THE SPLEEN STRUCTURE AND ABNORMALITIES

BY DR. KIBET PETER SHIKUKU

MBCHB III

AUGUST 27, 2015

ANATOMY OF THE SPLEEN

- Parts:
  - Capsule – Separated by various trabeculae
  - Red pulp –
    - Surrounds the white pulp and contains mainly RBCs and macrophages; the main function is to phagocytise old, damaged red blood cells; it may also have a reparative function.
  - White pulp – peri-vascular, it conglomerates around a blood vessel
    - It is a circular structure made up mainly of lymphocytes. It functions in a manner similar to the nodules of a lymph node
  - Splenic vein and arteries

FUNCTION

- The spleen is a sophisticated filter that monitors and manages blood cells and immune functions
- During fetal development, the spleen produces red and white blood cells
- By the 5th month of gestation the spleen no longer has hematopoietic function but retains the capacity throughout life
- Red cells that pass through the spleen undergo a `cleaning` or repair
- Abnormal and old cells are destroyed.
- Reticulocytes loose their nuclear remnants and excess membrane before entering the circulation
- RBCs coated with IgG and IgM are removed and destroyed
  - The spleen is the site of destruction in autoimmune disease states (Immune Thrombocytopenic Purpura [ITP] and hemolytic anemia)
  - Parasites such as malaria can be removed as well
- The spleen is involved in specific and non-specific immune response (promotes phagocytosis and destruction of bacteria)

SITES OF HEMOPOIESIS

- Yolk sac
- Liver and spleen
- Bone marrow
  - Gradual replacement of active (red) marrow by tissue inactive (fatty)
  - Expansion can occur during increased need for cell production

CAUSES OF SPLENOMEGALY

- Infection
  - Bacterial - typhoid fever, endocarditis, septicemia, abscess
  - Viral – EBV, CMV and others
  - Protozoal -malaria, toxoplasmosis
- Hematologic process
  - Congenital or acquired hemolytic anemia
  - Benign hematoma, harmatoma
- Metabolic diseases
  - Lipidosis: Niemann-Pick, Gaucher disease
  - Mucopolysaccharidosis infiltration: histiocytosis
- Congestion
- Cirrhosis
- Cysts
- Miscellaneous

HYPERSPLENISM

- Refers to a variety of ill effects resulting from increased splenic function that may be improved by splenectomy
- The criteria for diagnosis include:
  - Anemia, leucopenia, thrombocytopenia or a combination of the 3
  - Compensatory bone marrow hyperplasia
  - Splenomegaly
- Hypersplenism can be categorized as **primary** or **secondary**

SPLENIC INVOLVEMENT IN HODGKIN`S LYMPHOMA

- The probability of splenic involvement increases with increasing spleen size
- The absence of splenomegaly does not exclude splenic involvement
- Upon gross examination of the spleen a greyish white nodule ranging from several millimetres to several centimetres is apparent with Hodgkin`s disease
- Liver involvement with Hodgkin`s disease rarely occurs in the absence of splenic disease

FELTY`S SYNDROME

- It is a syndrome consisting of severe RA, granulocytopenia and splenomegaly
- It usually occurs in patients with a long Hx of RA
- Severe, persistent and recurrent infections are characteristic
- Moderate splenomegaly is common
- Splenectomy is effective in most patients

GAUCHER`S DISEASE

- It is a disorder of lipid metabolism that may result in massive splenomegaly and hypersplenism
- Commonly found in the Jewish population
- Diagnosis is made by finding the typical Gaucher`s cells in biopsy tissue
- Massive splenomegaly is usually the most common form of presentation
- The adult form is most common form
- Splenectomy (subtotal) shows great benefits

CYSTS AND TUMORS OF THE SPLEEN

- The differential diagnosis of splenomegaly should include splenic masses and primary tumors (these conditions are rare however they must be considered)
  - Cystic lesions comprise parasitic and non-parasitic cysts
    - Parasitic cysts are due to almost exclusively to echinococcal disease
    - Non-parasitic cysts are classified as primary (true) which have an epithelial lining or pseudocysts
  - Symptoms of splenic cysts are vague and are caused primarily by mass effect (compression of adjacent viscera)
- Selected non-parasitic cyst may be managed by aspiration
- Splenectomy should be performed for all large cysts and those with an uncertain diagnosis
- Malignant and benign primary tumors of the spleen are rare
- Most primary malignant tumors are **angiosarcomas**

