Idiopathic (Immune) Thrombocytopenic Purpura (ITP)

Background
1. Definition
   - Isolated thrombocytopenia with normal bone marrow and absence of other causes of thrombocytopenia
2. General info
   - One of the most common causes of symptomatic thrombocytopenia in children
   - 2 major forms of ITP:
     - Acute thrombocytopenic purpura
       - Most commonly seen in children 2-6 yrs of age
       - May follow viral illness
       - Usually very sudden onset
       - Symptoms disappear in <6 mos (often within few wks)
       - Spontaneous remission occurs in >80% of children w/acute ITP, usually without recurrence
       - Male to female ratio 1.2:1
     - Chronic thrombocytopenic purpura
       - Can occur at any age, usually between ages 20-30 yrs, not in children
       - Usually does not follow an infection
       - Subtle onset
       - Symptoms last a minimum of 6 mos to several yrs
       - Female to male ratio 2-3:1
       - Spontaneous remission rate is <20%

Pathophysiology
1. Incidence/prevalence
   - Incidence of acute ITP
     - 3-8 cases per 100,000/yr
   - Incidence of ITP in adults
     - 6-7 cases per 100,000/yr
   - 40% of pts are <10 yrs
2. Pathogenesis
   - Autoantibodies (usually IgG) are directed against platelet membrane antigens, such as glycoprotein complex IIb/IIIa
   - Antibody-coated platelets have a shortened half-life because of accelerated clearance by tissue macrophages in spleen and other portions of reticuloendothelial system
   - Net effect is a decr in platelet count
3. Risk factors
   - Age: bimodal peak
     - 20-30 yrs old
     - 2-6 yrs old
   - Gender:
     - Females more likely to develop ITP during adulthood than males
   - Prior viral infection (measles, mumps and rubella) or MMR vaccine
     - 60% of acute ITP preceded by viral infection or MMR vaccination
4. Morbidity/ mortality
   o Hemorrhage
     ▪ Most serious complication
     ▪ Intracranial hemorrhage is most significant
     ▪ Mortality rate:
       ▪ 1% in children
       ▪ 5% in adults
     ▪ In pts w/severe thrombocytopenia (platelet count <20,000)
       ▪ Predicted 5-yr mortality from bleeding significantly raised in pts
         >60 yrs versus pts <40 yrs, 47.8% versus 2.2% respectively
     ▪ Previous Hx of hemorrhage incr risk of severe bleeding in adult ITP

Diagnoses
1. History
   o Focus on symptoms of bleeding
     ▪ Type
     ▪ Severity
     ▪ Duration
     ▪ That may exclude other causes of thrombocytopenia
   o Elicit risk factors for HIV and systemic symptoms linked to other illnesses
     or meds that can cause thrombocytopenia
     ▪ Liver dz, thrombosis, and autoimmune dz
     ▪ Heparin, alcohol, quinidine/quine, sulfonamides
   o Address risk factors for incr bleeding, as these may determine
     aggressiveness of Tx or mgmt
     ▪ GI dz
     ▪ CNS dz
     ▪ Urologic dz
     ▪ Active lifestyle
   o Common Sx/S
     ▪ Purpura
       ▪ Tiny red dots (3-10 mm) under skin that are a result of very small
         bleeds
       ▪ Menorrhagia/ metrorrhagia in women of child bearing age
       ▪ Epistaxis
       ▪ Gingival bleeding
       ▪ Bruising tendency

2. Physical exam
   o Abdominal
     ▪ Inspection, auscultation, palpation, percussion
     ▪ Note tenderness, masses, organomegaly (liver and spleen)
   o Skin
     ▪ Inspection, palpation
     ▪ Note for nonpalpable petechiae, which mostly occur in dependent area,
       bruising
   o Oral and nasal cavity
     ▪ Inspection, palpation
     ▪ Look for gingival swelling and bleeding
     ▪ S/S of nasal bleeding
Menstrual
  • Cycle (freq, duration, quality)

