* **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 (>106 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