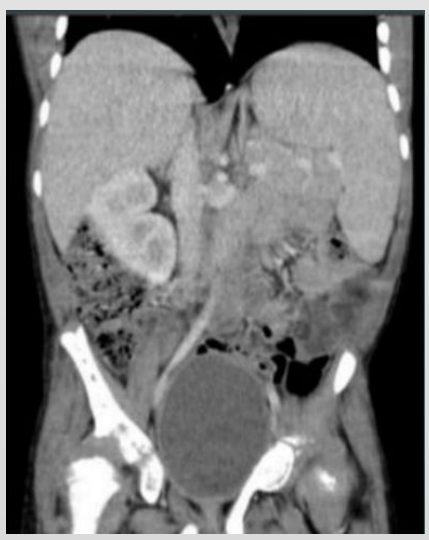


Figure 3

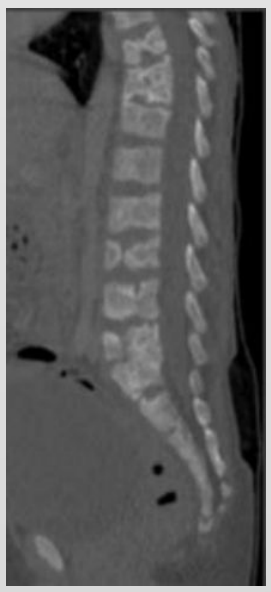


Figure 4

1: Sickle cell Anemia

Sickle cell cases:

1- A 40-year-old man with sickle cell disease.

Figure 5 shows Axial unenhanced CT scan at thoracoabdominal level, findings:

- Arrows → two uniformly low-attenuation (compared with liver parenchyma), well circumscribed lesions.
- Bilobed hypodense liver due to iron overload because of multiple blood transfusions.
- Percutaneous biopsy showed extramedullary hematopoiesis (here, CT with contrast is not enough)

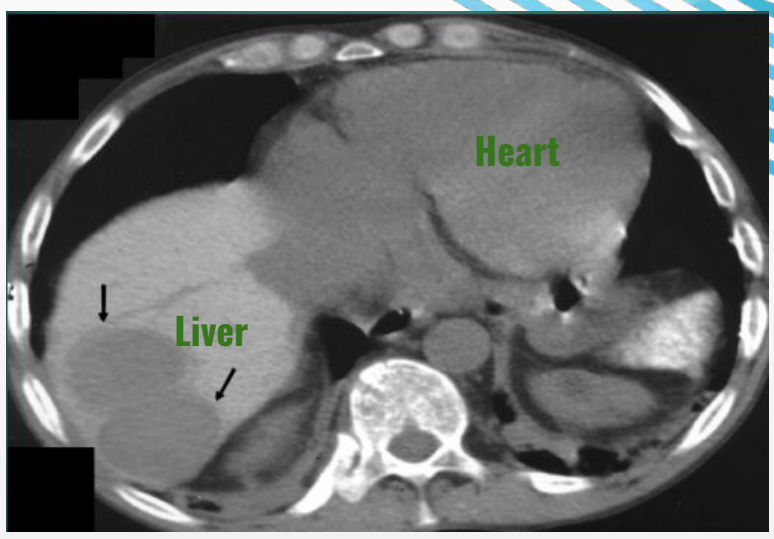


Figure 5

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

- Figure 6 is a Sagittal T1-weighted MRI (we knew it is T1 because the CSF is black) of spine shows Low signal intensity in vertebral bodies compared to discs. Can be seen in any kind of anemia not just sickle cell.
- H-shaped vertebrae (only with sickle cell anemia) (arrows in right image) due to **osteonecrosis** of vertebral endplates "Honda sign".

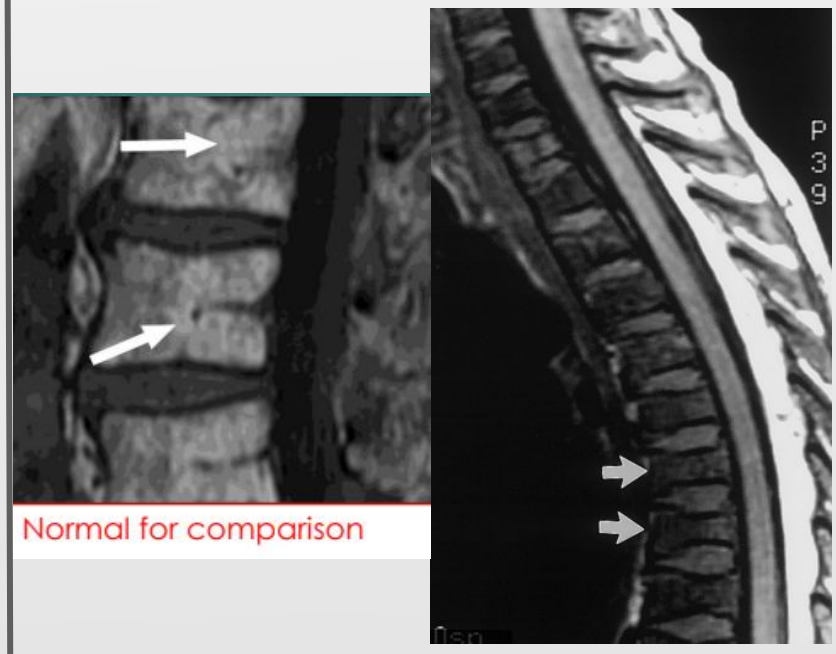


Figure 6

3- H-shaped vertebrae in a 15-year-old patient with SCA. Findings: (Figure 7)

Classic boxlike endplate depressions in middle portion (see the lowest vertebra shown) due to osteonecrosis of the vertebral endplates.

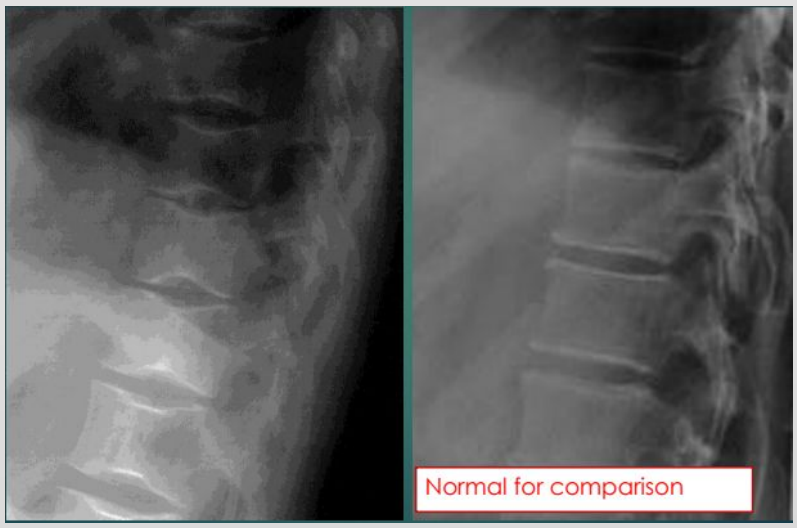


Figure 7

1: Sickle cell Anemia

Sickle cell cases:

4- Frontal radiograph of right shoulder in a 22-year-old SCA patient. Findings:

In figure 8, we see areas of patchy sclerosis, Osteonecrosis, and radiolucency

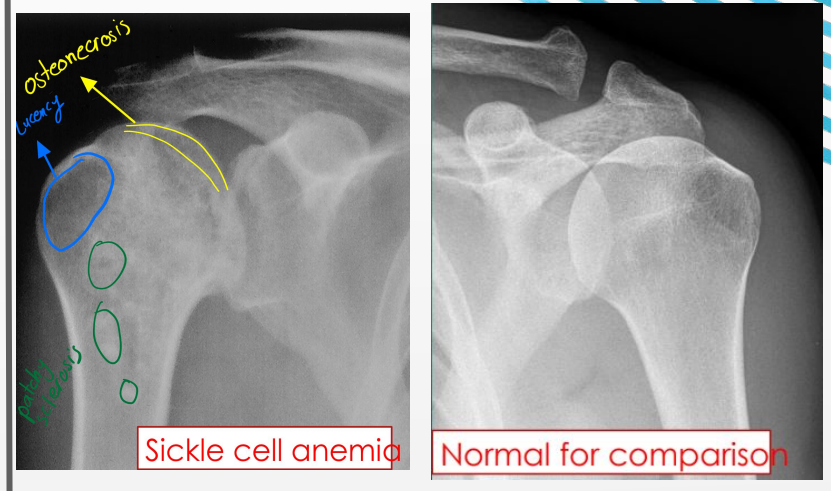


Figure 8

5- AP radiograph in a 44-year-old man. Findings:

Figure 9 demonstrates avascular necrosis with flattening of bone, Sawing of the articular surface, and heterogeneous densities in left hip and a normal right hip

- Signs of avascular necrosis in SCA:
  - Flattening of the Femoral/Humeral head.
  - Irregularity of the articular surface.
  - Heterogeneous density of the bone.

