Abnormal CBC

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Abnormal CBC

• What I look at in a CBC
• Approach to specific abnormalities
What I look at in a CBC

- Hct
- MCV
- MCHC
- Plts
- WBC
- Diff - # not %!
MCV

- < 70 fl
  - Either thalassemia or iron deficiency
- > 100 fl but not anemic
  - Alcohol
  - Smoking
  - Dysproteinemia
  - Normal variant
Microcytosis

- Iron Deficiency
- Thalassemia
- Anemia of chronic disease
  - Rarely < 70fl
- Sideroblastic
  - Rare
Meltzer Index

- MCV/RBC
  - > 13 – Iron deficiency
  - < 13 – Thalassemia
MCHC

• Mean Corpuscular Hemoglobin
  – Moves with MCV
• > 36 can be a sign of hereditary spherocytosis
Differential

• Absolute counts not percent that matters.
Anemia

• My approach
Work-Up: I

- Reticulocyte Count
- Smear Review
- Nutritional
  - Ferritin
  - Methylmalonic acid
  - Homocystine
  - Copper
    - Neutropenia
    - Sensory deficits/ataxia
Ferritin: Bottom Line

- Ignore lab reference ranges!
  - < 15 ng/ml 100% specific
  - > 100 ng/ml rules-out
- In older patients ferritins < 100ng/ml consider GI work-up
- Iron supplementation to women with ferritins < 50ng/ml improves fatigue
Work-Up II

- ACD/Renal
  - Erythropoietin Level
  - CMP
- Hemolysis
  - Reticulocyte count
  - LDH
  - Bilirubin – total and direct
  - Direct antibody test
  - Haptoglobin
Work-Up III

- SPEP/Serum Free Light Chains
  - Older patient
  - Back pain
  - New onset renal disease
  - Severe anemia
When to Do a Bone Marrow?

- Circulating immature cells
- Severe pancytopenia
- Very low reticulocyte count (<0.01%)
- Nucleated red cells
- Evidence of marrow infiltration
- Staging of malignancies
- Unexplained anemias
Erythrocytosis

• Hemoglobin > Men: 18.5 (16.5) or Women 16.5 (16)
• High hematocrit and other blood counts up
• Big question – Polycythemia vera vs other causes
Differential Diagnosis

- Polycythemia vera
- Hypoxia
  - Lung disease
  - High altitude
  - Sleep apnea (nocturnal desaturation)
- Impaired oxygen delivery
  - Smoking
    - $> 1$ PPD $\rightarrow$ Hbg by 1
Testosterone

- Increased sensitivity to EPO
- Onset months
  - Can take several months to resolved
- Phlebotomy with hct >54%
- Space out injections
- Transdermal
Other Important Causes

• Renal
  – Cancer
  – Big renal cysts
  – Renal artery stenosis
• Hepatic
  – Hepatomas
  – Hepatitis
• Endocrine Tumors
Genetic Causes

• Abnormal Hemoglobinins
  – Impaired oxygen delivery
  – Most common
• EPO-R mutations
• HIF pathways
Work-up I

• Suspicion for PRV increases if
  – Other counts elevated
  – Splenomegaly
  – Aquagenic pruritus
• JAK2 mutation assay
  – Abnormal in 99% of PRV
  – Diagnostic test
Work-Up II

- Erythropoietin levels
  - PRV if below normal
- Oxygen saturation
- Sleep Studies
- Carboxyhemoglobin
- Renal/Liver imaging
- Hemoglobin electrophoresis
- \( P_{50} \) studies (Mayo Clinic)
Therapy

• PRV
  – Phlebotomy
  – Hydroxyurea
  – Ruxolitinib

• Secondary
  – Congenital cardiac – NO!
  – Lung disease hct > 57
  – Oxygen, CPAP, …
Neutrophilia

• Neutrophils > 10,000/ul
• Red Flags
  – Immature forms (blasts)
  – > 20,000/ul
Neutrophilia - DDX

• Neoplastic
  – Acute myelogenous leukemia
    • Blasts
  – Chronic myelogenous leukemia
    • Immature cells
  – Chronic neutrophilic leukemia
    • High neutrophils counts
Neutrophilia - DDX

