Central Nervous System Manifestations of Antiphospholipid Syndrome

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KEYWORDS

• Antiphospholipid syndrome (APS) • Central nervous system (CNS) • Stroke • Chorea • Psychosis • Cognitive disorder • Seizure • Sinus thrombosis

KEY POINTS

- Neurologic involvement is common in patients with antiphospholipid antibody syndrome.
- The most prevalent central nervous system manifestation of antiphospholipid syndrome is stroke, and the cerebral vasculature is the most commonly involved arterial bed in the body.
- Other thrombotic and nonthrombotic manifestations also have been reported that include cognitive disorders, dementia, seizures, chorea, migraine, psychosis, and demyelinating disease.
- In addition to infarction, neuroimaging often reveals white matter lesions throughout the brain that are nonspecific and also are seen in other conditions.
- Treatment of antiphospholipid antibody–associated neurologic disease consists of anticoagulation with or without additional immunosuppression as deemed necessary. The intensity of anticoagulation is a matter of some debate.

INTRODUCTION

The antiphospholipid syndrome (APS) is an acquired systemic disorder associated with circulating autoantibodies to anionic phospholipids and phospholipid binding complexes.[1] APS can occur independently (referred to as "primary APS") or in the setting of another autoimmune disease, most commonly systemic lupus erythematosus (SLE). The primary clinical manifestation of APS is thrombosis, which can occur in either the arterial or the venous circulation, or both. Neurologic involvement is prevalent in APS and responsible for significant morbidity and mortality from the disease.[2] APS affects the nervous system in myriad ways, with stroke and transient ischemic

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attack (TIA) being the most common.[3] Not all neurologic manifestations, however, are a consequence of thrombotic events. This article reviews many neurologic complications (**Box 1**) linked to APS and focuses primarily on those that affect the central nervous system (CNS), reviewing their clinical features, diagnostic evaluation, and treatment.

CLINICAL MANIFESTATIONS

Cerebral Vascular Accident

The neurologic manifestations of APS can generally be grouped into those that are caused by ischemia and those that are not ischemia-related, with the former being more prevalent than the latter. Cerebrovascular accident (CVA) is the most common and often consequential neurologic complication of APS,[2] and the cerebral circulation is the most common arterial system affected in APS.[4] CVAs linked to APS can be either thrombotic or embolic in origin and can affect any vascular territory.[5] Antiphospholipid antibody (APL)-positive patients with ischemic stroke tend to be younger and more likely to be female compared with stroke patients who are APL negative.[6,7] Indeed, the prevalence of APS is particularly high in younger stroke patients. At least 20% of strokes in individuals younger than 45 are attributable to APS,[8] and the presence of APL in younger individuals confers a more than fivefold risk of incident stroke or TIA compared with those who are not APL positive.[9] Conversely, the risk of incident stroke associated with APL in older patients is somewhat less clear, and, although most studies that have examined this question support an increased risk of CVA in older patients who are APL positive,[5] the mechanism of APS-associated stroke may be different in younger patients than in older patients.[5] For those patients who have already suffered a CVA, there is some controversy as to whether the presence of APL increases the risk of a subsequent cerebral ischemic event.[2]

Patients with secondary APS in the setting of SLE also may be at greater risk of having a cerebral ischemic event than those with primary APS.[7] In this population, the presence of lupus anticoagulant (LAC) has been shown to be a stronger predictor of thrombosis and intracranial ischemic events than are antibodies to cardiolipin.[6,7,10] Traditional cardiovascular risk factors, such as hypertension, also have

Box 1
Central nervous system manifestations of antiphospholipid syndrome

- Cerebral vascular accident
- Sneddon syndrome
- Venous sinus thrombosis
- Cognitive impairment and dementia
- Psychosis
- Seizure
- Movement disorder
- Headache (including migraine)
- Demyelinating disease
- Transverse myelitis
- Ischemic optic neuropathy