Thrombotic Microangiopathy (TMA)

Group of disorders characterized by:

- Thrombocytopenia
- Microangiopathic hemolytic anemia (MAHA)
- Organ dysfunction - the kidneys, brain, heart, pancreas, liver, lungs, eyes, and skin.

Primary thrombotic microangiopathy (TMA) – require specific therapy

- Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS)
    - Primary (without coexisting disease) - Atypical HUS - complement mediated
    - Secondary to Infection:
        - Shiga toxin-producing Escherichia coli (STEC)
        - Shigella dysenteriae
        - Streptococcus pneumonia
- Drug-induced TMA (DITMA)
- Heritable coagulation and metabolic mediated – usually in children

Secondary to systemic disorders – require therapy directed at the underlying disorder

- DIC
- Acute viremia (CMV, HIV, or EBV)
- Severe hypertension
- Malignancies
- After organ and hematopoietic cell transplant
- Catastrophic antiphospholipid antibody syndrome
- CTD – SLE, APS, SSc
- Pregnancy-related disorders such as preeclampsia or HELLP syndrome

Clinical suspicion of primary TMA:

- Thrombocytopenia and anemia with elevated LDH and reticulocytes (elevated unconjugated bilirubin is supportive) associated with organ dysfunction.

Primary TMA diagnosis confirmation:

- Schistocytes in peripheral smear
- Reduced haptoglobin
- Negative Coombs test
- Normal coagulation tests
- Exclusion of TMA secondary to systemic conditions

Primary TMA differential diagnosis:

- TTP
    - ADAMTS 13 activity <10%
    - Assessment with the PLASMIC score
- STEC HUS
    - EHEC/ Shiga-toxin positivity

    - aHUS - Atypical, complement mediated HUS
        - ADAMTS 13 activity >10% and EHEC/ Shiga-toxin negative

Primary TMA treatment:

- Supportive care: IVF, nutrition, electrolytes replacement and HD as needed
- RBC transfusion - threshold for transfusion Hb 6 – 7 g/dl
- Platelets transfusion - active bleeding, need for invasive procedure or platelets <10.000
- Specific therapy for TTP
    - Therapeutic plasma exchange, glucocorticoids, and rituximab is the standard therapy
        - When a diagnosis of TTP is first suspected therapeutic plasma exchange with up-front corticosteroids are recommended
        - When low ADAMTS 13 is confirmed
            - Consideration for aplacizumab for critically ill with severe neurologic or cardiac findings and other forms of critical illness
            - Treatment for TTP continues until the thrombocytopenia has resolved to the range of ≥150
- Specific therapy for STEC HUS
    - Supportive, antibiotics are not indicated
- Specific therapy for aHUS
    - Switch therapeutic plasma exchange to eculizumab as soon as a diagnosis of aHUS is confirmed ADAMTS 13 > 10% and STEC negative
    - If Eculizumab is given, meningococcal vaccine is required and prophylactic antibiotics should be given at the start of therapy and maintained for a minimum of 2 week
    - If Eculizumab is not available or “too expensive”, therapeutic plasma therapy is an alternative option (however, no conclusive evidence of benefit)