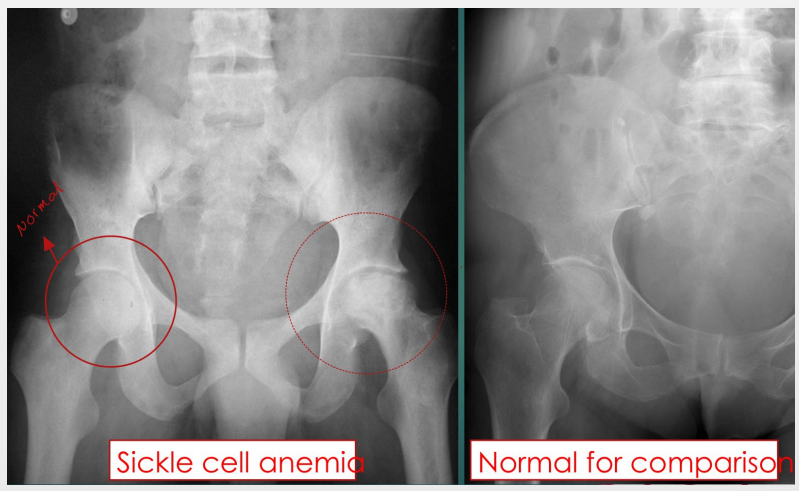


Figure 9

Coronal STIR MRI image in the same patient shows stage 1 avascular necrosis in right hip (arrow) as well, in addition to advanced changes of avascular necrosis of left femoral head (figure 10)

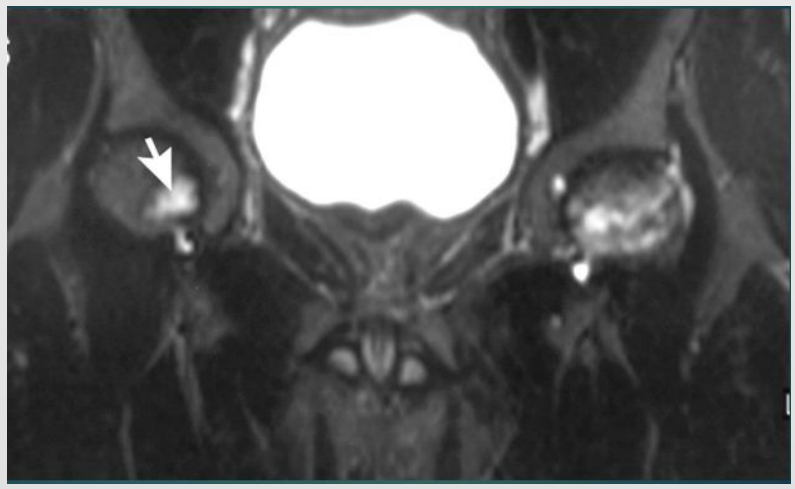


Figure 10

Note:

- 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

1: Sickle cell Anemia

Sickle cell cases:

6- Hand-foot syndrome (Dactylitis), in SCA. Findings:

Figure 11, a Frontal radiograph of right foot in a 3-year-old girl shows **thick periostitis** and subperiosteal new bone along the metatarsal shafts with bone expansion due to inflammation.

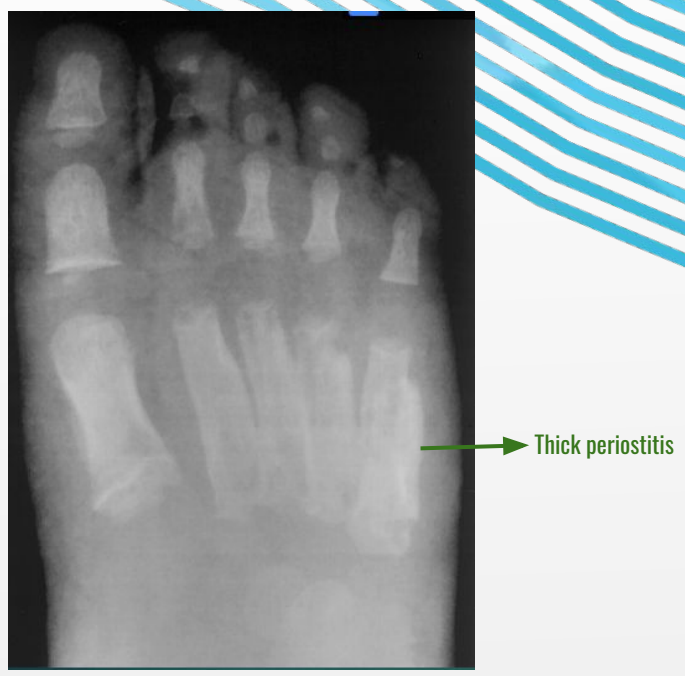


Figure 11

7- Salmonella osteomyelitis in a 10-year-old boy with SCA. Findings: Figure 12

- Left → Initial film at onset of lower shin pain and fever (normal).
- Right → Film 7 days later shows mottled lower tibial shaft and diffuse periostitis of the lower diaphysis.
- Heterogeneous density of the bone is a sign of bone infection (OM).
- Moth-eaten appearance. (it's a pattern of bone involvement by multiple lytic lesions that is described as permeative bone destruction (permeative process in bone).

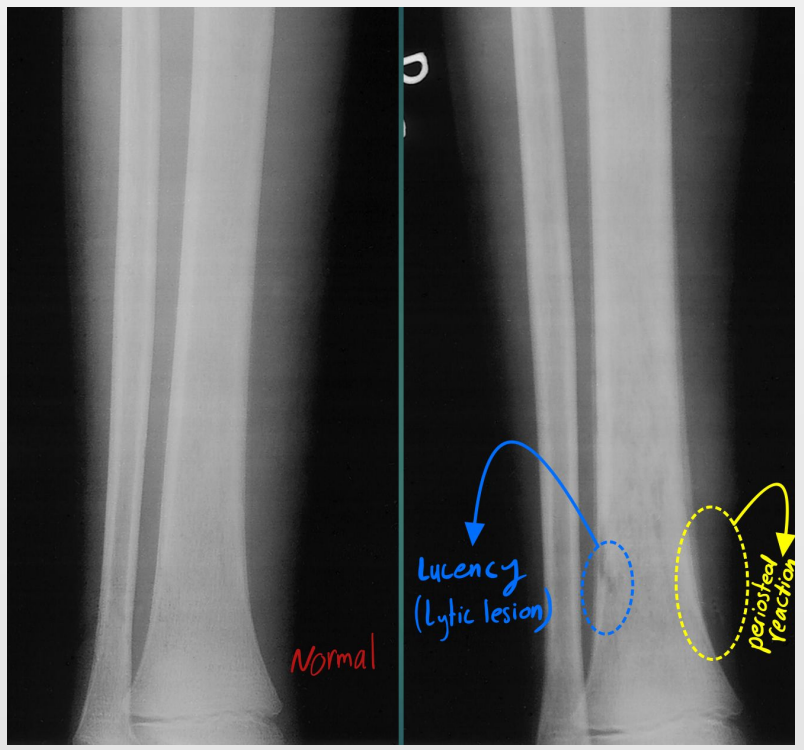


Figure 12

- Bone infarcts and osteomyelitis are difficult to differentiate on history (pain + anemia), clinical examination and plain x-ray images but they are very important to avoid complications of osteomyelitis.
- The treatment will be different in both, so we need an accurate Diagnose, how? By additional imaging (best by MRI, CT can be used, also can be done by US) because in X-ray they are similar, If you see fluid/abscess collection → Infection , NO → Infarction.
- **MRI findings that highly suggest infection:** (If 2 or 3 = infection)
  - Cortical defects in bone.
  - Adjacent fluid collections (abscess) in soft tissue.
  - Bone marrow enhancement.
- Ultrasound guided aspiration of fluid collection around the involved bone can be confirmatory.
- MRI is gold standard in differentiating between bone infarcts and osteomyelitis.