Eye
  • Look for retinal hemorrhages, papilledema for incr intracranial pressure from intracranial bleeding

3. Dx tests
   o Lab evaluation
     • CBC
       • Thrombocytopenia usually is only abnormality
       • Platelet count is usually <20,000/mL
       • WBC count and hemoglobin are generally normal
         o Although anemia can be seen in pts with significant bleeding
     • Peripheral blood smear
       • Examination of peripheral blood smear is mandatory and should detect no morphological abnormalities in WBC and RBC
       • Platelets are often large in size, particularly when Sx present several days or longer
     • Coagulation studies are normal and bleeding time is not useful
     • Antiplatelet antibody testing
       • Variety of tests are available for detecting platelet antibodies but are not routinely indicated due to lack of specificity
   o Imaging studies
     • CT scan of head is warranted if concern exists regarding intracranial hemorrhage

Differential Diagnosis
1. Active infection
   o Infectious mononucleosis
   o Hepatitis
   o HIV-1
2. Drug exposure
   o Heparin
   o Alcohol
   o Quinidine/ quinine
   o Sulfonamides
   o Furosemide
   o Gold salts
   o Cimetidine
3. Autoimmune dz
   o Systemic lupus erythematosus
   o Juvenile rheumatoid arthritis
4. Leukemia
   o CBC and bone marrow Dx
5. Acquired bone marrow failure syndrome
   o Aplastic anemia: anemia prominent, bone marrow Dx
6. Inherited disorders of thrombocytopenia
   o Inherited aplastic anemia
     • Prominent anemia, bone marrow dx
Therapeutics

1. Glucocorticoids
   - Helps bleeding by decr rate of platelet destruction
   - Usually results in an increase in platelet count within 2-3 wks
   - Side effects may include:
     - Hypertension
     - Irritability
     - Stomach ache
     - Wt gain
     - Acne
     - Growth delay in children
   - Most commonly used glucocorticoids
     - Prednisone
       - Adult dose for prednisone is 1-2 mg/kg/day
       - Children dose is 4-8 mg/kg/day by mouth
     - Methylprednisolone
       - Loading dose for adults 125-250 mg IV
         - Maintenance dose is 0.5 mg/kg/dose IV every 6 hrs for up to 5 days
       - Loading dose for children 2 mg/kg IV
         - Maintenance dose of 0.5 mg/kg IV every 6 hrs for up to 5 days
   2. IV gamma globulin (IVGG)
      - Can be used alone or in addition to glucocorticoids
      - It is an antibody mixture
      - Slows destruction of platelets
      - Works more quickly than steroids (within 24-48 hrs)
      - Adult dose
        - 1-2 g/kg IV admin over 1-5 days
      - Children's dose
        - 1 g/kg IV admin x1
      - Side effects may include:
        - Urticaria, pruritis, incr risk of infection
   3. Other Tx for ITP may include
      - Rh immune globulin
        - Temporarily stops spleen from destroying platelets
      - Medication changes
        - If drug is suspected as a cause, discontinuation or changing med may be necessary
      - Infection Tx
• If a treatable infection is cause for ITP, then Tx of infection may result in higher platelet counts
  o Splenectomy
    • Spleen may need to be removed since this is site of platelet destruction
    • Considered more often in older children w/chronic ITP to decr rate of platelet destruction
    • Tx of last resort if other Tx's fail
  o Hormones
    • Teenage girls may need OCP / hormone Tx to decrease excessive menstrual bleeding

**Follow-Up**
1. Hematology consultation is often helpful
2. Pneumococcal infection prophylaxis if pt required splenectomy for Tx
3. Monitor for SE of meds

**Prognosis**
1. Children
  o 83% of children have spontaneous remission
  o 89% of children eventually recover
  o >50% of pts recover within 4-8 wks
  o 2% of pts die
2. Adults
  o Only 2% of adults have a spontaneous recovery
  o 64% of adults eventually recover
  o 30% of pts have chronic dz
  o 5% of pts die from hemorrhage

**References**

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