Splenomegaly – Integrated Approach to Diagnosis

Basics

Causes of Splenomegaly

I. Primarily hematological
   1. Neoplastic
   2. Non Neoplastic

I.1. Neoplastic-
   a) Leukemias
      • Chronic lymphocytic
         Including prolymphocytic and hairy cell
      • Chronic granulocytosis
      • Acute lymphoblastic
      • Acute myeloblastic (less common)
   
   b). Polycythemia rubra vera
   C). Lymphoma
   d). myelodysplastic syndrome
   e) Histiocytosis

I.2. Non Neoplastic
   Hemolytic anemias (mainly)
   Megaloblastic, iron deficiency anemia (minimal enlargement)
   Auto immune thrombocytopenia (rare)

II. Non Hematological
   1. Infective
      (mechanism – accumulation of inflammatory cells)
      (splenic filtration of blood born pathogens may lead to indolent abscesses; as they enlarge, spleen also enlarges)
      a. acute and subacute infections
      . infectious mononucleosis
      . endocarditis
      . severe pyogenic infections
     a. Chronic
        TB, Syphilis, Brucellosis
b. Tropical Splenomegaly
c. Malaria, leishmaniasis, trypanosomiasis

The term tropical splenomegaly is generally reserved for chronic splenic enlargement in patients from malarial areas but its occurrence bears no relation to the apparent severity of infection; malarial parasite not routinely seen in peripheral smear

2. Congestive
   (Mechanism - Normal spleen helps to regulate portal blood flow;
   (Disordered splenic blood flow causes splenic congestion)

2a. Intrahepatic obstructive portal hypertension
   Portal cirrhosis, biliary cirrhosis, post necrotic scarring
   Hepato lenticular degeneration
   Hemochromatosis
   Hepatic venous occlusion
   Sarcoidosis
2b. Extra hepatic obstructive portal hypertension
   Venous malformations, thrombosis, atresia, stenosis, aneurysmal formation
   Extensive occlusion of i) portal vein ii) splenic vein
2c. Chronic passive congestion of cardiac origin

3. Infiltrative
   Malignant infiltration
   Leukemia - CML, Lymphoblastic
   Lymphoma - Hodgkin's, Non Hodgkin's
   Myelo proliferative syndrome
   Angio sarcoma
   Primary splenic tumor
   Benign
   Extra medullary hematopoiesis
   Storage diseases
   Gauchers
   Niemann-Pick disease
   (Mechanism - Metabolite laden macrophages)
   Amyloidosis
   Hurlers syndrome
   Eosinophilic granulomas
   Mucopolysaccharidoses

4. a. Conditions with Abnormal Erythrocytes
   Mechanism - sequestration and removal of abnormal blood cells
4a. Spherocytosis,
    Sickle cell disease, (before auto splenectomy occurs)
    Ovalocytosis
    Thalassemia
4b. Hyperplastic splenomegaly due to work hypertrophy
Extramedullary hematopoiesis-Myeloproliferative disease

5. Connective tissue disease
   (Mechanism-splenomegaly due to disordered immune regulation)
   . Rheumatoid arthritis-felty’s syndrome.
   (Components: arthritis, splenomegaly and leucopenia)
   . Systemic lupus erythematosus

6. Miscellaneous
   Sarcoidosis
   Cysts and hemorrhage
   Aneurysm of splenic artery
   Metastatic tumors primary hamartoma
   Idiopathic
   Thyrotoxicosis
   Iron deficiency anemia

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**DEGREE OF SPLENIC ENLARGEMENT AND DIAGNOSIS**

Note:
A palpable spleen is not always an enlarged spleen (visceroptosis or displacement)
‘Normal size-12cm length7cm width’;
Located along long axis of Left 9th, 10th and 11th rib-mid axillary line
Spleen should be twice the normal size to become palpable.

I. Causes of massive splenomegaly (beyond umbilicus)

In very large spleen - lower splenic pole may extend into pelvis and cross abdominal midline.
   1. Myeloproliferative disorder
      (proliferation of stem cells)
      Chronic myeloid leukemia
      Polycythemia
      Thrombocytosis
   2. Chronic malaria, kala Azar (Tropical splenomegaly)
   3. Storage diseases
      Gauchers, NemannPicks disease
   4. Thalassemia major
   5. Some cases of portal hypertension
   6. Sarcoidosis
   7. Congenital syphilis
   8. Hairy cell leukemia

Disease excluded by massive spleen are Acute infective diseases

II. SMALL SPLEEN (just palpable)
Mostly in acute infective conditions
Acute malaria, typhoid, kalaazar, septicemia

III. Moderate spleen (between costal margin and umbilicus)
Cirrhosis
Lymphoma
Hemolytic anemias
Amyloid
Splenic abscess, infarct
Hepatitis
Infectious mononucleosis

**Hypersplenism; Definition:**

Enlarged spleen with increase in normal destruction of blood cells.
Characterized by
1. Splenomegaly
2. Pancytopenia (Involving all 3 blood elements or one or two)
3. Presence of (normal) or hyper active marrow usually.
4. Reversible by splenectomy.