1: Sickle cell Anemia

Sickle cell cases:

8- Osteomyelitis of femur in a 24-year-old patient with SCA. Figure 13

Axial T1-weighted MRI after contrast shows heterogeneous enhancement of marrow cavity, a rounded low-signal-intensity area adjacent to the shaft that is non-enhancing (fluid collection, abscess), and enhancement of the soft tissues around the shaft and of the adjacent musculature. Areas of enhancement are likely infected

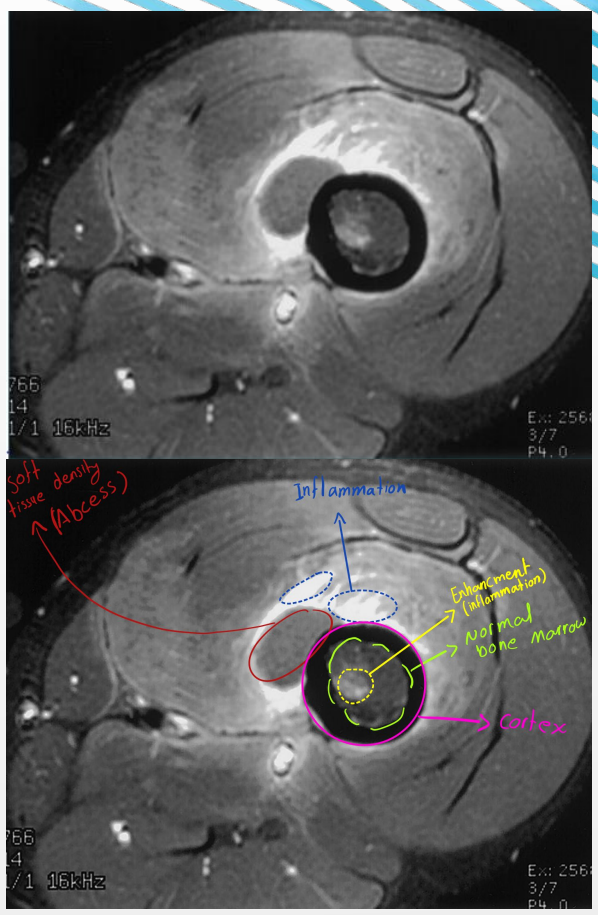


Figure 13

9- Soft-tissue infection in a 52-year-old man with homozygous sickle cell disease: Figure 14

Longitudinal high-resolution ultrasound image of left ankle shows a hypoechoic (dark) fluid collection (arrow) deep to Achilles tendon. Thick pus was aspirated from this area under ultrasound guidance

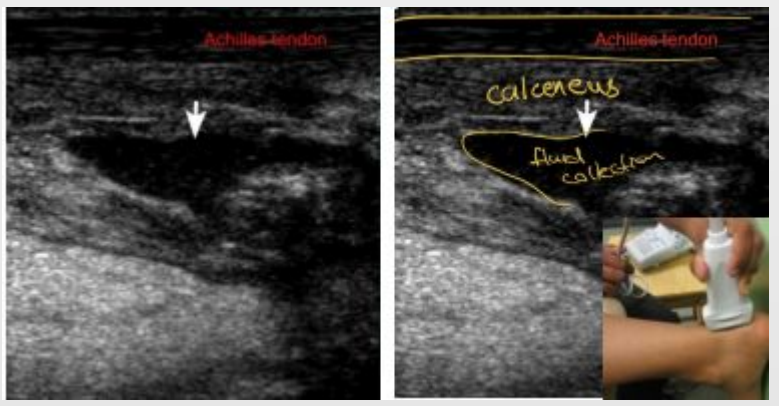


Figure 14

10- Chronic infarct in a 19-year-old patient with SCA and longstanding mild left sided weakness. Figure 15

- Axial T2-weighted MRI shows an area of high signal intensity and enlargement of overlying CSF spaces, compatible with chronic infarction and atrophy
- Multiple Infarction in right cerebral hemisphere, unusual in normal person, but expected in SCA patient.

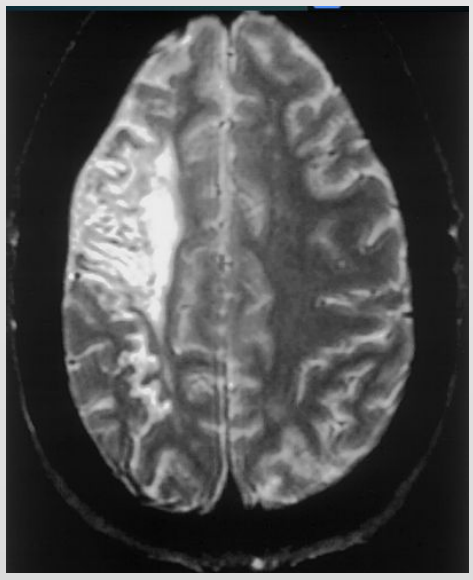


Figure 15

1: Sickle cell Anemia

Sickle cell cases:

11- Growth disturbance in distal radius in a 12-year-old girl: Figure 16

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. There is sequestration of the growth plate

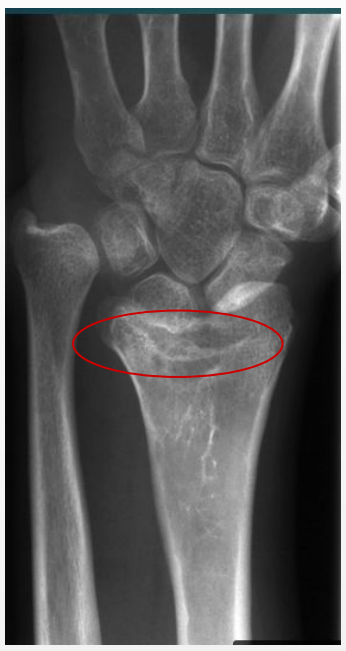


Figure 16

12- Sequestration syndrome with splenic infarction in SCA: Figure 17:

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.

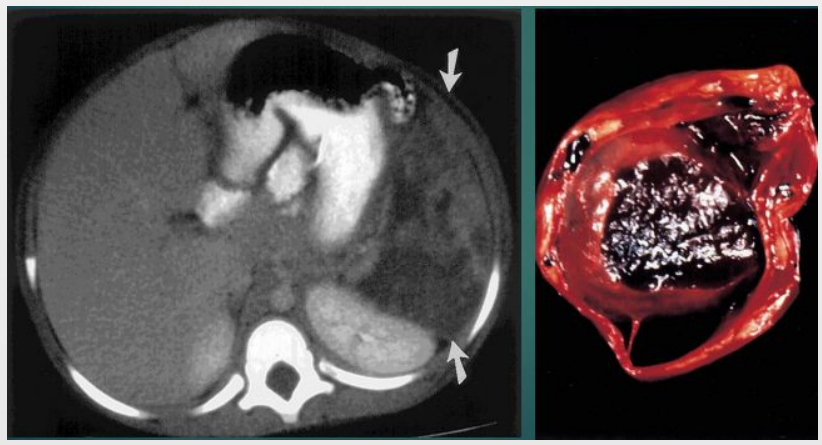


Figure 17

32-year-old man with SCA. Figure 18:

Frontal view of kidney during excretory urography in a 32-year-old man with SCA shows small, round collection of contrast material in a missing papillary tip (arrow). contrast is leaking out

