**Approaches in Hematology**

**Hematology Made Easy**

## Anemia of Chronic Disease

Q: What is anemia of chronic disease ACD? Associated chronic diseases? Characters in iron profile? Treatment?

- ACD is Normocytic Normochromic anemia in its early stages, then it might become Microcytic hypochromic anemia. It is one of the hypoproliferative anemias.

- Causes of anemia of chronic disease (ACD)
  1) Chronic disease: the most common is chronic renal failure (ESKD), Heart failure, COPD, DM.
  2) Chronic inflammatory diseases: Rheumatoid arthritis, SLE, all collagen rheumatological diseases.
  3) Chronic infections: TB, recurrent abscesses, Osteomyelitis, recurrent septic arthritis, recurrent cellulitis.
  4) Anemia of malignancy
     - Solid cancers like Cancers in lung, liver, kidney, etc.
     - Hematologic: Lymphoma, MM
  5) Anemia of endocrine disease particularly thyroid disease

- In ACD, there is a disturbance in iron utilization ---> hepcidin disturbance.

- Iron profile would be as follow:
  - Iron: low
  - Ferritin: high (often > 100)
  - TIBC: normal or low
  - Transferrin saturation (TSAT): low or normal often > 20%
  - CRP > 5
  - Retics < 2% (hypoproliferative anemia)
- Treatment
  - ℛ Treat the cause.
  - ℛ Packed RBCs if HgB < 8 g/dl
  - ℛ Consider adding iron replacement: In ACD, if Ferritin < 100 + TSAT < 20%. As it would be ACD + concomitant iron deficiency
  - ℛ Erythropoietin-stimulating agents (ESAs) / Erythropoietin (EPO) can be given in ACD with the following conditions:
    - ESKD
    - anemia of malignancy
    - anemia of inflammatory collagen disorders not responding to supportive therapy if serum EPO is low.

## Sideroblastic Anemia

Q: When do you suspect Sideroblastic anemia? DX?! Treatment?

- Sideroblastic anemia occurs when the BM fails to produce enough mature RBCs with production of premature stage called Sideroblasts.

- Causes:
  - Inherited:
    - X-linked
    - Or part of certain rare syndromes occurring in childhood.
    - X linked with ataxia
    - SIFD
    - MLASA
    - TRMA

  - Acquired:
    - A stage of Myelodysplastic syndrome:
      - RARS refractory anemia with ring Sideroblasts): old classification
      - Recently, it is found in the following stages:
        - ✓ MDS with ring Sideroblasts and single lineage dysplasia {MDS - RS - SLD}
        - ✓ MDS with ring Sideroblasts and multi-lineage dysplasia
        - ✓ Myelodysplastic/ myeloproliferative neoplasm with ring Sideroblasts and thrombocytosis
    - Drugs
      - INH (isoniazid)
      - Chloramphenicol
      - Linezolid
    - Alcoholism
    - Zinc toxicity
    - Copper deficiency

- Suspect Sideroblastic anemia in the following situations:
  - Refractory anemia (microcytic hypochromic anemia) is refractory to iron and not associated with chronic diseases after exclusion of thalassemia minor (trait)
  - New onset microcytic hypochromic anemia in old people after exclusion of Iron deficiency anemia, thalassemia trait, and anemia of chronic disease.
  - Microcytic hypochromic anemia with Splenomegaly (MDS/MPN)
  - Long-standing microcytic hypochromic anemia which transforms into bi or pancytopenia (MDS)
  - New onset of microcytic anemia in relation to intake of certain drugs like INH

- DX:
- Mainly laboratory
  - Definitive DX is done by bone marrow exam (aspirate and or biopsy) with demonstration of characteristic RING SIDEROBLASTS by Prussian blue stain.
  - Iron study may help.

- Treatment
  - ℛ Treatment of inherited cause & underlying syndrome (MDS).

  - ℛ Treatment plan for sideroblastic anemia includes the following:
    - ➢ Removal of toxic agents if found such as drugs & zinc & stopping alcohol.
    - ➢ Administration of pyridoxine, thiamine, or folic acid.
    - ➢ Transfusion (along with antidotes if iron overload develops from transfusion).
    - ➢ Other medical measures (not in all patients)
    - ➢ Bone marrow or liver transplantation (last line in certain cases)

  - ℛ Vitamin B6 may help.
    - Thiamine in TRMA syndrome: vitamin B6 may have a role in some acquired related to toxic/metabolic causes with stoppage of offending agent (drugs & Alcohol). Thiamine as would be expected from its name, thiamine-responsive megaloblastic anemia is treated with thiamine. In this acquired form of sideroblastic anemia, supraphysiologic doses of thiamine (25 to 75 mg daily) have been shown to improve the anemia.

    - Pyridoxine (vitamin B-6) deserves a trial in all cases of sideroblastic anemia as many acquired and certain congenital forms of sideroblastic anemia respond to this relatively safe agent. The response will be evident in a few weeks, with reticulocytosis and improving hemoglobin levels. The dose should be tailored to the patient's tolerance. Dosages up to 1 g/day have been used, but the goal is to find a dosage of pyridoxine (usually 50-200 mg/d) that will maintain the hemoglobin level and yet prevent toxicity (peripheral neuropathy). For patients whose condition responds, treatment is lifelong.

  - ℛ Folic acid by itself has been reported to reverse sideroblastic changes in some patients. It is advisable to supplement folate in pyridoxine-responsive cases to ensure an adequate supply during a period of increased hemoglobin synthesis.

  - ℛ Transfusion is the mainstay of treatment for patients whose sideroblastic anemia does not respond to pyridoxine therapy.
    - ⚠ It is problematic and should be avoided if the anemia is mild to moderate and asymptomatic patients.
    - ⚠ Even without transfusions, patients with sideroblastic anemia are prone to develop iron overload. Transfusion in sideroblastic anemia has been known to worsen iron overload and lead to secondary hemochromatosis.

  - ℛ Transplantation: Bone marrow transplantation is a treatment of last resort and is best saved for young patients whose conditions are pyridoxine resistant and transfusion dependent and who have a human leukocyte antigen (HLA)-matched sibling.