Hematology

438 teamwork

Polycythemia

Color index:

Red: Important

Gray: Extra, notes

Editing file

objectives

- **Myeloproliferative Neoplasms:**
  - **Polycythemia vera (PV)**
  - **Essential thrombocythemia (ET)**
  - **Primary myelofibrosis (PMF)**

MPN Features

01 Cytosis

02 Organomegaly (splenomegaly)

03 High uric acid

04 Hypercellular bone marrow

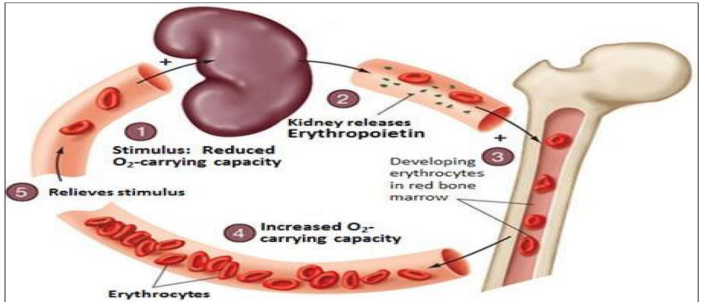
05 Progress to Acute leukaemia (mainly AML)

MPN Overview

1. **Myeloproliferative neoplasms (MPN)**
   - 1.1. Chronic myelogenous leukemia, *BCR-ABL1*–positive (CML)
   - 1.2. Polycythemia vera (PV)
   - 1.3. Essential thrombocythemia
   - 1.4. Primary myelofibrosis (PMF)
   - 1.5. Chronic neutrophilic leukemia
   - 1.6. Chronic eosinophilic leukemia
   - 1.7. Mast cell disease (MCD)
   - 1.8. MPN, unclassifiable

   BCR-ABL must be negative
2. **Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of *PDGFRA*, *PDGFRB*, and *FGFR1***
3. **MDS/MPN**
   - 3.1. Chronic myelomonocytic leukemia (CMML)
   - 3.2. Juvenile myelomonocytic leukemia (JMML)
   - 3.3. Atypical chronic myeloid leukemia, *BCR-ABL*–negative (aCML)
   - 3.4. MDS/MPN, unclassifiable
4. **Myelodysplastic syndromes (MDS)**
5. **Acute myeloid leukemia (AML)**

Erythropoiesis regulation

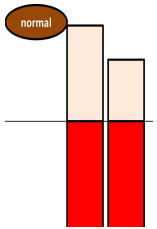


1- The kidney has hypoxia inducible factor which stimulates the production of Erythropoietin

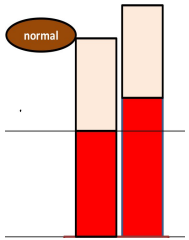
2-Hypoxia Inducible Factor has an activator (low oxygen) and an inhibitor(von hippel lindau Gene)

Polycythemia

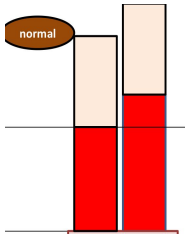
Characteristics	• In Greek “too many cells in the blood.”. • Absolute increase in total body red cell volume (or mass) • Manifests itself as a raised Hb or packed cell volume (PCV) • Hb is >16.5or 18.5 g/dl in women and men, respectively.	
Classification of polycythemia	**Relative polycythemia**	Decreased plasma volume due to severe dehydration
	Secondary polycythemia or reactive	**Increased RBC mass due to high EPO:** • COPD, Sleep apnea, smoking • High altitude • High affinity HB • Renal disease • Epo secreting tumor (Parathyroid adenoma)
	polycythemia vera	Increased RBC mass due to malignant proliferation