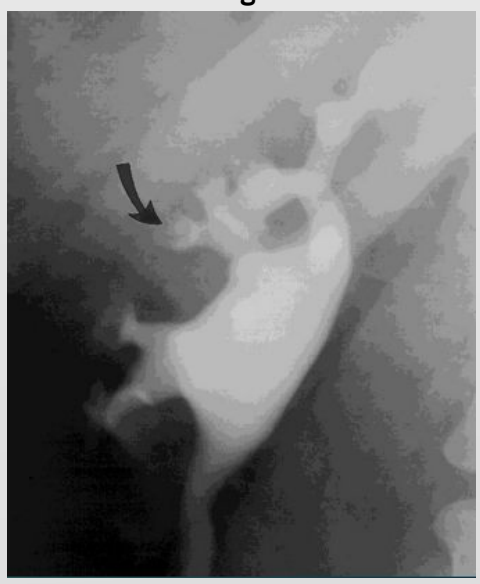


Figure 18

A 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). Figure 19

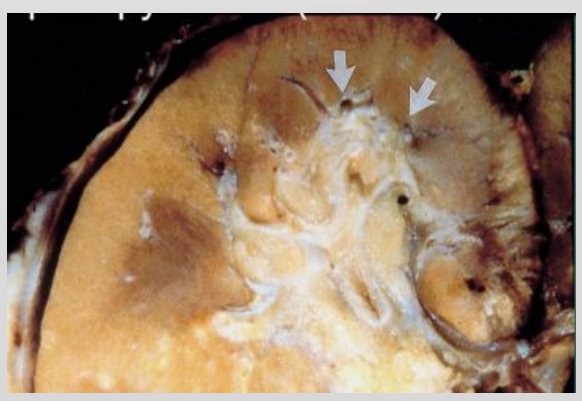


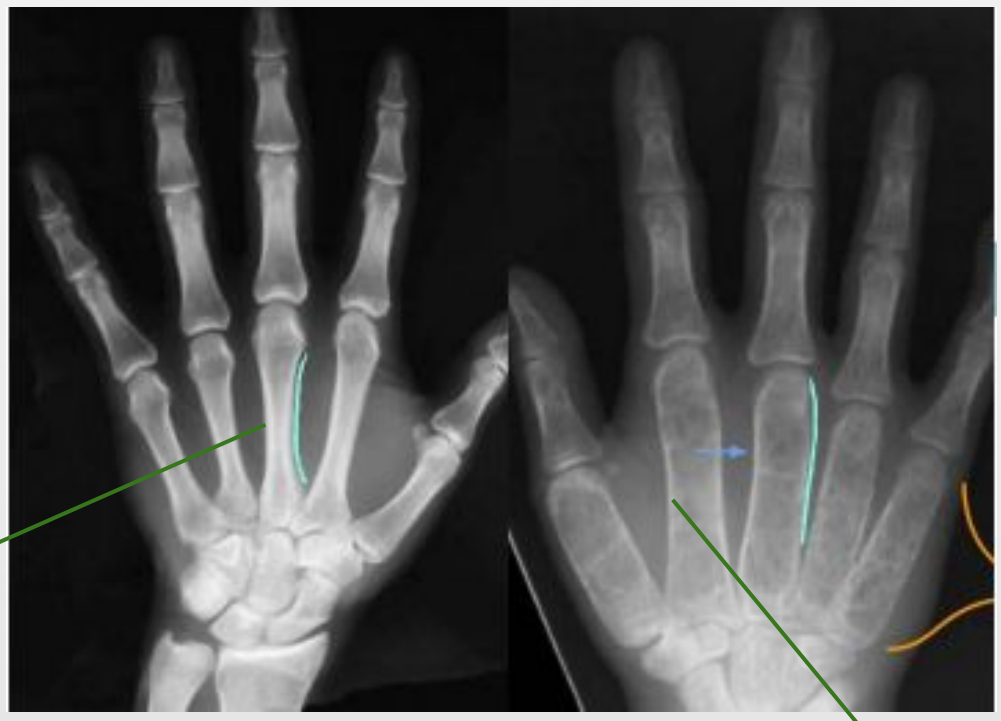
Figure 19

2: Thalassemia

General features:

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

Normal **(Concave)**



Abnormal (**Convex** or straight). There is decreased space between the periosteum and the endosteum due to bone marrow expansion

Figure 20

خط واحد كأنه مرسوم بقلم رصاص

Thalassemia cases:

1- 25-year-old man with β-thalassemia:

PA radiograph of chest (left) shows diffuse expansion of ribs due to expanding red marrow and right upper paraspinal (paravertebral) thoracic mass (arrow) compatible with extramedullary hematopoiesis. (Figure 21)

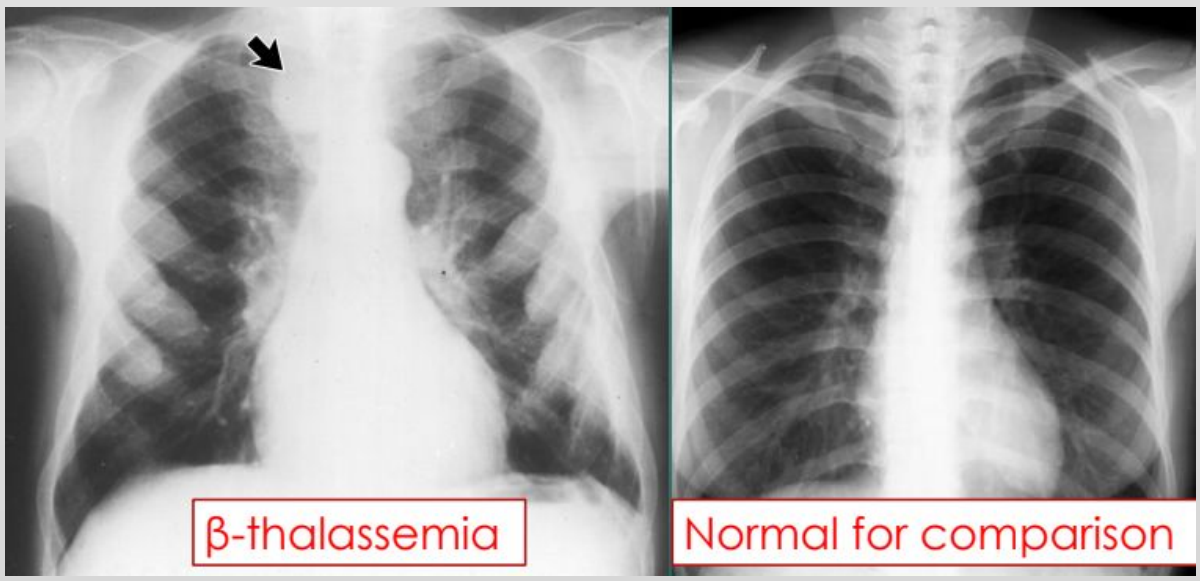
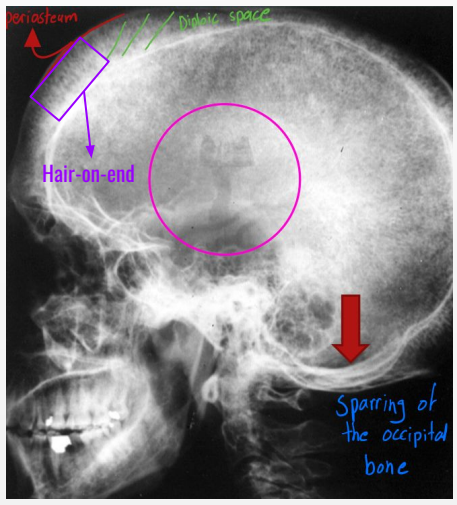
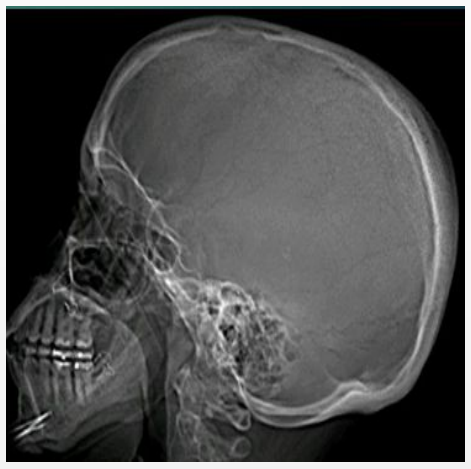


