Essential Learning

Thrombotic Thrombocytopenic Purpura

- **Differential diagnosis (for seizure and rash)**
  - Thrombotic thrombocytopenic purpura (TTP)
  - Hemolytic uremic syndrome (HUS)
  - Disseminated intravascular coagulation (DIC)
  - Immune thrombocytopenic purpura (ITP)
  - Infection (meningitis, encephalitis)
  - Sepsis
  - Endocarditis
  - Heparin-induced thrombocytopenia (HIT)
  - Drug-induced thrombotic microangiopathies
  - Malignancy
  - Eclampsia should also be considered in a female patient who is pregnant or postpartum.

- **Pathophysiology of thrombotic thrombocytopenic purpura**
  - Life-threatening thrombotic microangiopathy.
  - Multi-organ dysfunction results from systemic microvascular ischemia secondary to thrombosis.
  - TTP is a consumptive thrombocytopenia
  - Severely decreased activity of metalloprotease ADAMTS13.

- **Morbidity and mortality of thrombotic thrombocytopenic purpura**
  - TTP is a rare disease
  - Mostly seen in 30-50 year old females.
  - True medical emergency, carrying a 90% mortality if untreated.
  - With prompt recognition and treatment, the survival rate is 90%.
  - TTP can begin with a flu-like prodrome, including a GI component.
    - It is twice more common in women and is associated with pregnancy (10-25% of cases), infection (HIV), familial causes or certain drugs (estrogens, clopidogrel, ticlopidine, quinine, cyclosporin, mitomycin C).

- **Important findings indicative of TTP**
  - The classic pentad of TTP includes fever, thrombocytopenia, microangiopathic hemolytic anemia, renal impairment, and CNS impairment.
  - Uncommon to have all components of the pentad (only 40%) and the presence of all five indicates severe end organ ischemia.

- Thrombocytopenia and hemolytic anemia are the most common features and manifestations of bleeding may be evident on exam.
- Neurologic findings may fluctuate and can include headache, personality changes, seizure activity, coma, focal deficits, or intracranial hemorrhage.

- **Work up for TTP**
  - TTP is a clinical diagnosis, but characteristic laboratory findings include:
    - Severe microangiopathic hemolytic anemia
    - Thrombocytopenia (< 20,000 platelets/µL)
    - Fragmented RBCs on the peripheral smear
    - Signs of renal disease
    - Decreased haptoglobin, elevated reticulocyte count, elevated indirect bilirubin, and elevated LDH are also common findings
    - Urinalysis may show RBC's
    - ADAMTS13 assay may help distinguish TTP from HUS but is usually a send out lab.
  - Hematologic studies including d-dimer, fibrinogen, haptoglobin, lactate dehydrogenase (LDH), coagulation studies, and peripheral smear can help differentiate TTP from DIC
    - DIC: elevated d-dimer, decreased fibrinogen and prolonged coagulation studies
    - TTP: elevated LDH, decreased haptoglobin and normal coagulation studies

- **Treatment of thrombotic thrombocytopenic purpura**
  - Emergent treatment with plasmapheresis and FFP infusion (i.e., plasma exchange transfusion) is essential and should be initiated as soon as possible, without delay.
    - Plasma exchange transfusion removes the platelet aggregation factors and immune complexes associated with endothelial damage and can continue daily until platelets have normalized and hemolysis has ceased.
  - Steroids may be beneficial to limit immune-mediated damage and support adrenal dysfunction.
  - Benzodiazepines or anticonvulsants may be needed to treat seizures initially.
  - Dialysis may also be necessitated in severe renal impairment.
  - Avoid platelet transfusions unless there is risk of intracranial bleeding or hemorrhage.
    - Transfused platelets can augment platelet aggregation and cause worsening of thrombosis and ischemia.
  - FFP may be given while arranging plasma exchange transfusion.
  - Splenectomy may be necessary in refractory cases or relapse.
  - Patients should be monitored closely as relapse occurs in up to 40%.
  - Antiplatelet agents are controversial.
  - Rituximab, anti-CD20 monoclonal antibody which normalizes ADAMTS 13, is being used increasingly in the treatment of TTP as evidence shows improved rates of resolution of acute disease and rates of remission.

- **Attributions**

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