PURE RED CELL APLASIA (PRCA)

WHAT IS PRCA?
- Normocytic normochromic anemia with reticulocytopenia (<1%) and almost complete absence of erythroblast in the bone marrow (<0.5%).
- Uncommon disorder, presents at any age, affects men and women equally, does not display any significant ethnic or racial predisposition.
- Clinically, may present as either an acute, self-limiting illness or a chronic disease

WHAT CAUSES PRCA?
- Autoimmune disruption of erythroblast maturation
  - IgG antibodies to erythroblasts or erythropoietin,
  - NK cells secrete factors that selectively inhibit erythroid colonies
  - Direct T-cell lysis of erythroblasts via TCR-antigen recognition.
  - Erythroblasts loose MHC I complex and are destroyed by NK cells

WHAT IS THE ETIOLOGIC BREAKDOWN?
- Childhood aplasia
  - Diamond-Blackfan anemia: sporadic, rare disease that presents in infancy with short stature, ASD/VSD, microcephaly, cleft palate, micrognathia, macroglossia, anemia usually macrocytic.
  - Transient erythroblastopenia of childhood: presents at >1 y.o. spontaneous resolution with 4-8 weeks
- Associated with infection
  - Parvovirus B19 infection: transient (5-10 day) aplastic crisis in patients with shortened RBC life span (sickle cell, G6PD def., pyruvate kinase def., hereditary spherocytosis, elliptocytosis, thalassemias, etc.). Patients’ present with fever, chills, nausea, vomiting, headache and abdominal pain. Virus directly attacks erythroid progenitor cells. Typical bone marrow reveals abnormally large proerythroblasts, diagnostic of infection, despite negative immunostaining for B19. Chronic aplastic anemia in patients’ with immunosuppression (HIV, post transplant, chemotherapy, immunosuppressive therapy). Bone marrow is similar, diagnosis made by PCR for virus, antibody titers not useful.
  - EBV, CMV, viral hepatitis, staph bacteremia, menongococcemia
- Associated with neoplasms:
  - Thymoma (9%), CLL (6% large granular lymphocyte leukemia), hodgkin’s disease, MM, waldenstrom’s macroglobulinemia, CML, essential thrombocythemia, acute lymphoblastic leukemia, solid tumors of stomach, breast, lung, bile duct, renal cell, thyroid, KS.
- Associated with autoimmune disorders:
RA, SLE, Sjogren’s syndrome, MCTD, autoimmune hemolytic disorders, autoimmune hypothyroid, autoimmune hepatitis, ulcerative colitis, anti-epo antibodies post epo treatment.
- Associated with medications: AZT, allopurinol, tegretol, chloramphenicol, tacrolimus, INH, rifampin, suldinac, penicillin
- Idiopathic, Pregnancy

**HOW DO YOU MAKE THE DIAGNOSIS?**
- Blood smear: severe normocytic, normochromic anemia
- Retic count: very low, <1%
- Bone marrow biopsy: near absence of erythroblasts within an otherwise normal cellular marrow (myeloid and megakaryocytes exhibit normal maturation). May see a mild increase of lymphoid aggregates, plasma cells and mast cells. However, if RBC’s show any other abnormalities or any of the other cell lines show abnormalities; must send marrow for additional testing to exclude myelodysplasia or other underlying disorders.
- Normal B12, folate, ferritin
- Look for associated condition: Chest CT eval thymoma, parvovirus B19 PCR or IgM titers, age-appropriate cancer screening, ANA, HIV.
- Must distinguish from myelodysplasia with refractory anemia: retic is usually not too low, red cells are macrocytic and white cells reveal dysplasia, marrow is hypercellular, myeloid maturation is left shifted, presence of mononuclear megakaryocytes, erythroblasts rarely absent and display megaloblastoid features.

**IS THERE ANY TREATMENT? 5-10% remit spontaneously**
- Stop all drugs: syndrome should resolve within 3 weeks
- Treat underlying disorder
  - Parvovirus: IVIG controls infections and allows marrow recovery
  - Thymoma: thymectomy resolves anemia in 40% cases within 8 weeks
- If failing primary disorder treatment, or idiopathic, start immunosuppressive
  - Prednisone 1 mg/kg/day: 40% cases remit within 4 weeks, usually treat for 3-4 months. Start slow taper when HCT reaches 35. If no response within 3 months, likely NOT to respond.
  - Azathioprine, cyclophosphamide, cyclosporin, and antithymocyte globulin: no good data to recommend one over the other. Usually used in combination with low dose steroid, which improves efficacy.
  - In refractory cases, plasmapheresis and splenectomy have been used. Weekly blood transfusions may be required for symptoms.

**References:**