Antiphospholipid Antibody Syndrome

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KEYWORDS

- Antiphospholipid syndrome • Antiphospholipid antibodies
- Recurrent pregnancy loss • Fetal demise • Unfractionated heparin
- Complications of pregnancy

KEY POINTS

- Antiphospholipid antibodies (aPLs) are acquired antibodies directed against negatively charged phospholipids, a group of inner and outer cell membrane antigens found in mammals.
- Obstetric antiphospholipid antibody syndrome (APS) is diagnosed in the presence of certain clinical features in conjunction with positive laboratory findings.
- Although obstetric APS was originally reported in association with slow progressive thrombosis and infarction in the placenta, it is most often associated with a poor obstetric outcome.
- Several pathophysiologic mechanisms of action of aPLs have been described.
- The most common histopathologic finding in early pregnancy loss has been defective endovascular decidual trophoblastic invasion.
- Treatment with heparin and aspirin is emerging as the therapy of choice, with approximately 75% of treated women with RPL and aPL having a successful delivery, compared with less than 30% without treatment.

INTRODUCTION

Antiphospholipid antibodies (aPLs) are acquired antibodies (immunoglobulin [Ig] G, IgM, and/or IgA isotypes) that react against negatively charged phospholipids. They were originally associated with a slow progressive thrombosis and infarction in the placenta[1] and thus have been classified as thrombophilic factors. aPLs should additionally be classified as autoimmune factors when considering implantation and

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pregnancy because of the complex nature of the interaction of aPLs with target tissues. They have been shown to inhibit the release of human chorionic gonadotropin from human placental explants; to block in vitro trophoblast migration, invasion, and multinucleated cell formation; inhibit trophoblast cell adhesion molecules; and to activate complement on the trophoblast surface, inducing an inflammatory response.[2–5]

Antiphospholipid syndrome (APS) is an autoimmune condition characterized by the production of aPL combined with certain clinical features. The presence of aPL (including anticardiolipin [aCL] and lupus anticoagulant [LAC]) during pregnancy is a major risk factor for adverse pregnancy outcome.[6] In large meta-analyses of studies of couples with recurrent pregnancy loss (RPL), the incidence of APS was between 15% and 20% compared with about 5% in nonpregnant women without a history of obstetric complications.[7,8] It is not yet understood how aPLs arise in patients with APS. Genetic factors and infection may play a role. Family studies suggest a genetic disposition to APS, either when it presents as a primary condition or when it is seen in the context of systemic lupus erythematosus (SLE). This genetic disposition is accounted for, at least in part, by the major histocompatibility complex. The antibodies generated in patients with APS seem to recognize epitopes on phospholipid-binding proteins, unlike the antibodies that arise following infections such as syphilis and Lyme disease, which recognize phospholipids directly.[9]

DIAGNOSIS OF APS

APS is a syndrome that is defined based on both clinical and laboratory criteria. The diagnosis can be based on the presence of the clinical manifestation together with the laboratory detection of abnormal antibodies (**Box 1**). APS is designated as primary in patients without clinical or laboratory evidence of an underlying condition or disease, and secondary when it is associated with other diseases or conditions.[10] SLE is the disorder in which APS is most commonly associated but it may be associated with other conditions.[11,12] **Box 2** lists the conditions associated with secondary APS that may be relevant to obstetricians.

Widespread interest in APS among all areas of medicine led to the First International Symposium on Antiphospholipid Antibodies in 1984. The purpose of this group was to bring together the international research and clinical communities with the goal of clinical and scientific sharing and standardization of APS. Meetings have been held periodically with research and clinical data reviewed and discussed at preconference meetings and committees. An article was published with the latest suggested criteria for the diagnosis of APS with the current version referred to as the Sydney criteria.[13] These criteria should be useful for research investigations because the criteria result in specific diagnoses; however, in the clinical setting, these criteria are not very sensitive. These committee recommendations have been widely published, but the committee is not sanctioned or supported by any governing body such as the American College of Obstetricians and Gynecologists. The committee is primarily composed of rheumatologists, hematologists, and internists, with minor representation from obstetricians.

Clinical Criteria

The clinical manifestations of primary and secondary APS are diverse and may involve most organ systems.[10,14] Based on currently available evidence, vaso-occlusive disease is the pathologic basis for many of the complications of primary and secondary APS. Therefore, preconception counseling of the patient with APS regarding the risks