Anemia in Your Office

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Disclosures
Activities in Last Three Years

- Honoraria for lectures
  - Beckman Coulter
Objectives

- Outline a practical diagnostic approach to anemia that identifies anemia syndromes requiring early specialist referral
- Outline the diagnosis and management of common anemia syndromes

Scenario

- On a CBC ordered for another purpose, unsuspected anemia is found

-OR-

- Based on clinical symptomatology or physical findings, you suspect that anemia is present
Confirm abnormal CBC
- Include differential, manual slide review if available, reticulocyte count

Obtain further studies which will let you evaluate anemia etiology
- Chemistry panel: should include creatinine, total bilirubin, total protein and albumin
- PT/PTT if platelets are low
- Fe, TIBC/Transferrin, B12/Folate

Rubric for Early Referral: “Anemia and ….”

Jaundice/hyperbilirubinemia
- Hemolysis – an emergency if anemia is severe
- Mild hemolysis in a patient with known hemoglobinopathy (T Bili < 2-4) generally not an emergency
  - Send direct/indirect Coombs (DAG/IAG) if possible

Schistocytes
- TTP – fever, thrombocytopenia, renal abnormalities, neuro abnormalities, abdominal pain – an emergency needing admission/transfer

Blasts
- Usually needs prompt referral – degree of emergency depends on proportion of blasts, associated cytopenias
Rubric for Early Referral: “Anemia and …”

- Increased WBC count
  - Lymphocytosis/monocytosis
    - If in the setting of a mono-like illness in an otherwise healthy patient, observation may be appropriate
  - Increased granulocytes with metamyelocytes, myelocytes
    - What makes the emergency is the immature forms
    - Granulocytosis in the setting of acute inflammatory illness likely does not need referral

- Neutropenia, Thrombocytopenia/Pancytopenia
  - If in the setting of a mono-like illness in an otherwise healthy patient, observation may be appropriate

- Monoclonal gammopathy
  - Suspect with elevated globulin fraction (= Total Protein – Albumin)
  - Check SPEP – if monoclonal protein, refer

If Still Holding the Bag While Awaiting Transfer of an Inpatient...

- Autoimmune hemolysis
  - DAG positive – prednisone 1 mg/kg po
  - Can be managed until stable in community
    - OK to transfuse type-specific blood cautiously

- TTP
  - Give FFP 2-4 units per 24 hrs
  - Avoid platelet transfusions unless life-threatening bleeding

- Treat fever in neutropenic (ANC < 1500) patients with broad spectrum antibiotics
- Usual good attention to hydration, etc.
Iron Deficiency

- Suspect with history of bleeding (GI or menses), pregnancy with inadequate iron supplements, MCV with low MCHC
  - Most common etiology of anemia – consider in all anemic patients
- Diagnosis: Serum ferritin, serum iron, serum TIBC/Transferrin
  - Ferritin < 25-30 µg/L
  - Elevated TIBC/transferrin with % saturation < 10%
    - % Saturation = (Iron ÷ TIBC/Transferrin) x 100

Factors confusing studies
- Ferritin rises with inflammation; iron, TIBC fall with inflammation
- Oral iron or hemolysis artifactually elevate serum iron
- Inflammation may cause RBC clumping, falsely elevating MCV

Other tests
- Soluble transferrin receptor (sTfR) – elevated in iron deficiency
  - Becoming more obtainable
  - Most specific as ratio with ferritin
- Bone marrow examination
  - Usually requires consultation
  - Patient comfort/convenience issues
Iron Deficiency

- **Management**
  - Oral Iron salts/saccharates
    - FeSO4 325 mg TID
    - Others work, need to dose ≥150 mg elemental iron/day
  - Intravenous iron
    - Generally requires referral

- A sign of disease, not a disease itself
  - GI endoscopy on all males, females after menopause

Anemia of Chronic Disease

- Suspect with moderate anemia in setting of an inflammatory syndrome, whether acute or chronic