Figure 21

2: Thalassemia

Figure 22





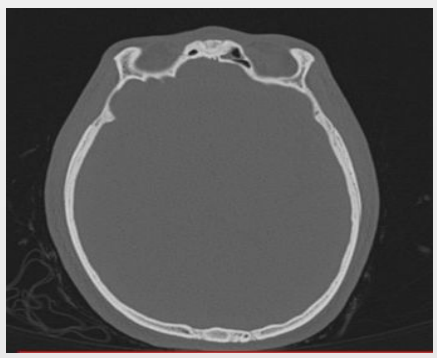
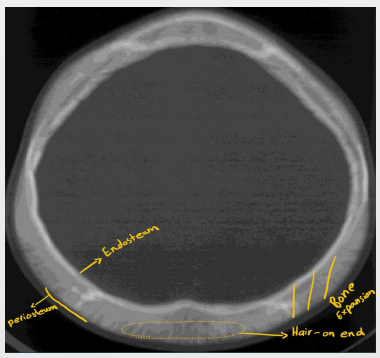
Normal

Thalassemia cases:

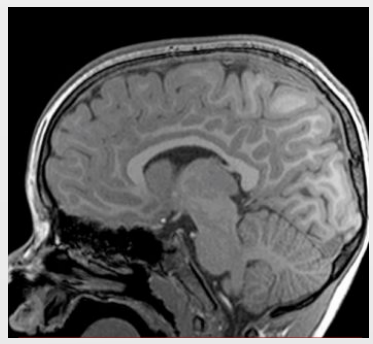
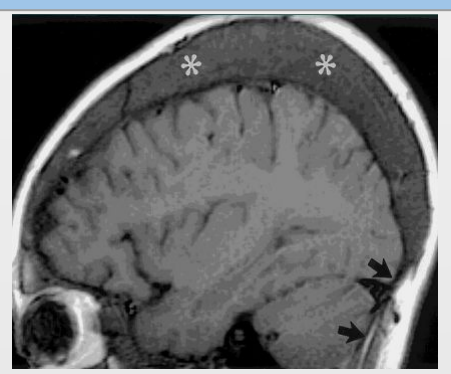
2- 25-year-old man with β-thalassemia. (Figure 22)

Lateral skull radiograph shows:

- expansion of diploic space with hair-on-end appearance.
- Spared occipital bone (has no red bone marrow but have yellow bone marrow) (arrow)
- Widened groove of middle meningeal artery (Circle)

Normal	Axial CT image of upper skull
	

Axial CT image of upper skull (left) shows diploic space widening and trabecular prominence

Normal	Sagittal MRI Brain
	

Sagittal MRI of brain (right) shows diploic space widening representing red marrow (*). Note spared occipital bone (arrows), which has no marrow elements

3- 23-year-old woman with history of thalassemia and known extramedullary hematopoiesis.

PA chest film shows well-marginated bilateral, paraspinal masses compatible with extramedullary hematopoietic tissue. However we must Do CT to rule out malignancy (Figure 23)

Axial contrast-enhanced CT scan through chest shows uniformly enhancing paraspinal hemopoietic masses **with no bony erosion.** **(Infiltration) This excludes sarcoma** (Figure 24)

Figure 23

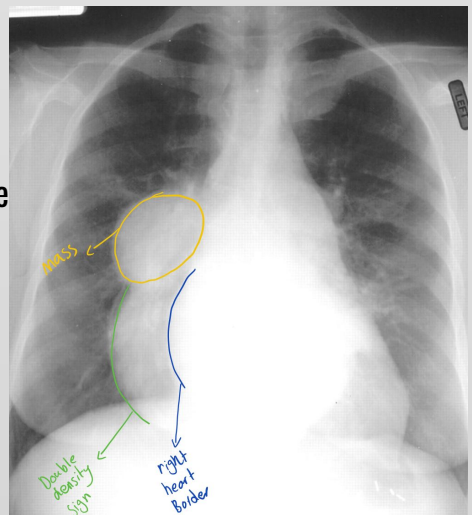
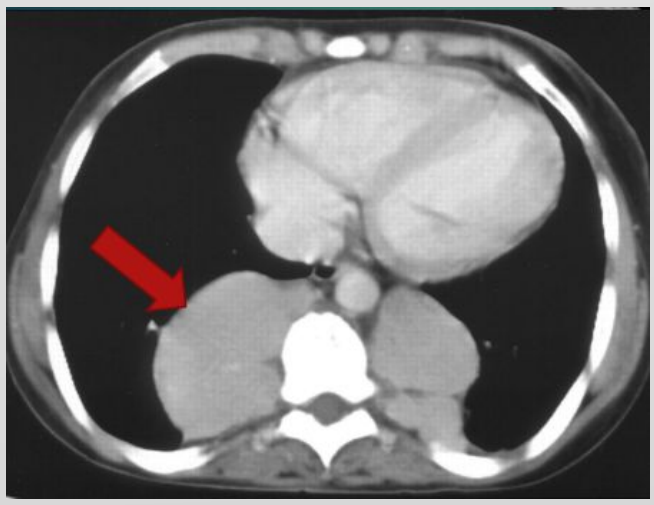
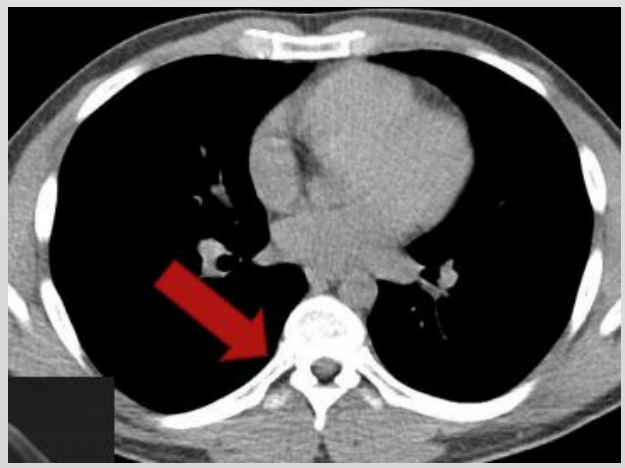


Figure 24





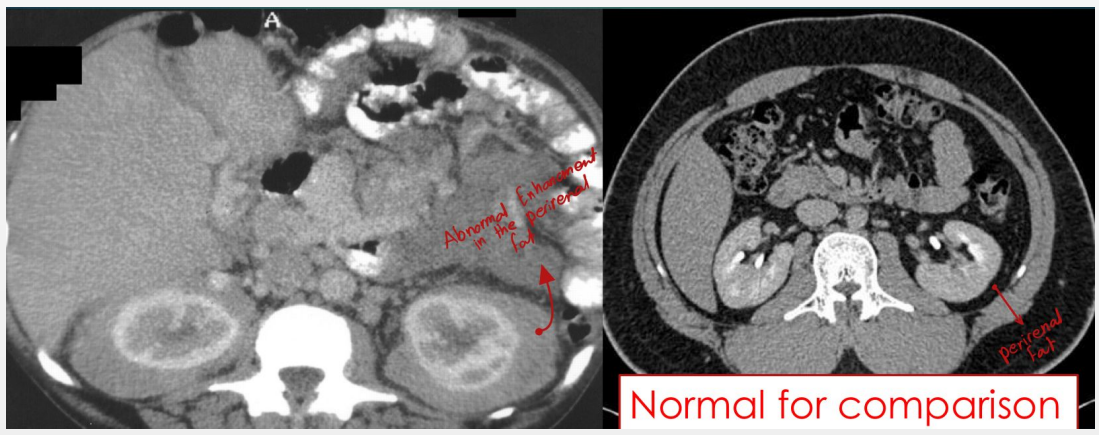
Normal

3: Myelofibrosis

Myelofibrosis cases:

1- 56-year-old man with myelofibrosis

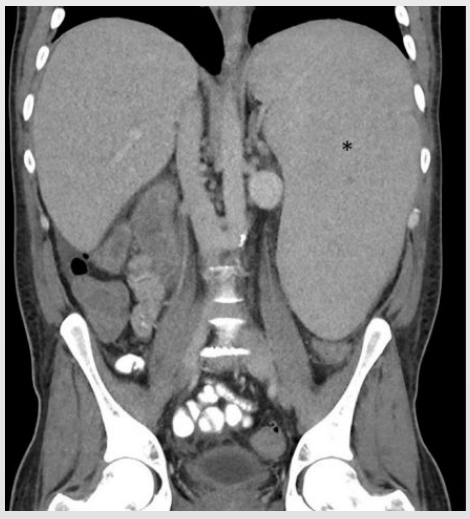
- Axial contrast-enhanced CT scan through kidneys reveals bilaterally symmetric enhancing perinephric masses.
- **Biopsy** showed extramedullary hematopoiesis

