The Top 10 From The CBC

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Interpreting a "CBC w/ Differential"

- General Topics
  - RBC abnormalities – high vs low
  - Platelet abnormalities – high vs low
  - WBC abnormalities – high vs low

  vs

  - Bicytopenias
  - Pancytopenia

Cytopenias

General first steps

- Review old labs. Is there a pattern?
  - Progressive decline (rapid vs slow decline over years)
- New symptoms? Is there a correlation in timing?
- New medication(s)?
  - Hold or discontinue.
  - Retest
- Order a PERIPHERAL SMEAR… it’s never a wrong answer

RBC Abnormalities

Evaluating RBC Values

- Typically we don’t rely on the “rbc” but rather, only the
  - hemoglobin &
  - hematocrit

- RBC values are typically more scrutinized in the
  - Thalassemias &
  - Sickle Cell diseases

Abnormal MCV and MCHC can present with & without anemia

MCV

Mean Corpuscular Volume

(measured in fL)

Anemia can be present w/ any of the following:

- Microcytic <80
- Macrocytic >100
- Normocytic 80-100

MCV

- Microcytosis(<80fL)= small size
  - Iron deficiency
    - Iron loss from pregnancy, colorectal bleeding mass, AVM, etc
  - Copper deficiency (DC all chronic use of Zinc please…)
    - *Discuss "false MDS" diagnoses*
  - Thyroid disorders
  - Thalassemia
  - Sideroblastic Anemia
  - Rx ?
  - +/- Anemia of Chronic Inflammation
  - Hookworm infection (leads to chronic GI blood loss)

Iron Deficiency

Keys for iron absorption

- When supplementing patients with PO Iron
  - Take with vitamin C
  - Avoid Dairy within the window of when Fe taken
  - No BID dosing (equivalent to daily)

  - Absorbed better w/o food (if can tolerate)
  - Tolerated better with food
  - Give a prn stool softener for likely constipation

MCV

- Macrocytosis(>100fL)=larger size
  - Megaloblastic anemias
    - B12
    - Folate
    - Thiamine (B1)
  - Copper deficiency
  - Reticulocytosis (hemolytic anemia?)
  - Rx-induced
  - MDS
  - Aplastic anemia
  - Multiple myeloma
  - Hereditary stomatocytosis

Multifactorial:

- Thyroid disorders
- ETOH
- Liver disease
- HIV
- Pregnancy
- Bariatric surgery
- Downs Syndrome

MCV

- Clinical Keys
  - Impaired absorption B12
    - Hypochlorhydria: age, gastric atrophy, Rx (ppi, H2 antagonists, Metformin)
    - Inadequate pancreatic protease

MCV

- Normocytic = normal size
  - Thyroid disorder (Addison's)
  - Anemia of chronic disease
  - Anemia of chronic inflammation
  - Anemia of chronic kidney disease
  - Malignancy +/-Myelophthesis
  - Autoimmune disease
  - Trauma
  - Post-surgical
  - Secondary hypoparathyroidism

MCHC

- Mean Corpuscular Hemoglobin Concentration
- Commonly used as a *surrogate for iron stores*

- Typically you will only see
  - Normochromic
  - Hypochromic
  - …but, *sometimes you will see* Hyperchromic (unique)

MCHC

- Normochromic
  - “iron stores are typically **replete**”

MCHC

- **Hypo**chromic
  - "iron stores are typically **DEPLETE**"
  - Thus, consider checking iron studies even if no actual anemia

MCHC

- "Hyperchromic"
  - Very uncommon
  - Not always, but if >60 → think: **Spherocytosis**
    - Order a peripheral smear to be read by pathology to rule out spherocytosis.
    - Yes, these patient can be confused with "Chronic Iron Deficiency" due to a low MCV.
    - They will always "fail supplemental iron"
    - Hereditary condition
    - Highly variable clinical presentation & history
    - Send them to Hematology to evaluate.

Platelet Abnormalities

THROMBOCYTOPENIAS
“low platelets”

Thrombocytopenia

- Mild: (150-100k /µL)
- Moderate (99-50k /µL)
- Severe (<50k /µL)

Thrombocytopenia

The basics:

- If the platelets are slowly declining over time, especially if <100k, consider an out-patient Hematology referral
- If abrupt decline, especially if symptomatic bleeding, easy bruising, strongly consider ER/in-patient referral for urgent evaluation

Thrombocytopenia

Urgency,

- TTP, HUS, aHUS
- Eclampsia, HELLP syndrome
- DIC
- ITP
- …others. Lets look at some of the others

Thrombocytopenia

- Etiology
  - ADAMTS13 d/o – urgent
  - ITP – recent viral infection vs idiopathic?
  - Cirrhosis or other liver disorders (chronic & typically irreversible but sufficient for life)
  - Meds – most common.
  - Consumption – thrombosis?
  - Sequestration – splenomegaly?
  - Dysplasia? …r/o bone marrow failure syndrome.
  - Laboratory phenomenon?
  - Malignancy

Unexplained Thrombocytopenia w/o Symptomatology

Laboratory Phenomenon?