- **Diagnosis**
  - Low iron, usually low TIBC/transferrin, with high normal/elevated ferritin
  - Low iron with ferritin > 200 µg/L essentially makes diagnosis
  - sTfR, sTfR ferritin ratio, normal
  - MCV occasionally as low as 78 fL, rarely ever lower
Anemia of Chronic Disease

- May be confused with iron deficiency due to low iron, occasional low MCV
  - Ferritin, sTfR will usually distinguish
  - Bone marrow rarely required
  - Serum erythropoietin usually relatively low
  - Often evidence of inflammation (high ESR, CRP)
  - Referral may be needed to confirm diagnosis

- Management
  - Anemia usually moderate; specific management not required
  - Treat underlying disease
  - Administering iron not helpful
  - No need for colonoscopy/EGD to find blood loss site
  - Treatment with erythropoietin corrects anemia but not approved in US

B12/Folate Deficiency

- Suspect with elevated MCV; in elderly, malnourished, institutionalized or heavy EtOH users; after gastric/upper small bowel surgery; in neuropathy

- Diagnosis: Serum B12 and serum folate – if you suspect one, check both
  - If MCV > 105, hypersegmented neutrophils, or neuropathy, B12 < 200-250 ng/L makes diagnosis of B12 deficiency
    - If clinical suspicion high but B12 normal, check methylmalonic acid level
  - Serum folate < 3.5-4.0 µg/L diagnostic of folate deficiency
    - If clinical suspicion high but serum folate normal, check RBC folate level
B12/Folate Deficiency

- Management: B12
  - Evaluate for etiology: intrinsic factor antibodies, gastrin
  - Give 3-4 1000 µg SC injections cyanocobalamin over 1-3 weeks, then monthly for life
  - Follow Hct/Hgb for response, not B12 levels
  - Oral B12 works but requires 2000 µg/day forever
- Management: Folate
  - Folate 1mg po/day; can go up to 5mg if poor response
  - Follow Hct/Hgb for response
- No harm to treat with both until results come back

Anemia of Renal Insufficiency

- Due to erythropoietin deficiency
- Suspect in patients with eGFR < 45 ml/min, or Cr > 2.0 AND no other etiology of anemia on evaluation
- Diagnosis
  - Requires measured or estimated CFR/Creatinine clearance < 45 ml/min
  - Otherwise negative evaluation
  - Serum erythropoietin levels not usually necessary or helpful
Renal Insufficiency

Predicted prevalence of hemoglobin level less than 11, less than 12, and less than 13 g/dL among men (A) and women (B) 20 years and older who participated in the Third National Health and Nutrition Examination Survey (1988-1994)


Anemia of Renal Insufficiency

Management

- If not symptomatic and hemoglobin consistently > 9-10 g/dL, no anemia treatment needed
- Otherwise can be treated with recombinant erythropoietin products
- Typically requires referral to either nephrologist or hematologist/oncologist
Thalassemia/Hemoglobinopathy Trait

- Suspect with microcytosis, minimal anemia, reticulocytosis greater than expected for anemia and normal iron studies
  - Often MCV very low and out of proportion to degree of anemia
  - MCHC, RDW often normal
- Diagnosis
  - Hemoglobin electrophoresis – usually > 45% Hgb A
    - Abnormal hemoglobin – hemoglobinopathy trait
    - Elevated Hgb A2 and/or Hgb F – β thalassemia trait
    - No abnormal hemoglobin, A2, or F, but microcytosis – infer α thalassemia trait
      - Can confirm by showing family member in same situation
  - Blood smear
    - Microcytosis with or without target cells
- Management
  - No specific management required
  - Folate 1 mg po/day to support reticulocytosis
  - May become anemic with minor infections due to suppression of increased reticulocytosis
    - Corrects rapidly when infection resolves
  - Has somewhat higher risk of gallstones than age-matched controls
  - May have total bilirubin at upper border of normal due to increased RBC turnover
References
