Myeloproliferative Disorders (Neoplasm)II

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Objectives

- Discuss definition, types, pathophysiology, clinical features, laboratory findings, complications and treatment of essential thrombocythsaemia
- Discuss definition, pathophysiology, clinical features , laboratory findings , complications and treatment of myelofibrosis

Introduction

Essential Thrombocythemia (ET)

- Marked increase in megakaryocytes & platelet mass

- ❑ Predisposition to thrombotic and hemorrhagic events
- ❑ Generally indolent course
- ❑ Transformation to acute leukemia uncommon, but occurs

- **ET: Epidemiology**
- Uncommon, but not *very* rare
- Predominantly older population
- Men ~ women:
  - Frequent occurrence in young women described in some series

- **ET: Thrombosis**

- ❑ Arterial > venous
- ❑ Small vessels (arterioles) >> large vessels
- ❑ Any system in body can be affected
- ❑ Neurologic & distal extremities most commonly involved
- ❑ Headache
- ❑ Paresthesias

- Transient ischemic attacks:

• ET: Thrombosis

• ET: Thrombotic Manifestations

• ET: Hemorrhagic Manifestations

- Tends to occur with high platelet counts (>10^6 platelets/mL)
- Bleeding is generally mild
- GI tract most common site of bleeding
- Other sites: skin, eyes, urinary tract, gums, joints, brain

• ET: Differential Diagnosis

- Reactive thrombocytosis
- Other chronic myeloproliferative neoplasms
- Pseudothrombocythemia:
  - WBC fragments (leukemia), schistocytes, microspherocytes (severe thalassemia)

- Must exclude chronic myeloid leukemia (CML)!

- **Causes of Reactive Thrombocytosis**
  - ❑ Infections
  - ❑ Inflammation of any type
  - ❑ Malignancy (non-hematologic)
  - ❑ Trauma
  - ❑ Blood loss or iron deficiency
  - ❑ Haemolysis etc

- **ET: Investigations**

❑ CBC & Blood Smear

- Threshold platelet count >450,000/mL
  - May be >1,000,000/mL

❑ Leukocytosis common:

❑ Hemoglobin usually normal

❑ Giant & bizarre platelets on smear

- **ET: Investigations**

- **ET: Treatment**

First question: *Who* to treat?

- ❑ Older patient (>60 years) or patient with previous thrombotic episodes: treat
- ❑ Young (<40 years), asymptomatic patient: May not require treatment
- ❑ In between, asymptomatic: controversial

- **ET: Treatment**

- ❑ Control of platelet count reduces both thrombotic & hemorrhagic complications
- ❑ Treatment options:
  - Hydroxyurea
  - Aspirin
  - Interferon-a
  - Anagrelide
  - Plateletpheresis

• Primary Myelofibrosis (PMF)

- ❑ Fibrosis in marrow (myelofibrosis)
- ❑ Leukoerythroblastic reaction in blood:
  - Nucleated RBCs, teardrop RBCs, immature granulocytes
- ❑ Splenomegaly, often massive
- ❑ Extramedullary haematopoiesis

• PMF: Pathophysiology

- ❑ Excessive production of growth factors by neoplastic megakaryocytes and other cells
- ❑ Growth factors stimulate fibroblast proliferation and production of collagen
- ❑ Fibroblasts are not part of malignant clone
- ❑ One third of patient has previous PRV

• PMF: Epidemiology

- ❑ Predominantly older population
- ❑ Male ≈ female (?)
- ❑ Possible etiologic factors:
  - – Ionizing radiation
  - – Organic solvents (benzene, toluene)
  - – No obvious underlying cause in most cases

• PMF: Clinical Features

- ❑ Fatigue due to anemia
- ❑ Abdominal discomfort, early satiety due to splenomegaly
- ❑ Bleeding: Petechiae & purpura to haematemesis from gastroesophageal varices

• PMF: Investigations

CBC & PBF

- ❑ Anemia common
- ❑ WBC variable: Leukocytosis in or Leukopenia in
- ❑ Platelets: Decreased rarely increased with megakaryocyte fragments & giant platelets

- Leukoerythroblastic reaction with teardrop RBCs:
  - Nucleated RBCs
  - Granulocyte precursors, including occasional blasts

• MF: Investigations

• MF: Investigations

Bone marrow:

- Usually “dry tap” (no aspirate)
- Fibrosis (may be subtle at first)
- Cellularity: Initially increased (“cellular phase”); later decreased
- Marked increase in megakaryocytes
- Osteosclerosis may develop late

• MF: Investigations

• PMF: Differential Diagnosis

- Other MPNs
- Metastatic neoplasms: Carcinoma, lymphoma
- Infections: Tuberculosis, fungi

- ❑ Other granulomatous diseases
- ❑ Hairy cell leukemia
- ❑ Others

• PMF: Clinical Course & Complication

- ❑ Median survival ~ 5 years
- ❑ Younger patients without anemia may have prolonged survival
- ❑ Causes of death:
  - Infection
  - Acute leukemic transformation (5-20%)
  - Heart failure
  - Hemorrhage

• PMF: Treatment

- ❑ Treatment is usually palliative
- ❑ Correct reversible factors: Iron, folate deficiencies
- ❑ RBC & platelet transfusions as needed
- ❑ Splenectomy (?)
- ❑ Interferon-a
- ❑ Stem cell transplant (experimental)

- **Summary: JAK2 in MPNs**

Questions

Thank you