- Simple evaluation option w/ repeated thrombocytopenia of *varying degrees over time*

- Platelet clumping caused +/- by EDTA-phenomenon?
  - Citrated platelet test, or citrated CBC, “purple top”
  - Perform with a peripheral smear read by pathology
  - If platelet values correct → due to EDTA

  - If not corrected, or minimally corrected can consider a heparinized tube.
  - If not correction, then consider an alternate diagnosis

Thrombocytopenia

- Due to Malignancy
  - Solid Tumors
  - Hematologic Malignancies

- Myelophthesis
  - displacement of hemopoietic bone-marrow tissue into the peripheral blood, either by fibrosis (myelofibrosis), tumors, or granulomas.

Familial Thrombocytopenia

- RUNX1 mutation
  - Identified on NGS or similar bone marrow genetics testing
  - Platelet function defect and aggregation defect, w/ ASA-like bleeding/bruising.
  - Considered a predisposition for MDS vs AML
  - Can also be seen with
    - TAR Syndrome – thrombocytopenia w/ absent radii
    - DiGeorge Syndrome (ch22-, R-heart defects)

Thrombocytopenia, Congenital Disorders

- MYH9 gene mutation
  - hereditary macrothrombocytopenia
  - giant platelets, dohle bodies in neutrophils

  - Four Disorders
    - May-Hegglin Anomaly
    - Sebastian Syndrome
    - Fechtner Syndrome
    - Epstein Syndrome

THROMBOCYTOSIS
“high platelets”

Thrombocytosis

- Elevated/High Platelets
- If climbing over time
  - DDx:
    - Reactive
    - Rx
    - thyroid disorder
    - secondary condition
    - Essential Thrombocythemia\ET (an MPN)

Thrombocytosis

- Differential:
  - **Primary:**
    - ET (essential thrombocythemia)
      - a member of the Myeloproliferative Neoplasms (MPNs)
      - Mutations of CALR, MPL, or JAK2
    - POEMS Syndrome
      - Polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes
  - **Secondary:** Reactive
    - Infection
    - Inflammation
    - *Iron deficiency* (corrects with iron supplementation)

- Note: never give ASA with plt >1million ➔ Acquired von Willebrand Syndrome

WBC Abnormalities

WBC

Leukocytosis

- Common Causes:
  - Infection
  - Reactive
  - Rx
  - Stress
  - Tobacco
  - Others: Castleman's Disease
    - HHV8+, B-cell lymphoproliferative d/o, releases IL-6

WBC

Leukocytosis

- Common causes in malignancy:

  "**Lymphoma**"

  – **CLL**: chronic & progressive climb in Lymphocytes (high teen's – hundreds)

  vs

  – B-cell vs T-cell Prolymphocytic Leukemia (WBC >100)

WBC

Leukocytosis, Common Hematologic Patterns

- Elevated WBC, plus
  - Elevated *Lymphocytes* → Think: CLL
  - Elevated *Basophils* → Think: CML
  - *Blasts* → Think: Acute Leukemia
    - Elevated *Eosinophils* → Eosinophilic Leukemia?
    - Elevated *Monocytosis* → CMML, AMML (AML M4) Acute Leukemia?
    - Elevated *Neutrophils* → Neutrophilic Leukemia?

WBC

Leukopenia

- Common Causes:
  - Viral infection, HIV, tuberculosis
  - Autoimmune (lupus, RA)
  - Malnutrition (B12, folate, Cu, Zn)
  - Meds (bupropion, clozaprine,
  - Malignancy (T-cell LGL, …)

WBC

Lymphocytosis

- Common Causes:
  - Malignancy
    - Chronic NK-cell Lymphocytosis
    - Chronic Lymphocytic Leukemia (CLL)

WBC

Neutropenia

- Common Causes:
  - Myelosupression (chemotherapy)
  - Malignancy (ANC <1,000)
  - Kostmaan Syndrome (congenital, ANC <500, HAX-1 or G6PC3 mut)
  - Severe Congenital Neutropenia (ELANE mut)
  - Cyclic Neutropenia – draw serial weekly cbc's to identify this pattern
  - Benign Ethnic Neutropenia (BEN)

- Uncommon Causes:
  - WHIM Syndrome (warts, hypogammaglobulinemia, immunodeficiency, myelokathexis)
  - Felty Syndrome (splenomegaly, neutropenia, thrombocytopenia, arthritis)
  - Barth Syndrome
  - Shwachman-Diamond Syndrome (SBDS gene mut)

WBC

Neutrophilia

- Sweets Syndrome “Acute Febrile Neutrophilic Dermatosis”

WBC

- **Monocytopenia**
  - GATA2 mutation
    - Chronic monocytopenia
    - Recurrent mycobacterial infections
    - Lymphedema

Questions?