Updates in the Management of Anemia in Cancer

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Objectives

- Recall common causes of anemia in patients with cancer
- Understand risks/benefits of blood transfusion in patients with cancer
- Understand the risks/benefits of erythropoiesis stimulating agents (ESAs) for anemia in patients with cancer
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Anemia in Cancer

Today’s focus is on anemia in patients with solid tumors or lymphoid malignancies
Prevalence of Anemia

- 40%-63% of patients with cancer are anemic prior to treatment
  - 32% of patients with Non-Hodgkin’s lymphoma
  - 49% of patients with gynecologic malignancies

- Degree of anemia correlates with
  - Cancer stage
  - Inflammatory markers
  - Albumin, cholesterol, leptin

- 90% of patients treated with chemotherapy are anemic

NCCN Guidelines, Cancer and Chemotherapy induced Anemia, v 2.2017
Etiology of Anemia in Cancer

- Impaired production/hypoproliferative anemia
  - Low reticulocyte count
    - Nutritional deficiency
    - Malignancy-induced
    - Myelosuppressive chemotherapy or radiation-induced
    - Decreased erythropoietin production
  - High reticulocyte count
    - Intra/extra-vascular hemolysis

- Red cell destruction/decreased RBC survival

- Blood loss
  - Hemorrhage via intraluminal bleeding or RP/hepatic internal bleeding
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Hypoproliferative anemia in cancer:
Nutritional deficiencies

- Cancer/chemotherapy-induced nausea and anorexia
- Neoplastic-induced malabsorption
  - Secondary to involvement of duodenum/jejunum
- Surgical resection
  - Gastric tissue/terminal ileum -> B12 def
  - Gastrectomy->achlorhydria -> iron malabsorption
Hypoproliferative anemia in cancer:
Bone-marrow infiltration

- Common in leukemia, lymphoma, plasma cell dyscrasia
- Uncommon in solid tumor malignancies
  - Can be seen in gastric and prostate Ca.
Bone marrow infiltration by gastric carcinoma

Guner SI, J Ca Clin Trials, 2015
Myelophthisis with dacrocytes/teardrop cells
Hypoproliferative anemia in cancer: Anemia of inflammation

- Cancers frequently produce IFN-α/β/γ, TGF-β, IL-1/6
- Causes a block in iron utilization or erythropoietin production
  - Increased hepcidin
    - Iron sequestration within macrophage
    - Decreased duodenal absorption
    - Decreased mobilization of stored iron
Hypoproliferative anemia in cancer:
Myelosuppressive Chemotherapy

- Frequently accompanied by thrombocytopenia and neutropenia
- Expected timing of anemia varies by chemotherapy regimen, schedule
  - Hgb trend is less dynamic than WBC/ANC during chemotherapy; is more “cumulative”
  - Recent labs are critically important to determine expected change in hgb over subsequent days
Example during one cycle of myelosuppressive chemotherapy
Hypoproliferative anemia in cancer:
Myelosuppressive Chemotherapy

- Two common mechanisms for anemia
  - Direct suppression of RBC precursor synthesis in bone marrow
    - Usually through impaired DNA synthesis/mitosis
  - Decreased erythropoietin production
    - Nephrotoxic effects

- Ex: Cisplatin
  - Platinum-containing DNA cross-linker
    - Interferes with RBC precursor synthesis
  - Also has direct nephrotoxic effects
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- Red cell destruction/decreased RBC survival
  - High reticulocyte count
    - Autoimmune
    - Microangiopathic hemolysis

- Blood loss
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Increased RBC destruction: Autoimmune Hemolytic Anemia

- Can be seen in
  - Chronic lymphocytic leukemia
- Less frequently in
  - Carcinoma
  - Non-Hodgkin lymphoma
  - Myelodysplastic syndrome
  - Others
Increased RBC destruction: Autoimmune Hemolytic Anemia

- IgG or complement mediated
- Labs notable for
  - Elevated
    - Reticulocyte count
    - LDH
    - Indirect bili
  - Decreased
    - Haptoglobin
  - Positive Coombs/DAT
  - Spherocytes
- Cold-reacting autoimmune hemolysis is less common
Direct Coombs Test/DAT