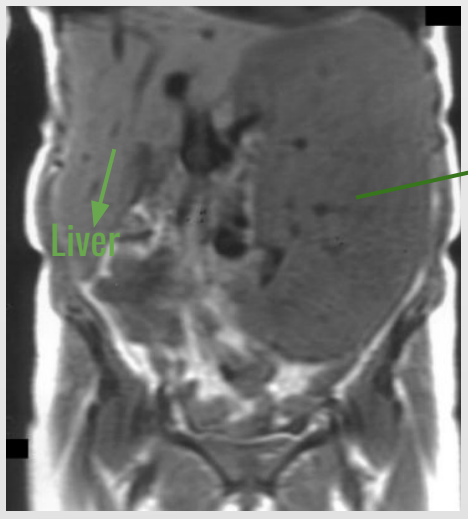


2- 51-year-old woman with myelofibrosis:

- Coronal T1-weighted MR image shows massively enlarged spleen (due to the extramedullary hematopoiesis)
- Splenic biopsy was followed by splenectomy.
- Pathologic examination revealed extramedullary hematopoiesis

CT

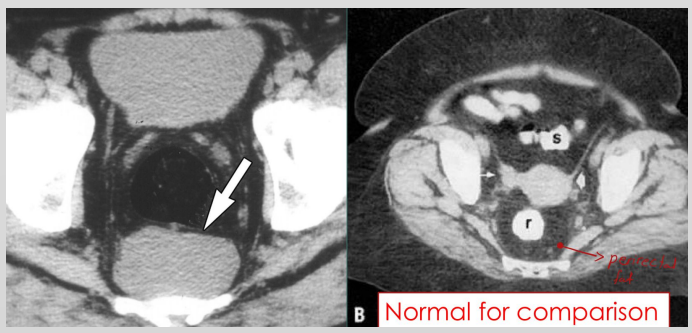




MRI

3- 48-year-old man with hemolytic anemia and myelofibrosis:

- Axial CT scan through pelvis shows well-marginated presacral soft-tissue mass (arrow) with no bony erosion or areas of necrosis
- Any soft tissue mass below therectum and sacrum (presacral space) is abnormal.
- No bony erosion = sign of benign mass.
- Biopsy (not often needed) showed extramedullary hematopoiesis



4: Lymphoma

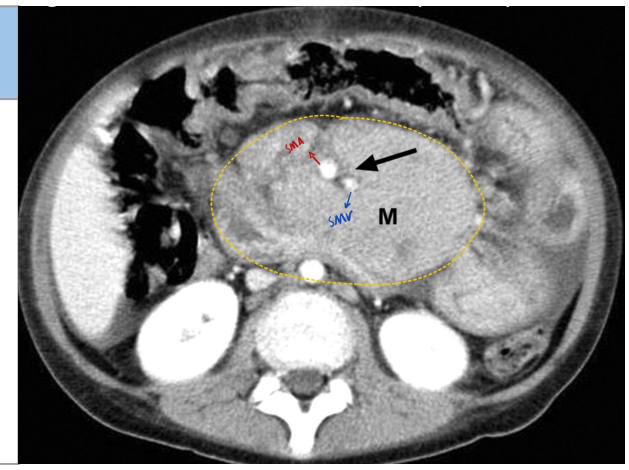
- It's neoplastic proliferation of the lymphocytes.
- Again, radiology has no role in diagnosing the subtypes of lymphoma, but we can identify the disease extent because sometimes it's hard to do physical examination of these masses especially if it is in a deep location ex: near the aorta
- Most of 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.
- Lymphoma can present as mass anywhere in the body

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.	➔ Large B-cell lymphomas (abdomen and nodes) most common. ➔ Burkitt lymphoma (jaw and abdomen). ➔ Burkitt-like lymphoma (abdomen and nodes). ➔ Lymphoblastic lymphoma (Mediastinum, nodes, bone marrow). ➔ Anaplastic large cell lymphoma (Nodes, skin, soft tissue, bone). ➔ Other peripheral T-cell lymphomas. ➔ MALT lymphoma.

Cases:

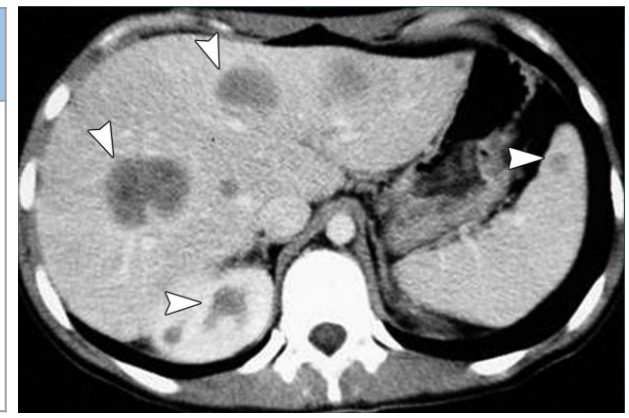
1- Non Hodgkin's Lymphoma (NHL) in an 11-year-old boy.

Axial CT scan with contrast shows Large lymphomatous mass (M)* encasing the mesenteric vessels (arrow).
Note: Lymphoma mass does not compress (displace) or invade (not aggressive), it encases and respect other surrounding structures.



2- 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.

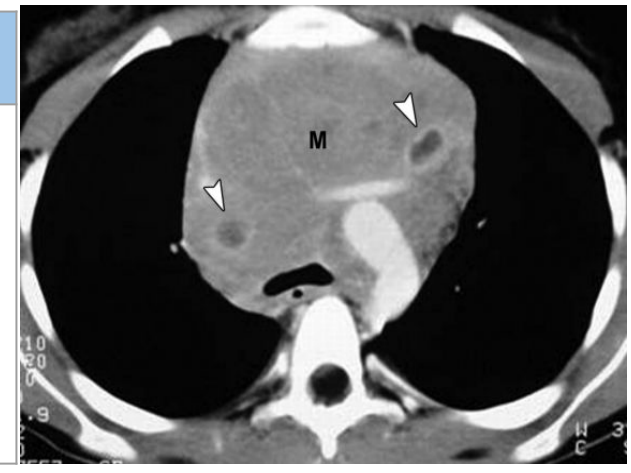


4: Lymphoma

Cases:

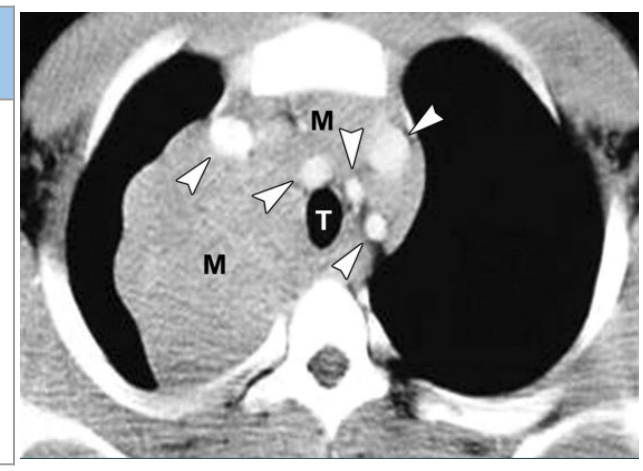
3- NHL in a 14-year-old boy.

Contrast-enhanced CT scan shows a large anterior mediastinal mass (M) that originates from thymus. A few cysts with central low attenuation and a peripheral enhancing ring are present (arrowheads). There is decreased blood supply in the center



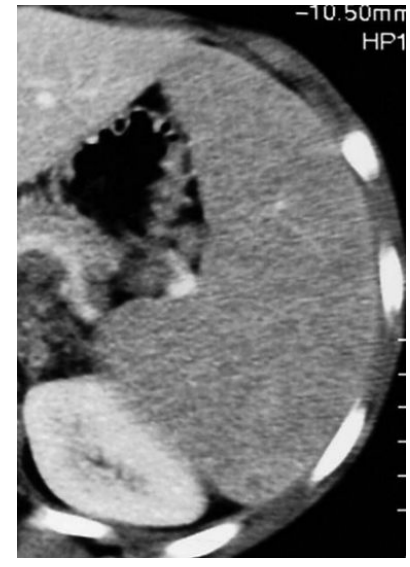
4- HD in a 17-year-old boy.

