PEARLS OF LABORATORY MEDICINE

Therapeutic Plasma Exchange in TTP

Edward J. Yoon, MD

Chief Resident, Clinical Pathology
Beth Israel Deaconess Medical Center
Harvard Medical School

DOI: 10.15428/CCTC.2016.261867
Presentation Outline

- Pertinent definitions and terminology
- Pathophysiology of TTP
- Therapeutic plasma exchange as treatment
Definitions & Terminology

Thrombotic Thrombocytopenic Purpura (TTP)

• Rare, life-threatening condition
• Ischemic end-organ damage due to microvascular thrombi (thrombotic microangiopathy)

Apheresis

• Extracorporeal therapy with automated cell-separator
• Physically separates blood components
• Goal – remove pathogenic substance from circulation
Apheresis – Schematic

Replacement Fluids

Centrifuge Separator

Removed Blood Components

Apheresis Machine

Patient
Definitions & Terminology (continued)

Therapeutic Plasma Exchange

• Apheresis procedure that exchanges native plasma with a replacement fluid
• Pathogenic component(s) exists within native plasma
• Extent of procedure – in terms of “plasma volumes”

\[
1 \text{ Plasma Volume (liters)} = [0.07 \times \text{weight (kg)}] \times [1 - \text{hematocrit}^*]
\]

*expressed as a decimal

American Society for Apheresis (ASFA)

• Guidelines on indications for therapeutic apheresis
• Systematic and evidence-based
• ASFA Categories and Grade of Recommendation
Pathophysiology of TTP

Deficiency of ADAMTS13 metalloprotease
- Normally cleaves unusually-large von-Willebrand factor multimers (UL-vWF)
- Auto-antibody formation ➔ Inhibits ADAMTS13
- Severe deficiency in the majority of cases
  - (<10% activity, with inhibiting antibodies)

Formation of microvascular thrombi
- Consequence of increased circulating UL-vWF
- Interaction of UL-vWF, platelets, endothelium, and high-shear flow (arterial microvasculature)
- Widespread ischemic end-organ damage
TTP – Schematic

Normal Microvascular Physiology

TTP

Figure Legend
- Von Willebrand factor
- Platelet
- ADAMTS13
- Inhibiting Antibody
Diagnosis of TTP

Classic teaching – Pentad of TTP

- Thrombocytopenia, microangiopathic hemolytic anemia (MAHA), neurologic changes, renal dysfunction, and fever
- May only see thrombocytopenia and MAHA (or other signs/symptoms) → Clinical diagnosis

Laboratory abnormalities

- Thrombocytopenia, anemia (schistocytes on smear)
- ↑Total (indirect) bilirubin, ↑LDH, ↓haptoglobin
- ↓ADAMTS13 activity, (+)inhibitor antibodies
Therapeutic Plasma Exchange in TTP

Proven first-line therapy (ASFA Category I)
- Significantly reduces overall mortality
- Initiate ASAP following diagnosis
- Exchange with donor plasma (FFP, FP24, etc.)
- ADAMTS13 testing – Do NOT delay treatment!

Physiology of plasma exchange
- Repletion of uninhibited ADAMTS13 enzyme
- Removal of inhibitor antibodies
Therapeutic Plasma Exchange in TTP (continued)

Treatment regimen
- Daily plasma exchange procedures
- Exchange 1 to 1.5 plasma volumes per procedure

Example: 70kg male, 45% hematocrit

\[
1 \text{ Plasma Volume} = [0.07 \times 70] \times [1 - 0.45^*] = 2.7 \text{ liters}
\]

*expressed as a decimal

- Donor plasma infusion → Temporizing measure only

Monitoring response to treatment
- Platelets sustained at >150,000 /µL, LDH near-normal for 2-3 consecutive days (without plasma exchange)
- Improved clinical signs and symptoms
Therapeutic Plasma Exchange in TTP (continued)

Supplemental treatment options

- Corticosteroids
- Rituximab
- Other immunosuppression
Special Considerations

Blood component transfusion
- RBC’s – Transfuse judiciously, if medically necessary
- Platelets – Generally contraindicated

Cryoprecipitate-poor plasma (Cryosupernatant)
- For plasma exchange
- Rationale ➔ Cryoprecipitate contains UL-vWF
- No definitive proof of improved outcomes
Practical Considerations

Difficulties initiating treatment
- Availability of apheresis services
- Vascular access
- Machine accessibility

Potential adverse events
- Allergic reactions to donor plasma
- Any other transfusion reactions
- Reactions to supplemental treatment
- Complications of vascular access
Summary

TTP is a complex disease – Clinical diagnosis made with laboratory support

Therapeutic plasma exchange – Apheresis treatment is first-line in TTP

Clinical decision-making – Critical throughout the treatment course
References


Disclosures/Potential Conflicts of Interest

Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:

- Employment or Leadership: None Declared
- Consultant or Advisory Role: None Declared
- Stock Ownership: None Declared
- Honoraria: None Declared
- Research Funding: None Declared
- Expert Testimony: None Declared
- Patents: None Declared
Thank you for participating in this Clinical Chemistry Trainee Council Pearl of Laboratory Medicine.

Find our upcoming Pearls and other Trainee Council information at www.traineeuncil.org

Download the free Clinical Chemistry app on iTunes today for additional content!

Follow us: