ANTIPHOSPHOLIPID SYNDROME

Rishi Motkur (1), Shruti Sunil(1), Gitika Aggarwal (1), Atul Laddu (1), and Jawed Fareed (2), 1= Global Thrombosis Forum, Suwanee, GA, and 2 = Loyola University, Chicago, IL

INTRODUCTION

Antiphospholipid syndrome (APS) is a condition in which the immune system produces antibodies that mistakenly attack tissues in the body, leading to blood clots in multiple organs. In this presentation, we will review the literature on APS, its symptoms, and management.

INCIDENCE

The incidence of APS is estimated to be approximately 2.1 cases per 100,000 individuals in the United States, with a prevalence of around 50 cases per 100,000 (Fig.1). The prevalence of APS compared to other autoimmune conditions is generally low; however, it is essential to note that studies on the prevalence of autoimmune conditions may vary due to differences in methodology and definitions.

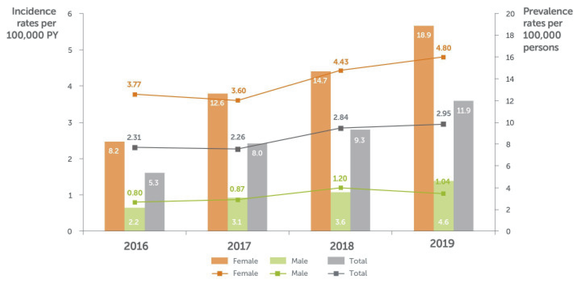

Figure 1: Yearly incidence and prevalence rates of APS cases. Lines represent incidence rates per 100,000 person-years and bars represent prevalence rates per 100,000 person-years.

ETIOLOGY

- Antiphospholipid Syndrome (APS) can be classified into two main categories: Primary and Secondary. In essence, this is based on whether the condition occurs alone or with other diseases.
- Primary APS occurs when the patient has no other autoimmune disease. These patients often develop blood clots or pregnancy issues, along with the presence of positive antiphospholipid antibodies. Approximately 60% of APS cases are primary, comprising the larger population with no other co-existing conditions.
- Secondary APS happens when patients also have another autoimmune disease, most commonly Lupus. Other autoimmune diseases that can lead to secondary APS include Rheumatoid Arthritis and Sjögren's Syndrome. Risk factors included OCs or Estrogen therapy, Pregnancy, and smoking cigarettes can facilitate Secondary APS.
- The distinction between the two types of APS matters because Primary APS tells physicians that only the antiphospholipid antibody system has malfunctioned, while the rest of the immune system works normally. Secondary APS tells physicians they must treat both the antiphospholipid antibody complications and the complications from the underlying autoimmune disease.
- This affects treatment planning and monitoring, as secondary APS patients require more comprehensive care for multiple conditions.

PATHOPHYSIOLOGY

- APS works through a "two-hit" model (Fig.2):
- In the First Hit, a type of stress damages the blood vessel walls. This stress could be in the form of infection, smoking, or inflammation. Due to this stress, in the "second hit", the antiphospholipid antibodies create blood clots.
- This amplification of antibodies heightens the likelihood of APL antibodies binding, leading to dangerously increased clot formation and the blocking of normal anti-clotting mechanisms.

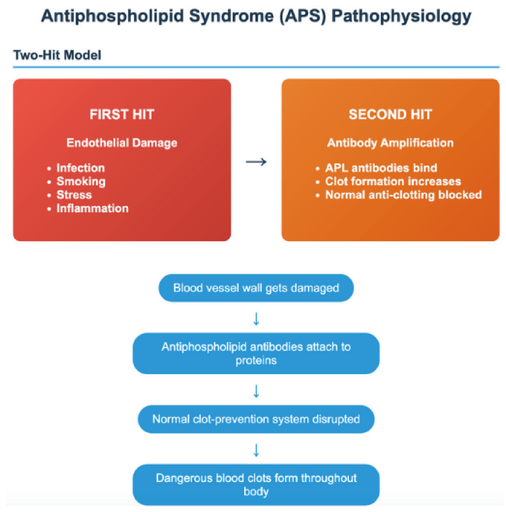

Figure 2: Explanation of APS two-hit model pathophysiology.

- There are three main types of antiphospholipid antibodies (Fig. 3) that doctors test for. These include anticardiolipin antibodies, Anti-beta-2-glycoprotein-1, and Lupus Anticoagulants. All three of these types are essentially autoantibodies that are associated with an increased risk of blood clotting.
- There are a handful of patients who test positive for all 3 antibodies. This is referred to as "Triple Positive." This triple positivity is associated with a higher risk of developing blood clots, or thrombosis, and pregnancy complications compared to patients with single or double positivity. Additionally, patients with triple-positive APS may require a more specific management plan to prevent complications.
- We can assess the severity of APS based on the presence of specific antibodies.

SIGNS, SYMPTOMS, AND COMPLICATIONS

Some signs and symptoms of APS include (Fig. 3,4): DVT, PE, red rashes, repeated miscarriages and stillbirths, preeclampsia, TIA, skin lesions (Fig. 5), and stroke.

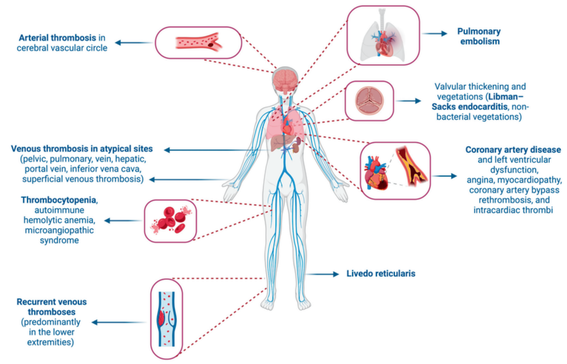

Figure 3: Clinical manifestations of antiphospholipid syndrome.

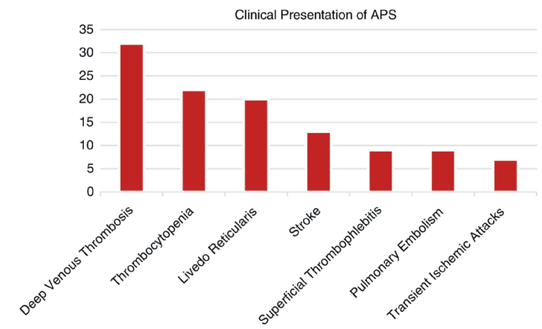

Figure 4: Illustration of the presenting symptoms and signs vs. percent of patients with APS.

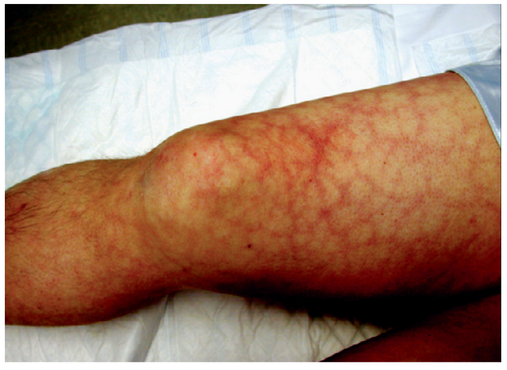

Figure 5: The skin lesions resulting from APS.

APS can lead to various organ complications, including fetal loss, stroke, pulmonary embolism, pulmonary hypertension, valvular abnormality, acute coronary syndrome, mesenteric thrombosis, or hepatic venoocclusive disease. Since surgery can increase the chances of blood clotting, patients with APS have a higher risk of complications during and after surgery. To prevent thrombosis, a clear anticoagulation strategy should be defined before any surgery in patients with APS.

DIAGNOSTIC TESTS

- APS is diagnosed through a blood test that searches for APLAs, which are specific to APS. To test for APLAs, a small blood sample is taken from a vein in the arm using a needle.
- Since antibodies can sometimes appear temporarily due to infection, two separate blood tests, taken 12 weeks apart, are usually performed to confirm the results.
- Diagnosis is confirmed if the patient has a history of blood clots and/or pregnancy complications such as miscarriages.
- Patients are referred to a hematologist or rheumatologist for treatment.

MANAGEMENT

- For thrombosis prevention in APS, low-dose aspirin is recommended for patients with high-risk antiphospholipid antibodies.
- Hydroxychloroquine is advised due to its protective effects against clotting. For secondary prevention, standard treatment is warfarin, with a target INR of 2-3, which acts as a vitamin K antagonist.
- Long-term anticoagulation should be considered for these cases. DOACs can serve as an alternative to warfarin in patient-specific instances, such as a warfarin allergy.
- For pregnancy management, the treatment varies depending on clinical history. If the patient has no history of pregnancy complications or clotting, no treatment is needed.
- In patients with a history of pregnancy loss or placental insufficiency, a combination of low-dose aspirin and LMWH is recommended throughout pregnancy.
- In women with a history of thrombotic APS, a combination treatment of low-dose aspirin and heparin at therapeutic dosage during pregnancy is recommended.
- For self-care, activities that could cause bruising, injury, or a fall should be avoided.
- Women should avoid using estrogen therapy for contraception or menopause. When considering food and dietary supplements, consuming large amounts of vitamin K-rich foods, such as avocados, broccoli, and Brussels sprouts should be avoided.

CONCLUSION

APS occurs when the immune system mistakenly creates antibodies that attack tissues in the body. There is no cure for this condition, but medications can reduce the risk of blood clots and pregnancy complications. APS may occur in individuals with systemic lupus erythematosus (SLE) or another autoimmune disease, or in those who are otherwise healthy. It is diagnosed only when these antibodies cause health problems. Management involves a combination of heparin, warfarin, and hydroxychloroquine, depending on the patient's risk and history. In pregnant patients, heparin or heparin with aspirin is recommended to prevent thrombosis. The patient should also be advised on self-care, including avoiding excessive consumption of vitamin K-rich foods, which can reduce the effectiveness of warfarin.