ANTIPHOSPHOLIPID ANTIBODY SYNDROME

FLAME LECTURE: 36

OAKES 3.27.17

LEARNING OBJECTIVES

- Describe the evaluation, diagnosis and treatment of antiphospholipid antibody syndrome (APAS) in pregnancy
- Describe how APAS affects pregnancy
- Prerequisites:
  - None
- See also – for closely related topics
  - None

ANTIPHOSPHOLIPID ANTIBODIES

- These are important because they are associated with:
  - Arterial and venous thrombosis
  - Autoimmune thrombocytopenia
  - Spontaneous abortion / IUFD
  - Pre-eclampsia (including early-onset pre-eclampsia)
  - IUGR
  - Placental insufficiency
  - Preterm delivery

DIAGNOSIS[1]

- Clinical criteria:
  - Unexplained vascular thrombosis (arterial or venous), new vascular thrombosis in pregnancy, or history of vascular thrombosis not previously worked up
  - Pregnancy Morbidity
    - 1+ unexplained death in a normal fetus at or beyond 10 weeks with normal morphology
    - 1+ premature birth of a morphologically normal neonate < 34 weeks because of pre-eclampsia/eclampsia OR features consistent with placental insufficiency
    - 3+ unexplained, consecutive spontaneous pregnancy losses before 10 weeks WITHOUT anatomic/hormonal/genetic cause

[1]Miyakis 2006

DIAGNOSIS[1]

- Requires one clinical criteria & one laboratory criteria
- Laboratory criteria: Must be on 2 occasions > 12 weeks apart to avoid false positivity
  - Lupus anticoagulant (LA)
  - Anticardiolipin (aCL) IgG or IgM titer >40 GPL/MPL, or >99th %ile depending upon how lab is reported
  - Anti-β_2 glycoprotein-I IgG or IgM titer >99th %ile

[1]Miyakis 2006

PATHOLOGICAL MECHANISM

- Largely unknown, though β_2 glycoprotein I is a multi-functional plasma protein with affinity for ALL negatively charged phospholipids
- This glycoprotein also holds regulatory roles in coagulation, fibrinolysis, other physiologic systems

MATERNAL SEQUELAE

- 5-12% of APAS patients will have a thrombotic event during pregnancy or in the postpartum period
- Venous thrombosis (65-70% of thrombotic events)
  - Most frequent site is the lower extremities
- Arterial thrombosis (30-35% of thrombotic events)
  - Stroke is most common consequence (most likely MCA)
    - However, may occur in atypical sites: retinal, subclavian, digital, brachial arteries
  - TIA and amaurosis fugax
  - Coronary artery occlusions

FETAL SEQUELAE

- Intrauterine Growth Restriction
  - 15-30% of women with ApL antibodies will have IUGR
- Recurrent pregnancy loss
  - 5-20% of women with recurrent pregnancy loss will test positive for ApL antibodies
  - Most occur at >10 weeks (the fetal period), but it can occur at any gestational age

OTHER OBSTETRIC SEQUELAE

- Pre-eclampsia
  - 11-17% of women with pre-eclampsia will test positive for ApL antibodies
  - Women with known APAS are 5-8x more likely to get pre-eclampsia
  - Strongest association is with severe pre-eclampsia being diagnosed at early gestations(< 34 weeks)
    - Pre-eclampsia can even occur during pre-viable gestations

OTHER AUTOIMMUNE SEQUELAE

- Autoimmune thrombocytopenia
  - Seen in 40-50% of APAS cases
  - Difficult to distinguish from immune thrombocytopenic purpura (ITP), but treated the same way (steroids and IVIG)
- Other associated medical conditions: autoimmune hemolytic anemia, livedo reticularis, cutaneous ulcers, chorea gravidarum, multi-infarct dementia, transverse myelitis
- Catastrophic APAS → progressive thromboses and multi-organ failure

MANAGEMENT

- ALL patient's with APAS should be on Aspirin 81mg or a stronger anti-coagulant
- Group #1: Women with prior thrombotic event
  - Prophylaxis with heparin throughout pregnancy
  - Prophylaxis with warfarin for a minimum of 6 weeks post-partum
- Group #2: Women without prior thrombotic event
  - Not well-studied yet
  - Aspirin alone vs. same prophylaxis regimen as those with a prior thrombotic event
  - Some data suggests combination of prophylactic heparin + low-dose aspirin may reduce pregnancy loss by 50%[1]

MANAGEMENT

- Antepartum surveillance
  - Recommended because of risk for fetal growth restriction and stillbirth
  - Serial growth scans and antepartum testing in the 3rd trimester
- Long-term management
  - Life-long risk of thrombosis and stroke (50% had a thrombosis in 3-10 years follow-up)
  - 10% were also diagnoses with systemic lupus erythematosus (SLE)
  - No evidence exists to support long-term treatment when thrombotic events occur in the presence of other risk factors (like pregnancy)
  - Avoid estrogen-containing oral contraceptives

IMPORTANT LINKS / REFERENCES

- PRACTICE BULLETIN 132 – Antiphospholipid Syndrome (December 2012; reaffirmed 2015)
- Empson M, Lassere M, Craig JC, Scott JR. Recurrent pregnancy loss with antiphospholipid antibody: a systematic review of therapeutic trials. Obstet Gynecol 2002; 99: 135-44.