**Differentiation between enlarged spleen and enlarged left kidney**

<table>
<thead>
<tr>
<th>Spleen</th>
<th>Kidney</th>
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<tbody>
<tr>
<td>1. Sharp edge</td>
<td>1. Rounded edge</td>
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<tr>
<td>2. A notch is felt in lower medial border</td>
<td>2. No notch felt</td>
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<tr>
<td>3. Upper border cannot be felt by pushing the fingers between the swelling and costal margin</td>
<td>3. Upper border can be felt by pushing the fingers between swelling and costal margin</td>
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<tr>
<td>4. It is not bimanually palpable</td>
<td>4. Is bimanually palpable</td>
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<tr>
<td>5. Dull on percussion</td>
<td>5. A band of colonic resonance anterior to the kidney</td>
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<td>6. Swelling grows downwards and towards left iliac fossa</td>
<td>6. Grows towards midline</td>
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<tr>
<td>7. Splenic swelling moves with respiration</td>
<td>7. Does not move freely with respiration-retroperitoneal</td>
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</tbody>
</table>

**Investigations**
- **Lab studies** to do: as appropriate:
  - CBC, blood smear for cellular morphology and parasites, culture of blood and other sites, serology (fungal, viral, HIV, Parasitic, TPI)
  - Mononucleosis screen,
  - PPD,
  - **BM aspiration and biopsy**, lymph node biopsy if significant lymph adenopathy is associated.
- **Imaging Studies**
  - Ultrasound Abdomen
  - CT scan/MRI of Abdomen
  - CXR if appropriate

**Treatment**: treat the cause.
Splenomegaly images

Spleen situated along long axis of 9th, 10th, and 11th ribs left side.
Organs in relation-
Diaphragm, Stomach, pancreas, colon, omentum, Left adrenal and kidney, ovary in female
Blood supply - splenic artery from celiac trunk
Venous drainage - splenic vein into portal
Lymph - celiac, para aortic nodes
Nerve - sympathetic from celiac plexus

Function of red pulp: Destruction of senile and abnormal RBCS
White pulp: contains small nodules rich in lymphoid cells
Called “malphigian nodules”-
Functions immunosurveillance

Bone marrow aspiration and biopsy

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I. Splenomegaly with Acute illness
   1. Rupture
      Splenic infarct
      Acute infective conditions
   2. Splenomegaly with fever
      Typhoid, malaria, kala azar, military tuberculosis,
      Infective endocarditis, leukemia, lymphoma
   3. Highly tender spleen
      Rupture with sub capsular hematoma
      Splenic abscess
      Splenic infarct
      (sickling of RBC in splenic artery, embolism-mural, endocardial, left atrial myxoma)

4.. Splenomegaly + acute illness + anemia
   Autoimmune hemolytic anemia
   Acute leukemia
   Myeloproliferative disease

5. Splenomegaly + fever + Lymphadenopathy
   (with or without arthralgia)
   Infectious mononucleosis
   Hodgkins/non Hodgkins/Leukemia
   (Acute lymphoblastic or myeloblastic leukemia)
   Systemic Lupus erythematosus
   Serum sickness
   Sarcoid

Learning point:
Normal palpable inguinal nodes-0.5-2ccm
Investigate-new nodes ≥1cm: not nodes from antecedent illness
Consider pt.’s age, physical characteristic of nodes, site, and associated clinical setting

Also Evaluate:
Complete history, clinical exam, presence and extent of adenopathy,
Systemic/localizing symptoms/signs; acute or chronic illness; any h/o risk factors for HIV
Inference:
Regional adenopathy indicates infection or malignancy
Lab studies to do: as appropriate:
CBC,culture of blood and other sites,CXR,PPD,serology(fungal,viral,HIV,Parasitic,TPI)
Mononucleosis screen,blood smear for cellular morphology and parasites,BM aspiration and biopsy

6. Rupture of spleen
Trauma
Infective conditions
- malaria, typhoid, infectious mononucleosis

7. Splenomegaly with anemia
Pernicious anemia
Hemolytic anemia
Hemoglobinopathies

8. Splenomegaly with suffused conjunctiva:
polycythemia

9. Splenomegaly with jaundice
cirrhosis
hemolytic anemia

10. Pulsatile spleen
Splenic aneurysm

11. Splenomegaly with high ESR
Connective tissue disorders

12. Splenomegaly with Leukopenia
Felty's syndrome (Rheumatoid arthritis + splenomegaly + leucopenia)
Septicemia

13. Bantis syndrome
Congestive Splenomegaly with hypersplenism occurring in cirrhosis and portal hypertension

14. Tropical splenomegaly
Massive Splenomegaly occurring in people of endemic area for malaria/kalaazar
But no parasite is demonstrable in blood.
IgM antibodies against malaria are detected in blood.
Cause of splenomegaly is obscure.;lymphocytic infiltration of splenic/liver sinusoids present.
This condition is rare before the age 8.
Synonym-HMS-Hyper reactive malarial Syndrome
It is a diagnosis of exclusion.Long term anti malarial therapy helps.
15. Myelo proliferative syndrome
Consists of
CML
Myeloid myelo fibrosis
Polycythemia
thrombocytosis

