CHRONIC NEUTROPHILIC LEUKEMIA (CNL)
Definition

- Sustained PB neutrophilia
- BM hypercellularity
- Hepatosplenomegaly

Should exclude
- all causes of reactive neutrophilia
- all other myeloproliferative diseases
Epidemiology

- Very rare disease, true incidence is unknown
- <100 cases reported
- Affects older adults
- No gender predilection
CNL

Sites of involvement

- PB and BM: always involved
- Spleen, liver: usually show leukemic infiltrates
Clinical features

- Most constant feature: splenomegaly
- Hepatomegaly usually present
- Up to 30% of cases: h/o bleeding from mucocutaneous areas or GI tract
- Gout
- Pruritis
CNL

- Etiology
  - Unknown
  - A/W multiple myeloma (up to 20% of cases)
**CNL**

- **PB Morphology**
  - Neutrophilia >25 x 10^9/L
  - Mostly PMNs (+/- toxic granules) and bands (>80% of WBCs)
  - Immature granulocytes (<10% of WBCs)
  - Blasts almost never seen (<1% of WBCs)
  - No dysplasia
  - Normal RBCs and platelets
**CNL**

- **BM morphology**
  - Hypercellular (neutrophilic proliferation)
  - M:E may reach 20:1
  - No increase in myeloblasts (<5% of nucleated marrow cells) or promyelocytes
  - Myelocytes and mature granulocytes increased
  - No dysplasia (if present→ consider atypical CML)
  - Look for a/w plasma cell dyscrasia
CNL

- **Cytochemistry/immunophenotype**
  - Increased Leukocyte Alkaline Phosphatase (LAP)

- **Genetics**
  - Normal in 90% of cases
  - Common abnormalities: +8, +9, del (20q), del (11q)
  - Beware of CML with P230 (with PB neutrophilia)
CNL

Prognosis

- Slowly progressive disorder
- Variable survival (6 mo to >20 y)
- Development of myelodysplastic features may signal transformation to acute leukemia
CHRONIC EOSINOPHILIC LEUKEMIA / HYPEREOSINOPHILIC SYNDROME

(CEL / HES)
CEL / HES

- Definition

- Persistently increased numbers of eosinophils in the blood ($>1.5 \times 10^9$/L), bone marrow, and peripheral tissues.

- Organ damage occurs as result of leukemic infiltration or the release of cytokines, enzymes, or other proteins by the eosinophils.
To make the Dx of HES

- Exclude all causes of reactive eosinophilia
- Exclude all neoplastic disorders in which eosinophils are part of the neoplastic clone
- Exclude T cell population with aberrant phenotype and abnormal cytokine production
CEL

To make the Dx of CEL

- Same as HES, and
  - Evidence of eosinophilic clonality
  - 2% - 20% myeloblasts in PB
  - 5% - 20% myeloblasts in BM
CEL / HES

- Epidemiology
  - Rare
  - True incidence is unknown
  - HES
    - M:F = 9:1
    - Peak in 4\textsuperscript{th} decade
  - CEL
    - Marked male predominance
CEL / HES

- Site of involvement
  - PB and BM always involved
  - Spleen and liver involved in 30-50% of cases
  - Also: heart, lungs, CNS, skin, GI tract
Clinical features

- Asymptomatic (10%)
- Constitutional Sxs (fever, fatigue, cough, angioedema, muscle pains, pruritis, diarrhea)
- Erythroderma in a man with HES.
- Indurated edematous plaques on the legs.
Clinical features

- Most serious findings are cardiac
  - Endomyocardial fibrosis with restrictive cardiomyopathy
  - Mitral / tricuspid valve scarring with regurgitation and embolization
- Other frequent findings
  - Peripheral neuropathy, CNS dysfunction, pulmonary Sxs, rheumatologic Sxs
CEL / HES

- Etiology
  - Unknown
CEL / HES

- **PB Morphology**
  - Striking eosinophilia (mainly mature eos.)
  - Possible abnormalities (not reliable criteria)
    - Sparse granulation with clear areas of cytoplasm
    - Cytoplasmic vacuolization
    - Nuclear hypersegmentation or hypossegmentation
    - Enlarged size
PB Morphology (cont’d)

- Neutrophilia
- Monocytosis
- If blasts >2% -> consider CEL
**CEL / HES**

- **BM Morphology**
  - Hypercellular (due to proliferation of eos.)
  - Orderly eosinophilic proliferation
  - Charcot-Leyden crystals in macrophages
  - Normal erythropoiesis and megakaryopoiesis
  - If blasts >5% -> consider CEL
  - Possible fibrosis
CEL / HES

- Cytochemistry / immunophenotype
  - MPO positive (cyanide-resistant)
CEL / HES

Genetics

- No single abnormality identified
- +8, i(17q)
- 8p11 translocations:
  - t(8;13)(p11;q12)
  - t(8;9)(p11;q32-34)
  - t(6;8)(q27;p11)

Notes: genetic abnormalities a/w eosinophilia in other diseases:
- inv16(p13;q22) AML-M4e
- t(5:12)(q33;p13) CMML
CEL / HES

Prognosis

- Variable 5 yr. survival rates (up to 80%)
- Unfavorable prognostic factors
  - Marked splenomegaly
  - Increased blasts in PB or BM
  - Cytogenetic abnormalities
  - Dysplasia in other myeloid lineages