Massive splenomegaly D/d

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spleen

In humans, its normal physiologic roles:

- Maintenance of quality control over erythrocytes.
- Synthesis of antibodies in the white pulp.
- The removal of antibody-coated bacteria and blood cells.
- Extramedullary hematopoiesis

Approach to the Patient: Splenomegaly

- Clinical Assessment
- Pain and a heavy sensation in the LUQ. Massive splenomegaly may cause early satiety.
- Pain may result from acute swelling of the spleen with stretching of the capsule, infarction, or inflammation of the capsule.

- Palpable spleen is the major *physical sign* produced by diseases affecting the spleen and suggests enlargement of the organ.
- The normal spleen weighs <250 g, has a maximum cephalocaudal diameter of 13 cm by ultrasonography

Splenomegaly

1. **Increased Demand for Splenic Function**
2. **Abnormal Splenic or Portal Blood Flow**
3. **Infiltration**

Diseases Associated with Splenomegaly

1.Enlargement Due to Increased Demand for Splenic Function

- Reticuloendothelial system hyperplasia

Eg. Hereditory spherocytosis

Thalassemia major

Hemoglobinopathies

Paroxysmal nocturnal hemoglobinuria

- Immune hyperplasia
  a)Response to infection
    - Infectious mononucleosis
    - Cytomegalovirus
    - Subacute bacterial endocarditis
    - Splenic abscess
    - Malaria,Leishmaniasis.

  b)Disordered immunoregulation
    - Rheumatoid arthritis (Felty's syndrome)
    - Systemic lupus erythematosus
    - Immune hemolytic anemias

2. Enlargement Due to Abnormal Splenic or Portal Blood Flow

- Cirrhosis
- Hepatic /portal /splenic vein obstruction
- Hepatic schistosomiasis
- Congestive heart failure

3. **Infiltration of the Spleen**

- Amyloidosis
- Gaucher's disease
- Niemann-Pick disease
- Leukemias
- Lymphomas
- Myeloproliferative syndromes

Massive splenomegaly

- Spleen palpable > 8 cm below the left costal margin or its weight is1000 g (Harrison 18e)

Causes of massive splenomegaly

Haemotological disorders

Chronic myeloid leukemia

Hairy cell leukemia

Polycythemia vera

Myelofibrosis with metaplasia

Chronic lymphocytic leukemia

lymphomas

Infiltrative disorders

Gaucher's disease

Niemann-pick disease

Other causes

Tropical splenomegaly

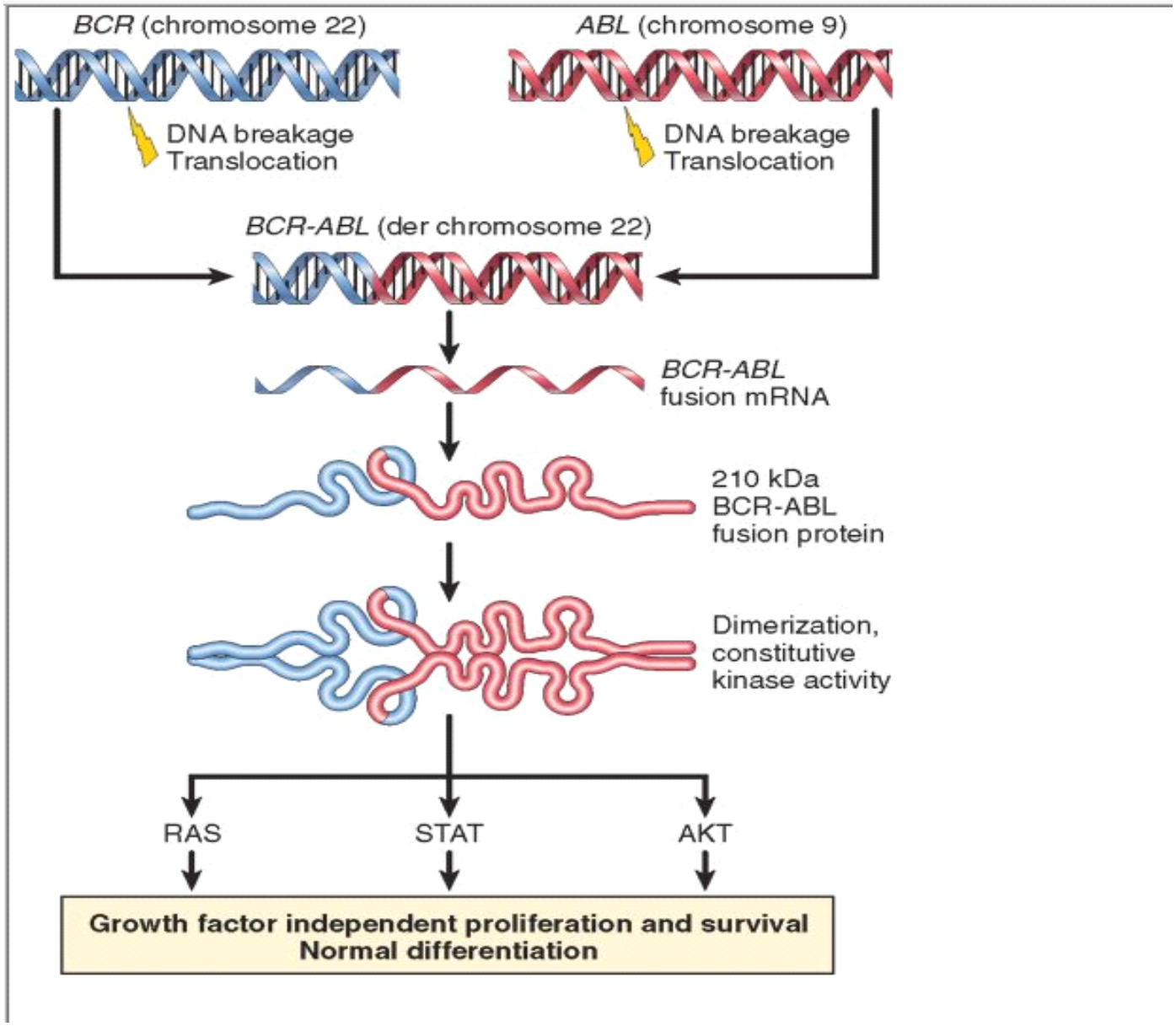
Visceral leischmaniasis

Congestive splenomegaly

Diffuse splenic haemangiosis

Chronic Myeloid Leukemia

- It is due to clonal expansion of stem cell with reciprocal translocation (t9;22).
- Philadelphia chromosome seen in >90%.
- Adults (25 to 60 yrs)


BCR (chromosome 22)
ABL (chromosome 9)
DNA breakage
Translocation
DNA breakage
Translocation
BCR-ABL (der chromosome 22)
BCR-ABL
fusion mRNA
210 kDa
BCR-ABL
fusion protein
Dimerization,
constitutive
kinase activity
RAS
STAT
AKT
Growth factor independent proliferation and survival
Normal differentiation

Clinical features

- The clinical onset of the chronic phase is generally insidious.
- Patients present with fatigue, malaise, and weight loss or have symptoms resulting from massive splenic enlargement.

  eg. early satiety, draging sensation in LUQ or mass.
- Less common are features related to granulocyte or platelet dysfunction

- splenomegaly is the most common physical finding.
- Lymphadenopathy and myeloid sarcomas are unusual.

- Elevated WBCs with increase in both immature and mature granulocytes, are present at diagnosis.
- Platelet counts are elevated at diagnosis, and a mild degree of anemia is present.
- Leukocyte alkaline phosphatase is low.
- At diagnosis, bone marrow cellularity is increased, with an increased myeloid-to-erythroid ratio.
- The marrow blast percentage is generally normal or slightly elevated

Treatment

- Imatinib inhibitis of tyrosine phosphorylation of proteins involved in Bcr-Abl signal transduction.
- In newly diagnosed CML, imatinib (400 mg/d) is more effective than IFN- and cytarabine.
- Treatment is currently recommended for life.
- Allogenic Stem cell transplation in imatinib resistant cases

Polycythemia Vera

- Panmyelosis (increase in RBC, granulocytes, platelets).
- Median age of onset is 60 yrs.
- Symptoms are related to increased red cell mass – hyperviscocity.

  headche, vertigo, visual disturbance,

  systolic hypertension
- Thrombosis (altered flow n platelet dysfn)

  cerebral, cardiac, mesenteric vessels are

  affected

- CBP

  Hb – 14 to 28g/dl

  WBC and platelets are elevated.
- Serum erythropoietin level is very low.
- Bone marrow initially hypercellular , later myelofibrosis develops leading to extra medullary haematopoiesis
- Massive splenomegaly is due to marrow failure.
- Phlebotomy to decrease red cell mass is treatment of choice.

Hairy cell leukemia

- It affects elderly males. (M : F = 4 : 1)
- Typical presentation involves Pancytopenia.
- Massive Splenomegaly is commom. Hepatomegaly less common, lymphadenopathy is rare.
- Bone marrow is typically not able to be aspirated (DRY TAP)
- biopsy shows fibrosis with diffuse infiltration by the malignant cells.

- Pancytopenia is due to marrow failure and spleen sequestration.
- Patients with this disorder are prone to m*ycobacterium avium intracellulare*.
- It is sensitive to interferon, pentostatin and cladribin.

Primary Myelofibrosis

- Seen in elderly males >60 yrs
- Characterized by marrow fibrosis, extramedullary hematopoiesis, and splenomegaly.
- usually detected by the discovery of splenic enlargement and/or abnormal blood counts during a routine examination.

- Present with night sweats, fatigue, weight loss in contrast to other MPDs.
- Blood smear shows tear drop cells and nucleated red cells.
- Marrow is usually inaspirable due to the myelofibrosis.
- Bone x rays may reveal osteosclerosis due to increased osteoprotegerin.
- No specific therapy exists for PMF.

Infiltrative diseases

Gaucher's disease

Niemann-pick disese

- These are lysosomal storage disorders.
- These are common in Askenazi Jews.

Disease	Enzyme deficiency	**Major Accumulating Metabolites**
Gaucher disease	Glucocerebrosidase	Glucocerebroside
Niemann-Pick disease: types A and B	Sphingomyelinase	Sphingomyelin

- Gaucher's disease is of three types
- Type I
  - hepatosplenomegaly
  - no CNS involvement
- Type II
  - severe CNS disease that leads to death by 2 years of age
- Type III
  - hepatosplenomegaly
  - myoclonic seizures,dementia.

Tropical splenomegaly

- Hyperreactive malarial splenomegaly.

- Etiology : although malarial parasite NOT demonstrated in smear, there are convincing evidence to support linkage.

1. It is prevalent in malaria endemic areas
2. High level of malarial antibodies seen.

3. Anti malarial drugs reduce size of spleen
4. Effective chemoprophylaxis has been shown to reduce spleen rates n incidence of HMS
5. It ia uncomon in children younger than 8yrs suggesting continuous exposure

- Chronic or repeated malarial infections produce cytotoxic IgM antibodies to CD8+ T cells and polyclonal production of IgM leads to formation of cryoglobulins.
- These cryoglobulins are cleared by spleen and liver leading to hyperplasia.
- Treatment : antimalarial chemoprophylaxis chloroquine and/or proguanil for one year

Visceral Leischmaniasis

- Caused by L.donovani and L.chagasi
- Two forms of parasite

  promastigote – sand fly (extracellularly)

  amastigote - man (macrophages)
- The parasites invade reticuloendothelial system and cause systemic disease with hepatosplenomegaly, lymphadenopathy, pancytopenia, fever, weight loss.
- Amastigotes in smears of tissue aspirates is the gold standard for the diagnosis of VL

- In the field, a rapid test based on the detection of antibodies to a recombinant antigen (rK39) used .
- liposomal AmB is the drug of choice
- The regimen is 3 mg/kg daily on days 1–5, 14, and 21 (total dose, 21 mg/kg).

Congestive splenomegaly

- Causes

  cirrhosis of liver(alcoholic, schistosomiasis)

  splenic or portal vein thrombosis

  cardiac failure.
- Long standing splenic congestion produces massive splenomegaly.
- Patients may have thrombocytopenia and leukopenia.
- Some patients will have fairly significant left upper quadrant abdominal pain related to an enlarged and engorged spleen.

- Spleen firm, fibrotic and capsule thickened
- Orgnization of focal haemorrhages gives rise to Gamma-Gandy nodules (consist of fibous tissue with haemosiderin n calcium deposits).
- Splenomegaly itself usually requires no specific treatment.

Thank you