- Infections
- Rheumatic conditions
- Obesity
  - Adipose cells make growth factors
- Smoking
  - Doubles WBC
- Pregnancy
- Steroids
  - Cushings
Leukemoid Reactions

- Very high blood counts (up to 100,000)
  - Predominantly neutrophil
- Chronic infections
- Bad C diff
- Solid tumors
Neutrophilia - Evaluation

- History/physical
  - Smoking/obesity
- Testing – rule out neoplasm
- CML – obtain FISH for BCR-ABL
- Other counts up – JAK2
- Bone Marrow if > 20,000/ul
Neutropenia

- Mild Neutropenia is very common!
- Concern
  - ANC < 1000
- Really concerned
  - ANC < 500
Neutropenia

- Ethnic
  - 800-1000
  - Lack of Duffy blood group

- SSRI
  - Mild neutropenia

- Copper deficiency
  - Usually anemic
  - Sensory neurologic defects
Drugs

• Antiseizure medications
  – Dilantin
• Nonsteroidal Anti-inflammatory
• Vancomycin
• Penicillins
• TMP-SMZ
• Anti-Thyroid
Neutropenia

• “Benign”
  – ANC < 500
  – Responds to infections

• NK/T-Suppresser cell leukemia

• Hairy cell Leukemia

• Felty’s syndrome
Neutropenia - Evaluation

- Sudden and sick
  - Admit
  - Stop new medications
  - Prophylactic antibiotics
  - Growth factors
Neutropenia - Evaluation

- History
- < 1000/ul
  - Flow cytometry for abnormal lymphocytes
  - Anti-granulocyte antibodies
- Copper levels
- Evaluation for other rheumatoid disorders
- Duffy blood group
Therapy

- Immune
  - Immunosuppression
- Hairy cell
  - Chemotherapy
- Benign - nothing
Eosinophilia

- Very common issue
- Almost always secondary to other process
- Hypereosinophilia syndrome rare but interesting disease
Causes of Hypereosinophilia

- Neoplastic
- Allergic/Asthma
- Addison
- Collagen Vascular
- Parasites
Neoplastic

- Hodgkin disease classic
- Solid tumors (lung, pancreas, colon, GYN)
- Lymphoma
- Hyper Eosinophilic Syndrome (HES)
What is HES?

• Eosinophil count > 1500/uL
  – 6 months*

• End organ damage
  – Heart
  – Neurological
  – Skin
  – GI

• No other obvious cause
Allergic

- Seasonal allergies
- Asthma
- Drug allergies
Addison

- Lack of endogenous steroids
Collagen Vascular

- Churg-Strauss
  - Pulmonary involvement
- Any Vasculitis
Parasites

- Any tissue invasive parasite
- Toxocara – dog and cat poop
- Strongyloides – can reoccur after many years
- Trichinella – why we need to cook our pork!
DDX of Eosinophilia by Eos
Counts
500-1,000/uL

- Endocrine disorders
- Allergies
- Dermatologic disorders
- Solid tumors
1,000-5,000/uL

- Asthma
- Aspirin allergies
- Parasites
- Vasculitis
- HES
5,000-50,000/uL

- Churg-Strauss
- Hypereosinophilic syndrome
- Visceral larva migrans
- Tropical pulmonary eosinophilia
Eosinophilia: Evaluation

- Detailed history
- Guided by counts
- May need stool samples, biopsies, etc.
Therapy

- Remove primary cause!
- HES:
  - Imatinib
  - Steroids
  - Hydroxyurea
  - IL-5 antibodies
Monocytosis

- The Poor Man’s Sed Rate
  - Any inflammation
- > 1000 or abnormal monocytes
  - Chronic myelomonocytic leukemia
  - Can be subtle
  - Worry about if other counts are low
Elevated Immature Granulocytes

- The curse of every hematologist's existence
- Essentially meaningless
  - Validity for a few conditions
  - Often up in inflammation
- Lab will call out blasts, etc..
- I ignore
Lymphocytosis

• Lymphocytes > 5000/μL
• Very common!!!
  – Up to 4-5% of the population will have clonal lymphocytes
  – Monoclonal B-lymphocytosis (MBL)
Lymphocytosis - DDX