INFECTIOUS MONONUCLEOSIS

- A disease characterized by fever, sore throat, lymphadenopathy and atypical lymphocytes
- Most patients are young
- Clinical symptoms are similar to those of a severe URTI
- The spleen is enlarged and palpable in over 50% of patients
- Splenic rupture may occur

INCIDENTAL SPLENECTOMY

- The spleen is vulnerable to injury during operative procedures in the upper abdomen
- Iatrogenic disease results

SPLENECTOMY

- Prior to removal of the spleen specific preparation Is necessary:
  - All patients should receive polyvalent pneumococcal vaccine, polyvalent meningococcal vaccine, Hib conjugant vaccine
  - Blood an blood products should be available well in advance of surgery

BLOOD COMPOSITIONAL CHANGES IN THE ASPLENIC OR HYPOSPLENIC PATIENT

- The absence of functional splenic tissue results in characteristic changes in the circulating blood:
  - Some of the predictable and desirable results
  - These changes are considered a measure of its success when splenectomy is performed for a hematologic disease
  - Howell-jolly bodies (nuclear remnants) and thrombocytosis (desired result)
    - Other findings include: target cells, Acanthoctyes (spur cells)., Heinz bodies (denatured Hb) and stippled RBCs

POST-SPLENECTOMY SEPSIS

- Asplenic patients have an increased susceptibility to the development of overwhelming infection
- The risk of sepsis is approximately 60 times greater than normal after splenectomy
- The risk is greatest in children younger than 4 years of age
- The risk of sepsis is higher among patients requiring splenectomy for inherited diseases
- The risk is sepsis after splenectomy is lowest after trauma
- Post-splenectomy sepsis syndrome typically occurs in a previously healthy individual after a mild URTI associated with fever
- Within hours N, V headache, confusion, shock and coma can occur; death follows within 24 hours
- The nature of the syndrome makes it difficult to diagnose early enough for therapy to be effective.

HYPOSPLENISM

- It is the lack of a spleen or its function
- **Congenital asplenia** – rare genetic disorder
- Is potentially lethal; it is characterized by diminished splenic function
- The patient peripheral blood smears appear as if they are asplenic
- Hyposplenism can occur in the presence of abnormal sized or enlarged spleen
- The danger of hyposplenism is the risk of developing potentially lethal sepsis
- SCA is the most common associated disease

CONGENITAL ASPLENIA

- Autosomal recessive genetic disorder
- Due to absence of **Hox 11 gene** in the embryo
- Causes a decreased adaptive immune response
- Associated with structural abnormalities in other organs of the body; causes death in infancy

SPLENECTOMY

- Removal of the spleen tissue
- Partial or total
- Resident splenic function on a quarter or two thirds of patients
- IgM levels decreases, IgG levels remain constant or increase, IgA and IgE levels increase
- ***Find out why***

IMMUNOLOGICAL CONSEQUENCES

- Causes slower and incomplete adaptive immune response against bacteria
- Low levels of **tuftsin** which stimulates phagocytosis by neutrophils, macrophages and monocytes
- Decreased neutrophil and macrophage activity
- Increased NK cell activity
- Limited capacity of circulating B-cells to differentiate into antibody-secreting cells
- Decreased levels of T-cells

DIAGNOSIS

- Determine anatomic presence or absence, size, and any lesions
- Functional Assessment
  - Radiologic techniques
    - X-ray, ultrasound, CT, MRI, radionucleotide scanning
  - Morphologically
    - PBS – presence of **Howell-Jolly bodies**

BONE MARROW STRUCTURE & BONE MARROW FAILURE

MBCHB III 2015

DR. P.M MATURI

SCOPE

- Definition
- Development and anatomy and structure of the BM
- Mechanisms of BM failure and causes
- Hematological changes in HIV
- Lab tests in BM failure

LECTURE OBJECTIVES

- Describe the BM structure in related to the function
- Define BM failure and describe the mechanisms of BM failure
- List causes of marrow failure
- Outline lab tests in evaluation of marrow failure

DEVELOPMENT OF BM

- BM first appears in the clavicle near the end of fetal life and becomes active about 3 weeks later
- BM supersedes the liver as the major hematopoietic organ at 32-36 weeks` gestation
- At birth, all BM is red (active haematopoiesis)
- With age, increasing volume of BM is progressively converted to the yellow marrow (fat)
- In an adult approximately half of the BM is red
  - Flat bones (hip bone, sternum, skull, ribs, vertebrae, shoulder blades)
  - Metaphyseal and epiphyseal ends of long bones (femur, tibia, humerus – spongy or cancellous part)
- Yellow BM – interior of diaphyseal portion (shaft) of long bones
- In old age, almost all marrow is yellow
- Yellow marrow can revert to red if there is increased demand for red blood cells