Mechanisms of Splenic enlargement
1. Reactive hyperkasia in infection and inflammation
2. Proliferation of lymphoma cells
3. Infiltration by other Neoplastic cells.
4. Extramedullary hemopoiesis
5. Proliferation of macrophages in response to increased destruction of blood cells.
6. Vascular congestion

Point to note in History
1. Age, occupation,
2. Race (congenital hemolytic disorders like thalassemia
3. Recent infections including malaria
4. Fever, weight loss, sweating (lymphoma, infections)
5. Fever or rigors - infective endocarditis
6. Pain in splenic area and or shoulder pain
7. Pruritis (lymphoma)
8. Abnormal bleeding/ bruising
9. Joint pains (Rheumatoid arthritis, SLE)
10. H/o alcoholism - Portal hypertension secondary to cirrhosis
11. H/o alcoholism - Portal hypertension secondary to cirrhosis
12. H/o alcoholism - Portal hypertension secondary to cirrhosis
13. H/o trauma - splenic hematoma
15. Residence and travel abroad
16. High risk sexual behavior (AIDS)
17. Drugs

Points to note in clinical examination
1. Size of spleen (measure in cm below the costal margin)
   note - consistency, tenderness, audible rub
2. Hepatomegaly size, consistency
3. Lymphadenopathy
4. Fever
5. Bruising
6. Oral and other superficial sepsis
7. Stigmata of liver disease
8. Stigmata of rheumatoid/SLE
9. Splinter hemorrhage, fundal hemorrhage
10. Cardiac murmur
11. Other signs of systemic diseases
12. Examination of post nasal space in cervical lymph adenopathy.

**Examination of Lymph nodes**

1. Size,
2. consistency, Firm in infections/hard in carcinoma/fluctuant in cold abscess, rubbery in lymphoma, matted in tuberculosis
3. Mobility and attachment to skin/subcutaneous tissue
4. Superficial inflammation or ulceration
5. Sinus formation
6. Tenderness and distribution

**Three methods of palpation of spleen**

1. Bimanual 2. ballotment 3. palpation from above

**Clinically Differentials for swelling in Left hypochondrial region**


**Investigations in cases with lymph adenopathy/Splenomegaly**

CBC, blood smear for cellular morphology and parasites, look for evidence of hematological malignancy
look for pancytopenia
culture of blood and other fluids/throat swab
serology (fungal, viral, HIV, Parasitic, TPI)
Mononucleosis screening
Tuberculin test, CXR (TB, Lymphoma, sarcoid)

**Lymph node** aspiration cytology if malignancy suspected
If unsuccessful- lymph node biopsy
i) process tissue for histological exam
ii) immunological studies of fresh tissue
iii) culture including TB 
frozen for lymphocyte studies and staining for other cell types.

**Lymph nodes of ‘uncertain significance’**
Non invasive tests as above
Observe the progress for few weeks
If does not resolve – biopsy
If nodes of unresolved histology: with hyperplasia or non diagnostic granuloma,
Observe for a short period and re-biopsy
Subsequent biopsy may show progression to lymphoma.

**IMAGING STUDIES**

**Ultra sonography:**
Non invasive, specific and highly sensitive – for evaluation of splenic size.

**CT SCANNING**
*Un enhanced CT image:*
Splenetic attenuation is similar to that of liver
Size of enlarged spleen in cranio caudal length > 10 cm
Preoperative Splenic volume can be measured by CT
Peri hilar lymph nodes detectable by CT+ accessory spleen, perisplenitis, splenic abscess
CT is study of choice to diagnose inflammatory changes
But CT cannot distinguish benign from malignant lesion
CT can also detect mass lesions, cyst, infarct, calcifications

**Spleno portography**
Makes out preoperative portal vein patency, distribution of collaterals in shunt operations
Can identify cause of idiopathic splenomegaly in children

**Angiography:**
To differentiate cyst from other splenic tumors

**Spleen liver colloid scan:**
Non invasive scanning test
Can evaluate spleen size, and spleen weight before splenectomy

**Procedures**
Splectomy and splenic biopsy can be performed in specialized institutions
But severe bleeding is a limiting complication

Histological findings
Large Foamy cells in NeimannPicks disease
Large hyaline masses in Amyloid
Reactive splenic vasculitis- rare complication of typhoid fever