- Antigen
- Erythrocyte
- In vivo antibody coating of erythrocytes
- Anti-IgG AHG reagent added after erythrocytes are washed
- AHG reagent causes IgG-coated erythrocytes to agglutinate
Increased RBC destruction:
Microangiopathic hemolysis

- TTP, HUS, DIC
- Can be seen in liquid or solid tumors
  - Adenocarcinomas
Schistocytes in microangiopathic hemolytic anemia
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Acute and chronic hemorrhage

- Intraluminal tumors (GI/GU tract)
- Coagulopathies are common in cancer patients
  - Many cancer patients are also treated with anticoagulants
  - DIC in leukemias, mucinous adenocarcinomas
- Stress and corticosteroids may contribute to gastric-mucosal erosive disease
Initial Assessment of Cancer Patient with Anemia

- **History**
  - Symptoms, nutritional status, EtOH
  - Recent transfusions
  - Bleeding, menses
  - Medications (including anticoagulants/antiplatelet agents)
  - Timing/duration of chemo/radiotherapy treatment
  - Recent labs

- **Physical Examination**
  - Stool guaiac*

* Digital rectal exams are relatively contraindicated in patients with absolute neutrophil count less than 500/uL
Laboratory evaluation

- CBC
  - MCV, platelets, other cytopenias
- Reticulocyte count
- Ferritin
- B12, folate, TSH, iron/TIBC
- Blood smear
- PT/INR, PTT
- Type and cross
- Additional studies
  - Haptoglobin
  - LDH
  - Fibrinogen, d-dimer
  - Coombs/DAT
  - Tbili/Dbili
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What is the goal hemoglobin?

- There isn’t one
  - Depends on
    - Timing of chemo/radiotherapy
    - Comorbidities
    - Symptoms

- Recent labs are critical to predict the trend

- In asymptomatic patients, short-term follow-up with repeat labs is reasonable
PRBC transfusion in cancer: Clinical pearls

- Understanding trend of Hgb versus chemotherapy administration guides transfusion
- Avoid transfusion in the setting of autoimmune hemolysis
- Ferritin prior to transfusion
- Leukoreduced (and irradiated) RBCs reduce
  - Febrile non-hemolytic reaction
  - Alloimmunization/platelet refractoriness
  - Viral infection
- 1 unit should increase Hgb by ~1g/dL
- In a patient with previous stem cell transplant, consult transplanter first

Risks of RBC transfusion

- Transfusion associated circulatory overload (TACO)
- Transfusion reactions
- Bacterial contamination/viral infection
- Alloimmunization

Cancer and chemotherapy induced anemia, NCCN Guidelines, 2.2017
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Erythropoiesis-stimulating agents

- ESAs (darbepoetin, epoetin alfa) may be suitable in patients with non-acute needs or who refuse PRBCs

- Risks
  - Increased thromboembolic events
  - Potential hastened progression of malignancy*
    - Breast, lung, lymphoid, head & neck, cervical cancers

* FDA REMS in effect thru April 2017

References:
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Leyland-Jones B, et al. JCO 2005
Overgaard J, et al. JCO, 2009
Smith RE, et al. JCO 2008
Wright JR, et al. JCO 2007
Epoetin alfa vs placebo in metastatic breast cancer

Leyland-Jones B, et al. JCO, 2005
Epoetin-β vs placebo in head and neck cancer

Henke M, Lancet, 2003
Anemia in cancer: Take-aways

- Start with a broad differential
  - Consider the categories of anemia
- Important to understand the patient’s point in their treatment course
- In patients on myelosuppressive chemotherapy, follow-up labs/visits and communication of lab results improves care
- Transfuse leukoreduced PRBC when necessary
- Avoid ESAs in patients with curable tumors
References

NCCN Guidelines, Cancer and Chemotherapy induced Anemia, v 2.2017
Bone marrow infiltration by gastric carcinoma; Guner SI, J Ca Clin Trials, 2015
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Epoetin alfa vs placebo in metastatic breast cancer; Leyland-Jones B, et al. JCO, 2005
Epoetin-β vs placebo in head and neck cancer; Henke M, Lancet, 2003
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Thank you
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