Relative polycythemia

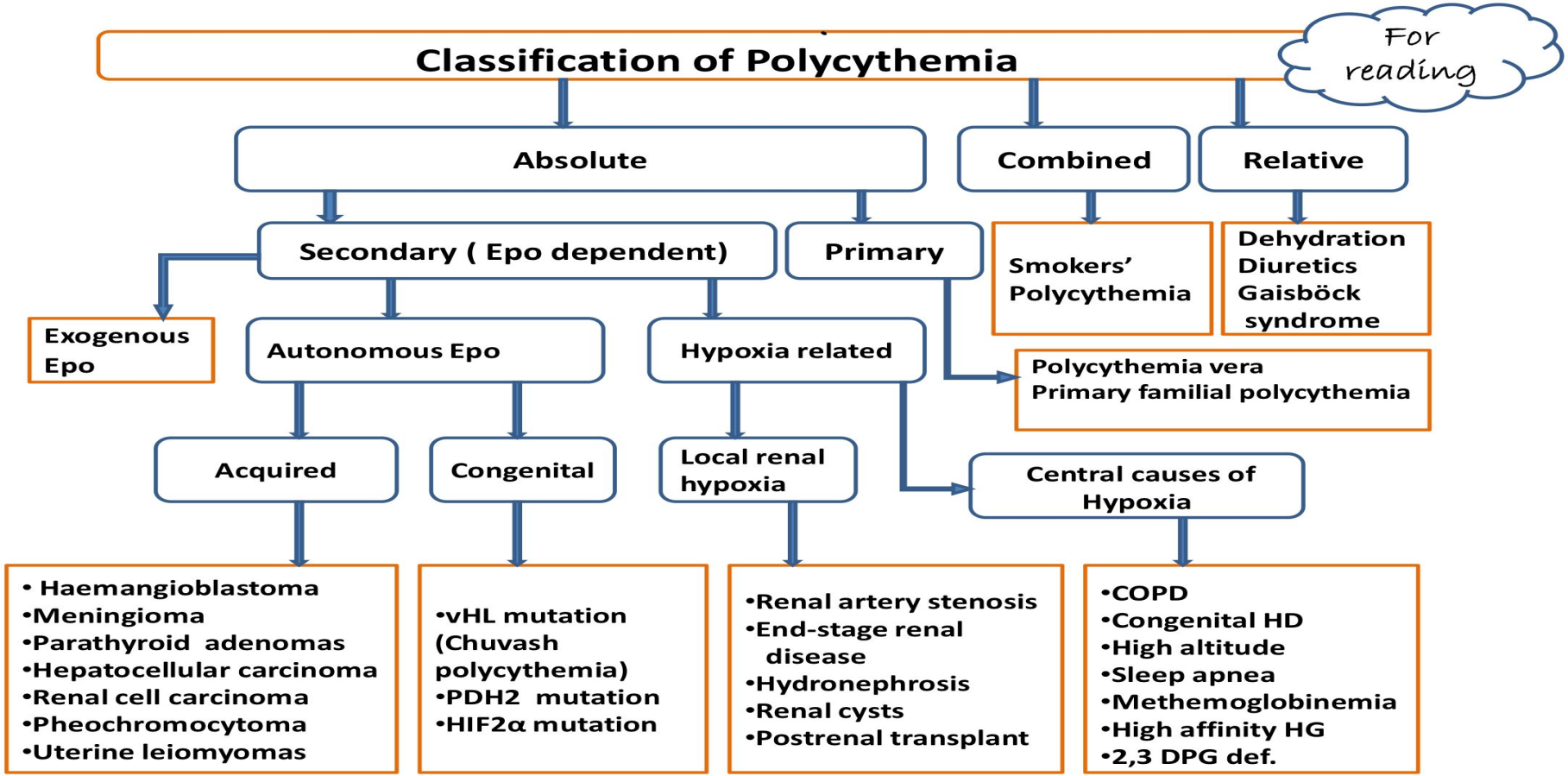


Secondary polycythemia or reactive



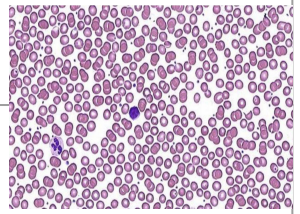
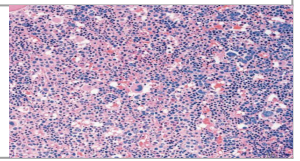
Polycythemia vera

For Reading


Classification of Polycythemia
For reading
Absolute
Combined
Relative
Secondary (Epo dependent)
Primary
Smokers' Polycythemia
Dehydration
Diuretics
Gaisböck syndrome
Exogenous Epo
Autonomous Epo
Hypoxia related
Polycythemia vera
Primary familial polycythemia
Acquired
Congenital
Local renal hypoxia
Central causes of Hypoxia
• Haemangioblastoma
•Meningioma
•Parathyroid adenomas
•Hepatocellular carcinoma
•Renal cell carcinoma
•Pheochromocytoma
•Uterine leiomyomas
•vHL mutation (Chuvash polycythemia)
•PDH2 mutation
•HIF2α mutation
•Renal artery stenosis
•End-stage renal disease
•Hydronephrosis
•Renal cysts
•Postrenal transplant
•COPD
•Congenital HD
•High altitude
•Sleep apnea
•Methemoglobinemia
•High affinity HG
•2,3 DPG def.

Polycythemia Vera

Definition: MPN characterized by increased red blood cell production independent of the mechanisms that normally regulate erythropoiesis.