ANATOMY OF THE BM

- Soft, spongy, gelatinous tissue found in the hollow spaces in the interior of bones
- Average weight of tissue is approximately 4% TBW (2.6 kg in adult of 65 kg)
- Contains the progenitor cells
- BM is also an important part of the RES
- BM consists of stem calls (large, primitive undifferentiated cells) supported by fibrous tissue – stroma
- There are 2 main types of stem cells hence 2 types of cellular tissue:
  - Haematopoietic tissue
  - Supporting stroma
- BM stroma contains mesenchymal stem cells
  - Multipotent stem cells that can differentiate into a variety of cell types including osteoblasts, osteoclasts, chondrocytes, myocytes, fibroblasts, macrophages, adipocytes and endothelial cells
- Stroma provides the microenvironment and CSFs needed to facilitate hematopoiesis by the parenchymal cells

ANATOMY OF THE BM CONT.

- The blood vessels constitute a barrier, inhibiting immature blood cells from exiting the BM
- Mature blood cells contain membrane proteins enabling attachment and passage through blood vessel epithelium
- Hemopoietic stem cells may cross the BM barrier, and may thus be harvested from blood (PBSC)
- Biologic compartmentalisation in the BM-certain cell types tend to aggregate in specific areas.

BONE MARROW FAILURE

DEFINITION

- Inability of the BM to maintain normal levels of circulating blood cells
- Characterized by anemia, leucopenia, thrombocytopenia
- Can affect a single or more (bicytopenia) or all the cell lines (Pancytopenia)
- Mechanisms
  - Destruction of BM tissue or suppression of normal hematopoietic cell growth and/or differentiation, stem cell failure)
    - Hypoplastic or aplastic
  - Replacement of marrow tissue by abnormal cells:
    - Infiltrative
    - Myelodysplasia

HYPOPLASTIC OR APLASTIC MARROW

- Marrow replaced by fat tissue (Hypocellular)
- No abnormal cells detected in PB or BM
  - Qualitative defect in multipotent stem cell
  - Defective marrow micro-environment
- Classification
  - Primary (constitutional)
    - Are inherited (congenital) disorders
  - Acquired
    - Idiopathic
    - Secondary

CLASSIFICATION OF PRIMARY AOR CONSTITUTIONAL SYNDROMES

- Fanconi anemia
  - Autosomal recessive or sex-linked inherited disorder presenting with physical and haematological abnormalities
- Dyskeratotis congenita
- Diamond Blackfan Syndrome

ACQUIRED

- Idiopathic – over 50% of the cases
- Secondary
  - Drugs – high risk, medium & low risk
  - Infections- Parvovirus B19, EBV, CMV, HBV, HIV
  - Chemicals e.g. DDT and metals (arsenic, lead, mercury)
  - Toxins

APLASTIC OR HYPOPLASTIC CAUSES - ACQUIRED

- Radiotherapy
- Immune related
- PNH (Paroxysmal Nocturnal Hemoglobinuria)
- Pregnancy

MARROW REPLACEMENT OR INFILTRATION

- Tumors
  - Leukaemia
  - Lymphomas
  - Plasma cell disorders
  - Metastatic malignancies to the BM
- Infections
  - Kala azar
  - Toxoplasmosis
- BM is cellular infiltrated by abnormal cells or tissue

BM FAILURE – LAB TESTS

- TBC
  - Pancytopenia
  - MCV may be high (100-103 fL) in aplastic anemia
- Reticulocyte count – low
- PBF
  - Macrocytes (round)
  - Poikilocytes (tear drops)
  - Abnormal WBC
- BME
  - Aspirate
  - BM trephine biopsy
- Test for cause
  - History of drug, chemical, toxin exposure in patient
  - Drug screen, viral screen, cytogenetics, flow cytometry

SITE OF BMA

- Infant < 1 year old
  - Anteromedial aspect of upper tibia (tibial tuberosity)
- Child
  - Iliac crest esp. PSIS; anterior superior iliac crest
- Adult
  - Iliac crest
  - Sternum – opp. 2nd intercostal space in the midline

END