THROMBOTIC MICROANGIOPATHIES


Take home points:
1. TTP “pentad” is only present in 1/3 of patients.
2. TTP presents with neurologic, systemic symptoms more commonly while HUS presents with renal involvement more commonly.
3. Any patient with elevated LDH, thrombocytopenia, and schistocytes on smear (with normal coags) should be considered to have TTP and plasmapheresis (plasma exchange) should be instituted immediately.

Thrombotic microangiopathies:
- Characterized by microvascular occlusion
- Systemic or intrarenal aggregation of platelets
- Thrombocytopenia
- Mechanical (intravascular) hemolysis
- Markedly elevated LDH but usually normal coags (differentiates from DIC)

Types of thrombotic microangiopathies:
- Systemic platelet thrombi: caused by failure to degrade large multimers of von Willibrand factor. Clinical presentations is that of thrombotic thrombocytopenic purpura (TTP)
- Predominantly renal platelet-fibrin thrombi: caused by exposure to E.Coli Shiga toxin or a familiar defect in plasma factor H. Clinical presentation is that of hemolytic-uremic syndrome (HUS)
- Renal or systemic thrombi: caused by transplantation or drugs (mitomycin, cyclosporine, tacrolimus, quinine, ticlodipine, rarely clopidogrel). Can present as either TTP or HUS.

TTP:
- Classic pentad (fever, thrombocytopenia, microangiopathic hemolytic anemia (MAHA), elevated creatinine, and neurologic symptoms) only seen in 1/3 of patients. Most patients have neurologic symptoms (seizures, altered mental status, strokes, etc).
- Look for triad of elevated LDH (due mainly to tissue hypoxia/injury and not hemolysis), schistocytes on smear, and thrombocytopenia.
- Presents as systemic platelet thrombi.
- Caused by low levels of ADAMTS 13 (a metalloproteinase that cleaves vWF) or antibody against vWF. No ADAMTS = large vWF clusters that cause platelet aggregation.
- Treat with plasma exchange (plasmapheresis). If you are at a place that doesn’t have plasma exchange, just infuse plasma (FFP). Adjunctive therapy: steroids, splenectomy (especially if relapsing or persistant). Rituximab and vincristine have been used as well in refractory cases.
- Avoid platelet transfusion at all costs (only use with life-threatening bleeds). Platelet transfusion associated with worse outcome from increased thrombotic complications.

HUS:
- Usually occurs in children; associated with E.Coli O157:H7 in most cases (there is a familial form)
- Most patients don’t have wide-spread systemic symptoms. Besides hematologic complications, renal involvement is the rule.
- In adults, the course is more virulent than in kids with progressive renal failure that can lead to ESRD
- Pathogenesis mainly platelet-fibrin aggregates (not a lot of vWF). Also endothelial damage plays a big role.
- Treatment can be supportive in children, but in adults, assume TTP and treat as above (mainly because TTP is a very bad disease). HUS has equivocal response to plasma exchange.
- Avoid anti-motility agents in E.Coli-associated HUS as this can exacerbate things.
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Teachable Cover Sheet

1. What is the classic “pentad” of TTP and how often is it present in cases of TTP?

2. What is the “triad” of TTP that alerts you to the diagnosis?

3. What is the underlying cause of TTP on a molecular level?

4. What differentiates TTP and HUS clinically?

5. What differentiates TTP and HUS pathophysiologically?

6. How can you differentiate TTP from DIC?

7. What is the treatment for TTP? When should it be initiated?

8. Can anything be done to prevent recurrent TTP?