- Clonal
  - CLL
  - MBL
- Reactive
- Post-splenectomy
CLL vs MBL

- Old criteria for CLL was lymphocytes > 15,000/ul
- With new lab techniques lowered to 5,000/ul
- MBL – clonal lymphocytes but less than 5000/ul
CLL vs MBL

• Risk of progression higher with counts > 10,000/uL
• BUT – can progress at any count (~ 1-2%/yr)
Rarer Causes of Lymphocytosis

- T-cell CLL
- Hairy cell leukemia
- Lymphoma
Work-Up

- Work-up if > 5,000/μL
- Flow Cytometry
  - Detects cell surface proteins
  - Looks for clonal populations
- Lymph node exam
Prognosis: MBL and Stage O CLL

- Overall good but moving target
- Unclear if more elaborate testing will help
Thrombocytosis

- > 450,000/μL
- Primary
  - Myeloproliferative
- Secondary
- Idiopathic?
Thrombocytosis

• Myeloproliferative
  – Essential thrombocytosis
  – Polycythemia rubra vera
  – Chronic myelogenous leukemia
Secondary

- Can be > 1,000,000/ul
- Inflammation
- Iron deficiency
- Post-splenectomy
- “Rebound”
Clues to ET

- Splenomegaly
- Erythromelalgia
- Thrombosis
  - Visceral vein thrombosis
- Bleeding
Work-up

- Myeloproliferative
  - JAK2/CALR/MPL
  - BCR-ABL
  - Splenic ultrasound
- Secondary
  - Ferritin
  - CRP
“Idiopathic”

- Patients with mild increases in platelets and no positive tests
  - Essential thrombocytosis
  - Congenital
  - ?

- Avoid labeling

- Treat with aspirin

- Follow closely
The Paradox of Essential Thrombocytosis

- The higher the platelet count, the greater the risk of bleeding!
Essential Thrombocytosis

- Very prolonged natural history

Therapy
- Aspirin if not bleeding
- Cytoreduction if
  - > age 60
  - Vascular risk factors
  - Previous thrombosis
Thrombocytopenia

• Classic definition
  – < 150,000
• DBM definition
  – < 100,000
Thrombocytopenia

• Production defects
• Sequestration
• Destruction
  – Immune destruction
  – Non-immune destruction
Thrombocytopenia

1. Production defects
   - Rare cause of isolated thrombocytopenia

2. Sequestration
   - “Hypersplenism”

3. Immune destruction
   - Immune thrombocytopenia

4. Non-immune destruction
   - Thrombotic thrombocytopenia purpura
< 10,000/ul Platelets

- Immune thrombocytopenia
- Drug induced thrombocytopenia
Thrombocytopenia

- 10-50,000/uL
  - DIC
  - TTP
  - ITP
  - Congenital
- 50,000-100,000/uL
  - Liver disease
  - ITP
  - TTP
  - Myelodysplasia
  - Congenital
Basic Question #1

• Is the patient sick?
  – Yes: TTP, HIT, DIC, Sepsis, etc…
  – Pregnant and sick: TTP, HELLP, fatty liver
Basic Question #2

- Other cell lines affected?
  - Yes – myelodysplasia, bone marrow issues, liver disease
  - No – ITP or congenital thrombocytopenia
Liver Disease

- Leukopenia common
  - ~ 1,000/ul
- Thrombocytopenia
  - ~ 50,000-90,000/uL
- Hypersplenism
- Lack of platelet growth factor
Immune Thrombocytopenia

- 1:50,000
- Autoimmune destruction of platelets
- Patients present with very low platelet counts (<1,000/uL)
- Clinical history is diagnostic test
  - No other cause of thrombocytopenia
  - Normal blood smear
Drug Induced Thrombocytopenia

- Most common autoimmune heme complication of medicine
- Implicated drugs:
  - Vancomycin
  - TMP/SMZ
  - NSAID
Congenital Thrombocytopenia

- Counts 10-150,000/uL
- Long history of abnormal counts
- Family history
- “Giant Platelets”
  - Missed by automatic CBC machines
Work-Up

- Guided by counts
  - Sick -> admit
  - <20,000 -> admit
- Review smear
  - Giant platelets
  - Schistocytes (TTP, HELLP)
- Splenic ultrasound
- Liver panel
The Abnormal CBC

• Find old CBC
• Sudden changes most worrisome
• Is the patient sick?