Diagnostic features		• HB >18.5g/dl in men ,16.5g/dl in women • Hypercellular bone marrow and Low Serum erythropoietin level • JAK2 mutation in >95% of cases	
Clinical features		**1-Increased blood viscosity** • Hypertension, Headache, dizziness, visual disturbances & paresthesia **2- Thrombosis** • Deep vein thrombosis, Myocardial infarction, Mesenteric, portal or splenic vein thrombosis **3-Splenomegaly in 70%, Hepatomegaly in 40%**	
Investigations	**CBC**	• RBC and Hb: Increased • WBC & PLT :mildly increased (usually)	
	Blood smear	• Excess of normocytic normochromic RBC • ± Leukocytosis & Thrombocytosis	
	Bone marrow	• Hypercellular , Predominant erythroid precursors • ± increased megakaryocytes & myeloid precursors • If Blasts increase (>20%) → AL transformation	

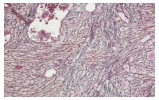
Polycythemia Vera cont.

Diagnosis of polycythemia vera

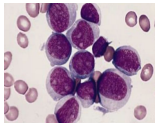
Treatment:
- **Venesection + Aspirin**
- **Myelosuppressive drugs (hydroxyuria)**

10-15 yrs

Myelofibrosis (20%)



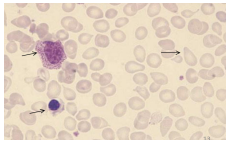
Acute leukemia (10%)



Primary myelofibrosis

The worst type in terms of prognosis

Definition: Clonal MPN characterized by a proliferation of megakaryocytes & granulocytes in the bone marrow that associated with deposition of fibrous connective tissue and extramedullary haematopoiesis



3-Teardrop RBCs shape is very characteristic for primary Myelofibrosis

Clinical features:

01 **Anemia**

02 **Leukoerythroblastic blood picture.**

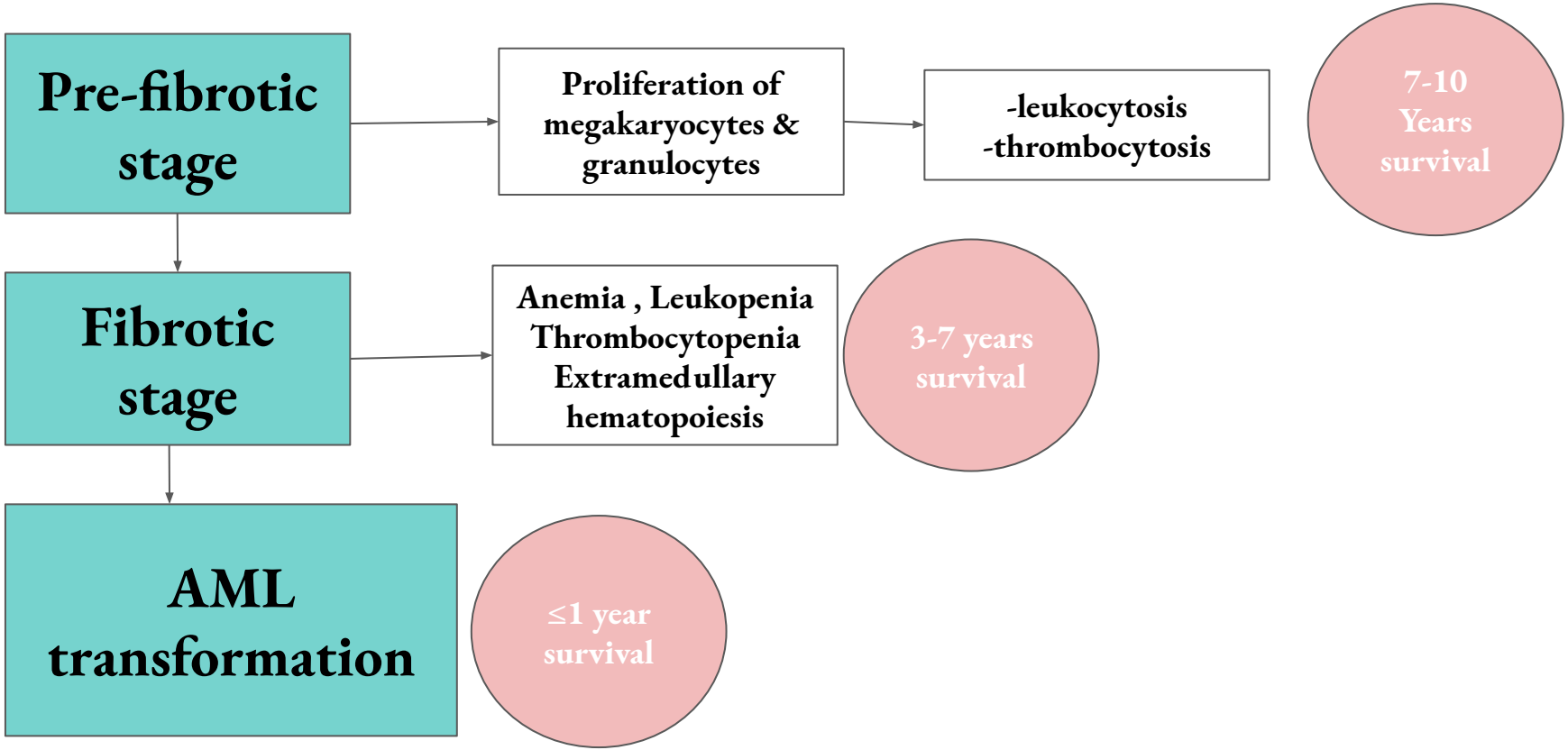
03 **Massive splenomegaly**

04 **Fibrotic bone marrow**

05 **JAK2 mutation (50%)**

06 **Risk of AML transformation (20%)**

Stages of Primary myelofibrosis



Essential Thrombocythemia

The Best type(Better prognosis) in terms of prognosis

4-Reactive Thrombocytosis must be differentiated from Thrombocythemia 5-In Thrombocythemia, if platelets are overactive there might be thrombosis, If platelets are inactive there might be bleeding

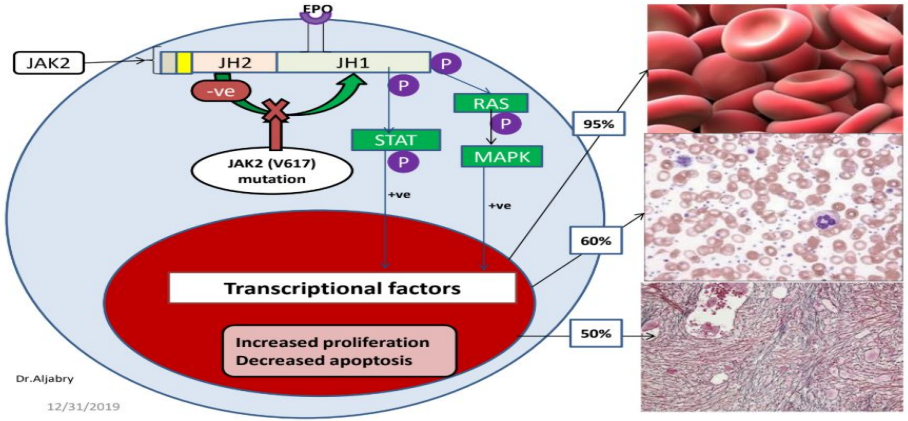
Definition: ET is MPN that involves primarily the megakaryocytic lineage. & characterized by sustained thrombocytosis .

Diagnostic features	• Sustained thrombocytosis ≥45O×109. • Hypercellular BM with megakaryocytic proliferation • Exclusion of: CML, MDS,PV & Primary Myelofibrosis • JAK2 mutation (60%),If negative ;no evidence of reactive thrombocytosis: ○ Iron def. ,splenectomy, surgery, infection ,autoimmune disease....
Clinical features (Very indolent: 5% risk of AML transformation)	• Asymptomatic (50%) • Thrombosis • Bleeding • Mild splenomegaly (50%) • Mild hepatomegaly (20%)
Treatment	Aspirin ±Hydroxyuria

JAK2 Mutation

What's JAK2? Non receptor protein tyrosine kinase involved in signal transduction pathway.

What's JAK2 Mutation? Point mutation (at codon 617 in JH2) leads to loss of auto inhibitory control over JAK2. The mutated JAK2 is in a constitutively active state,



Polycythemia vera

Essential Thrombocythemia

Primary Myelofibrosis

Negative Feedback

6-In Jak2 Gene, the JH2 segment is inhibitory for JH1 which is excitatory for transcriptional factors responsible for the proliferation of blood cells.
In JAK2 mutation the inhibition done by JH2 segment is disrupted, leading to abnormal proliferation

Quiz

Key answers:
1-B 2-B 3-C 4- C 5- D 6- C

1- What do you expect the level of EPO on polycythemia vera ? (from dr.notes)

A. High
B. Low
C. Normal
D. Normal or high

2- Which of the following is true about polycythemia vera?

A. Increased RBCs and Decreased Hb
B. Increased RBCs and Increased Hb
C. Increased RBCs and Decreased WBCs
D. Increased RBCs and Decreased Platelets

3- Which of the following is a clinical feature for polycythemia vera?

A. Vomiting
B. Arthritis
C. Paresthesias
D. Skin tags

4- Which of the following MPN has the worst prognosis?

A. Polycythemia vera
B. CML
C. Primary myelofibrosis
D. Essential thrombocythemia

5- Which of the following MPN has the best prognosis?

A. Polycythemia vera
B. CML
C. Primary myelofibrosis
D. Essential thrombocythemia

6- Which of the following is a common feature for primary myelofibrosis?

A. Increased RBCs and Monocytes
B. Hepatomegaly
C. Leukoerythroblastic blood picture
D. None of the above

THANKS

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