Primary Antiphospholipid Antibody Syndrome—Current Concepts

Dr Rukhsana Parvin
Associate Professor of Medicine
Enam Medical College & Hospital
Introduction

• Acquired autoimmune disorder characterized by recurrent venous or arterial thrombosis and/or recurrent fetal loss associated with persistence of antiphospholipid antibodies.
Epidemiology

- 1-5% healthy individuals have aPL antibodies
- Incidence is 5 cases per 100000 persons/year
- 50% of APS is **Primary** APS
- Mean age of onset: 31 years
- Risk of thrombosis: 0.5-30%
- Women: Men – 5:1
Criteria

- 1999, Sapporo, South Korea
- 2006, Sydney, Australia
Clinical Criteria

Vascular Thrombosis

• One or more clinical episodes of arterial/venous/small vessel thrombosis

• Thrombosis must be confirmed by objective validated criteria.
Pregnancy-related morbidity

• One or more unexplained deaths of a morphologically normal fetus at or beyond 10\textsuperscript{th} week of gestation.

• Three or more unexplained consecutive spontaneous abortions before 10\textsuperscript{th} week of gestation with maternal anatomical or hormonal abnormalities and paternal and maternal chromosomal causes excluded.
• One or more premature births of a morphologically normal neonate before 34\textsuperscript{th} week of gestation because of
  - eclampsia or severe pre-eclampsia
  - placental insufficiency
Laboratory Criteria

• Lupus anticoagulant
• Anti-cardiolipin antibody IgG or IgM subtype in serum or plasma
• Anti-beta 2-Glycoprotein 1 antibody IgG or IgM subtype in serum or plasma

• All should be present on two or more occasions at least 12 weeks apart
Diagnostic Criteria

• At least
  - one of the clinical criterion
  - one of the laboratory criterion
Noncriteria Manifestations

• Clinical
  - livedo reticularis
  - thrombocytopenia
  - autoimmune hemolytic anemia
  - cardiac valvular disease
  - multiple sclerosis-like syndrome, chorea or other myelopathy
• **Laboratory**
  - IgA anti-cardiolipin antibody
  - IgA anti-B2 GP1
Pathophysiology of APS

aPL

- Platelets
  - Activate platelet aggregation

- Coagulation cascade
  - Inhibit protein C/S, Thrombomodulin, ↓antithrombin III, ↓fibrinolysis

- Endothelial cells
  - ↑TF, Adhesion molecules, proinflammatory cytokines

- Placental tissue
  - ↓Trophoblastic cell growth, ↑apoptosis, ↓IL 3

- Complement system
• T cell hyperactivity and B cell overstimulation
• Role of TLR4
• Genetic factors
Treatment

• Asymptomatic individuals do not require specific treatment.
• Primary prevention of thrombosis in individuals who are persistently aPL positive lacks an evidence-based approach.
• For secondary thrombosis prevention, current recommendation is life-long warfarin, although the necessity, duration and intensity of warfarin treatment are still under debate.
• Prospective studies of patients with APS receiving antithrombotic therapy report an incidence of recurrent thrombosis of 3% to 24% per year.
• Retrospective studies report higher recurrence rates, ranging from 53% to 69%.
• General consensus is to treat patients with indefinite duration of anticoagulation.
• An observational cohort in 26 APS patients using **dabigatran** or **rivaroxaban** described a recurrent thrombotic event in only 1 patient after 8 months of treatment.

• The event-free survival rate was 87.9% at 12 months.

• Three controlled clinical trials are underway to evaluate the thrombotic risk of NOACs (RAPS, TRAPS, and ASTRO-APS).
Recent RAPS trial revealed that APS patients treated with rivaroxaban had a significant twofold-increased thrombin potential, suggesting a higher thrombotic risk, in comparison with warfarin users.
• **Rituximab** can be considered for recurrent thrombosis despite adequate anticoagulation.

• A non-randomized prospective study (**RITAPS trial**) showed rituximab to be effective for noncriteria **aPL manifestations** (ie, thrombocytopenia and skin ulcers).
• Prophylaxis during pregnancy is provided with subcutaneous heparin and low-dose aspirin.

• Therapy is withheld at the time of delivery and is restarted after delivery, continuing for 6-12 weeks or long-term in patients with a history of thrombosis.
• Corticosteroids have not been proven effective rather increase maternal morbidity and fetal prematurity rates.
Potential Future Therapy

• Statins
• Eculizumab
• Autologous hematopoietic stem cell transplantation
• Combination anti-aggregant therapy
Challenges for Future

• Physiological function of B2GP1
• Pathophysiology of thrombosis and pregnancy loss in PAPS patients
• Treatment is still poorly defined
• Evidence-based guidelines for management of neurologic manifestations remain unavailable
Conclusion

• There should be high index of suspicion for diagnosis of PAPS.
• Early recognition, appropriate treatment and lifestyle modifications can help the patients to lead a healthy life.
References


Thank You