Contrast-enhanced CT scan shows a large mediastinal mass (M). Trachea (T) is compressed, and great vessels (arrowheads) are displaced



5- HD in a 12-year-old girl.

Contrast-enhanced CT scan shows an enlarged spleen with a diffusely inhomogeneous appearance.



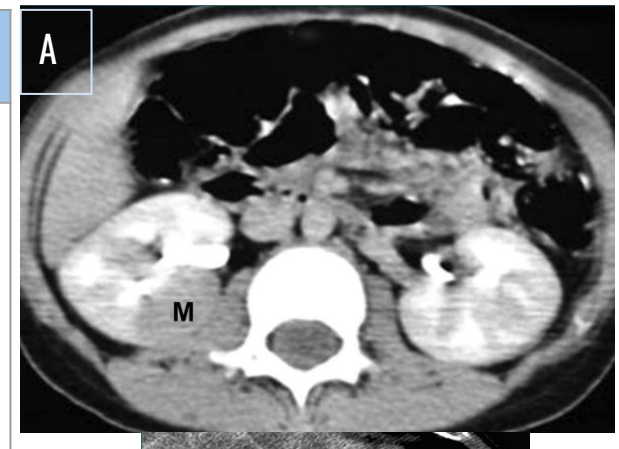
6- NHL in a 14-year-old boy.

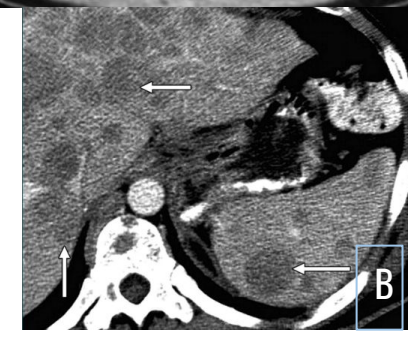
A- <u>Contrast-enhanced CT scan</u> shows single well-defined, low density mass (M) in right kidney

- 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.

B- <u>Axial CT scan</u> shows Diffuse hepatosplenic involvement in lymphoma, with multiple round, homogeneous, low density nodules (arrows) in liver and spleen

- There is involvement of bone, liver, and spleen here.

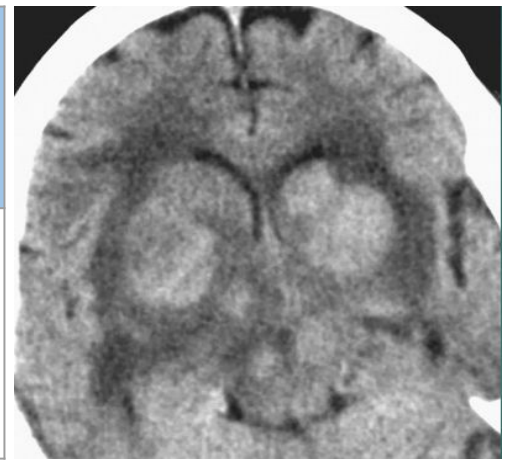




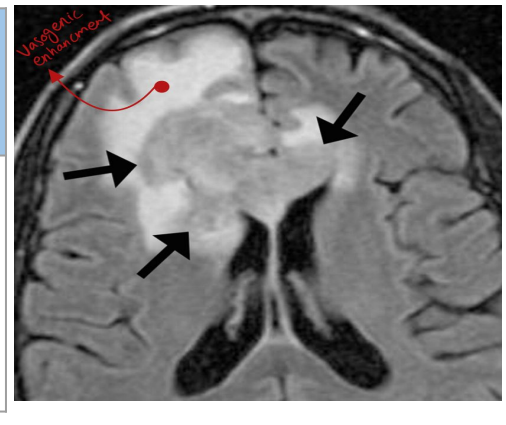
4: Lymphoma

Cases:

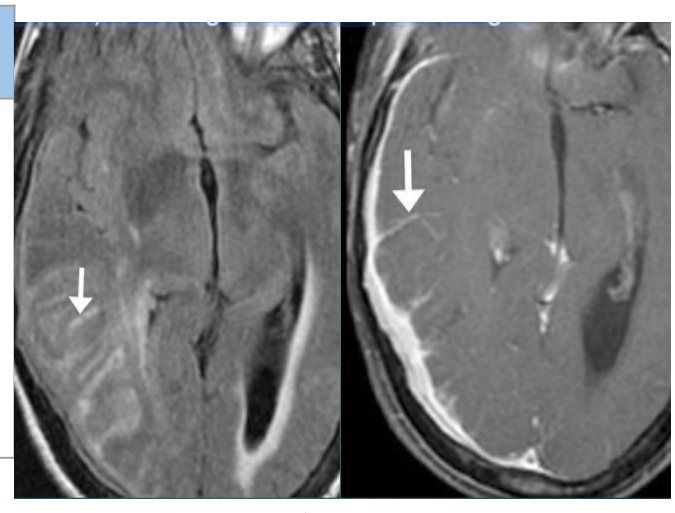
7- 72-year-old immunocompetent woman with primary CNS non-Hodgkin's B-cell lymphoma.
Unenhanced CT image shows classic hyperdense masses involving deep white and gray matter. + Basal ganglia



8- 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). + vasogenic enhancement

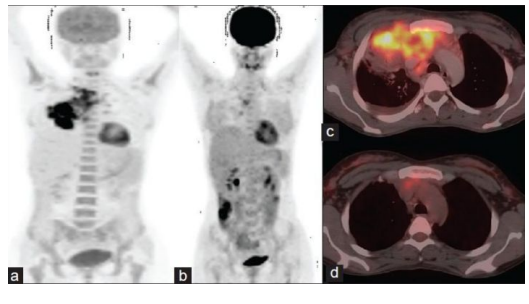


9- 63-year-old woman with primary meningeal lymphoma.
Axial FLAIR (left) and post contrast T1 weighted (right) MR images show hyperintensity and enhancement (arrows) involving sulci and leptomeninges (Arachnoid + Pia)



438 notes: Diagnosis of Lymphoma

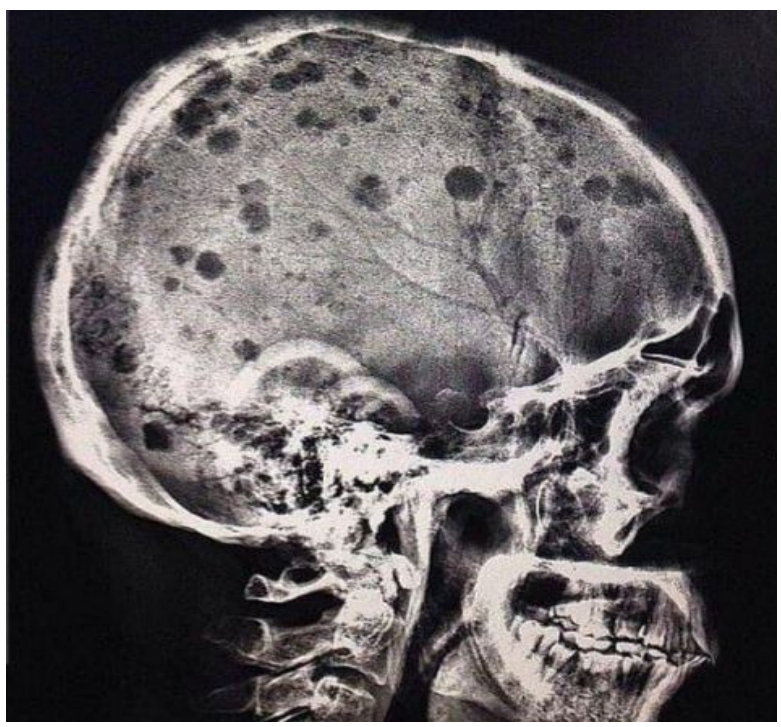
- If accessible area, then open-surgery-Biopsy is often performed (e.g. Axilla and groin).
- If not accessible, CT guided biopsy is done to reach final diagnosis.
- MRI is not commonly used unless you suspect a lymphomatous lesion in a specific area (e.g.brain)!! (forget about MRI, it's NOT used to assess 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!!!).
- Diagnosed by histopathology.
- **PET-CT IS GOLD STANDARD FOR (diagnosing) STAGING AND FOLLOW UP THERAPY of lymphoma.**

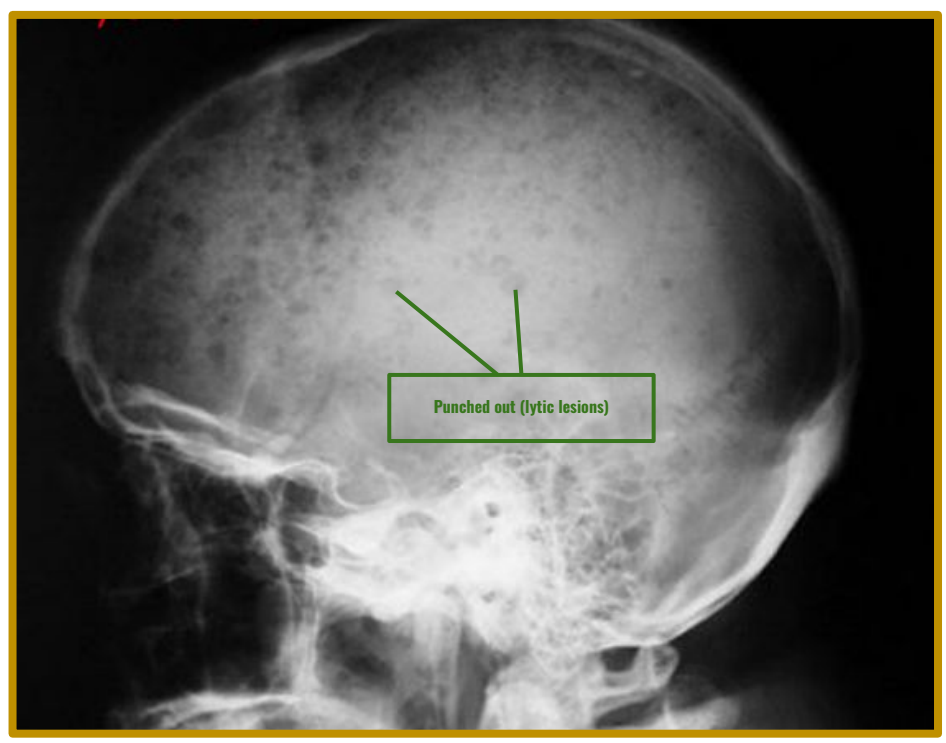


4: Multiple Myeloma

Case

Lateral skull radiograph showing multiple very sharply outlined (punched out) lytic lesions (Pathognomonic)

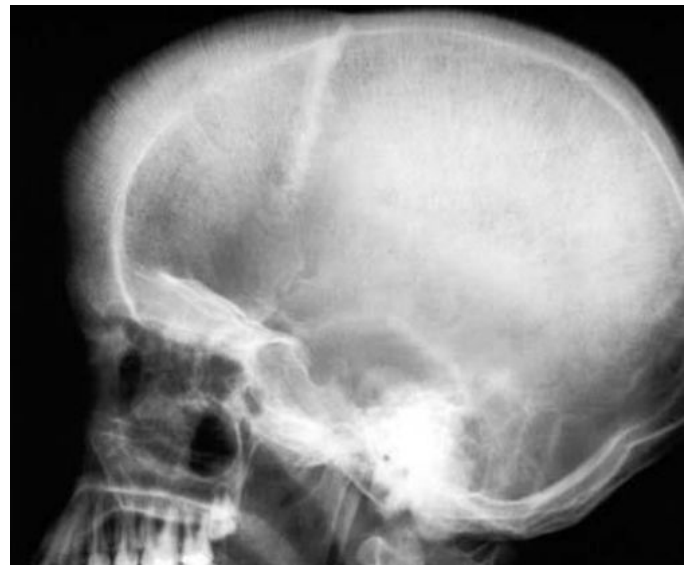




Drs' case: Findings shown here can be seen in:

1. **any severe chronic anemia**
2. thalassemia
3. Sickle cell anemia
4. Lymphoma

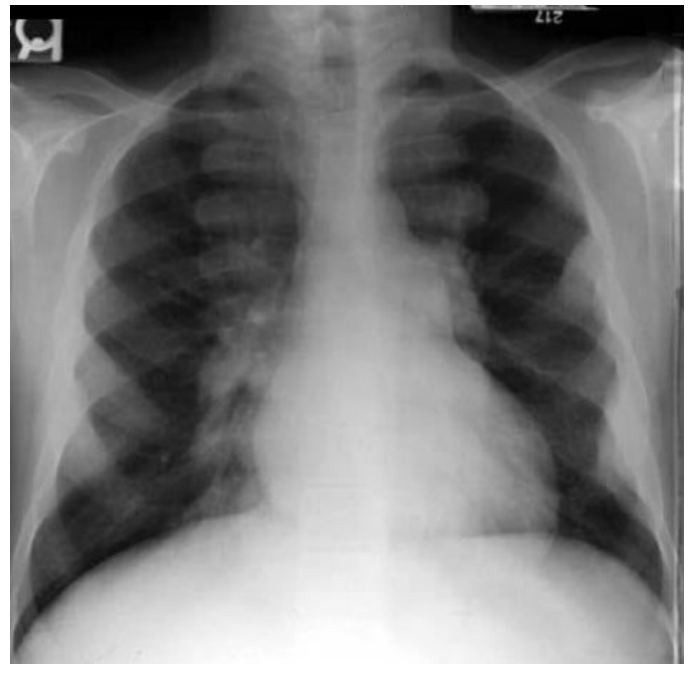
findings: Hair on end, Normal occipital bone & Expansion of diploic space



Drs' case: Findings shown here can be seen in:

1. **any severe chronic anemia**
2. thalassemia
3. Sickle cell anemia
4. Lymphoma

findings:Widening of ribs = hyperactive red marrow



Summary

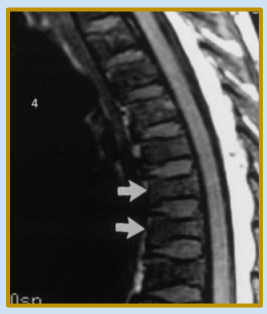
INTRA medullary hyperplasia	can be seen in Thalassemia, Sickle cell anemia, Iron deficiency anemia, Any severe chronic anemia except bone marrow failure. Signs of INTRA medullary hyperplasia include: 1. Expanded bone marrow in bones including long bones of hands, feet, limbs, skull. 2. Decreased T1 MRI bone marrow signal than adjacent discs.
Extramedullary 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	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.

Dr: Important to read the summary

Quiz 438

1- Which of the following diseases is supported by the finding on this image?

a. Thalassemia
b. Lymphoma.
c. Intramedullary hyperplasia
d. Sickle cell anemia



2- 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.

3- AH shaped vertebra is seen in:

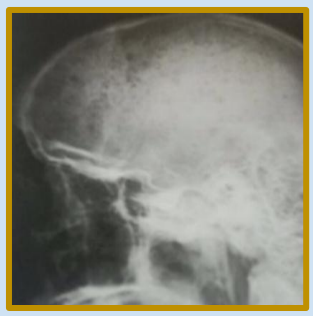
a. Sickle cell anemia
b. Thalassemia
c. Chronic severe anemia
d. Cancer

4- What is the gold standard for staging and follow up of lymphoma?

a. MRI
b. CT with contrast
c. CT without contrast
d. PET-CT scan

5- Findings in the shown skull radiograph can be seen in which ONE of the following:

a. Multiple myeloma
b. Lymphoma
c. Leukemia
d. Thalassemia



Answers
1) d
2) b
3) a
4) d
5) a

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- Bandar Alharbi

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- Sara Alrashidi
- Nouf Albrikan
- Renad Alosaimi
- Duaa Alhumoudi
- Norah Almasaad
- Salem Alshihri
- Ibrahim Alabdulkarim
- Mohamed Albabtain
- Abdulaziz Alamri
- Abdulrahman Alswat
- Munib Alkhateb
- Mohammed Alkathiri
- Omar Alhalabi
- Homoud Algadheb

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