5 Cardiac Manifestations in Antiphospholipid Syndrome

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Introduction

Cardiac manifestations may be found in up to 40% of patients with the antiphospholipid syndrome (APS), but significant morbidity appears in less than 10% of these patients. Most of these manifestations are explicable on the basis of thrombotic lesions either on the valves or in the coronary circulation, and they may mimic other similar conditions, such as rheumatic fever or infectious endocarditis. The APS coagulopathy in these patients requires the careful and judicious use of appropriate antiaggregant and anticoagulant therapy. For this reason, the estimation of antiphospholipid antibodies (aPL) in cardiological practice assumes considerable importance.

Valvular Disease

Heart valve lesions are the most common cardiac manifestations described in patients with aPL. The introduction of two-dimensional and Doppler echocardiography revealed a high prevalence of valvular abnormalities, such as thickening, stenosis, regurgitation, and vegetations, in patients with systemic lupus erythematosus (SLE). Additionally, it appears that, since the introduction of corticosteroid therapy, valvular involvement has become more prevalent among patients with SLE due to their increased longevity [1]. In several studies, these valvular lesions have been associated with the presence of aPL [2–6]. Furthermore, valvular lesions have also been described in patients with the primary APS (PAPS) [7–9]. Although most cases are symptomless, an increasing number of papers report cases with severe valvular dysfunction resulting in cardiac failure, sometimes requiring valve replacement [2–9].

Echocardiographic Findings

Valve Dysfunction and Thickening

In 1997, Nesher et al [10] performed a meta-analysis of 13 studies on valvular involvement in SLE, as documented by Doppler-echocardiography, and they found

valvulopathy in 35% of SLE patients. The mitral valve was involved most commonly, and lesions included leaflet thickening, vegetations, regurgitation, and stenosis. Most of these studies also looked at the possible relationship of valvulopathy to the presence of aPL. Although several studies documented a statistically significant association between aPL and valvulopathy [2–6], others found no significant difference in aPL-positive and aPL-negative patients [11, 12]. The meta-analysis of these studies showed that 48% of aPL-positive SLE patients had valvulopathy, compared with only 21% of aPL-negative SLE patients. Additionally, Nesher et al [10], in the analysis of studies involving patients with PAPS, found that 36% had valvulopathy.

Thickening of the valve leaflets is the most common lesion detected by echocardiography in both SLE and PAPS patients. Valve thickness increases by twofold to threefold or more compared with normal valves [7–9]. The mitral valve is involved most commonly, followed by the aortic valve. Most thickened valves develop hemodynamic abnormalities, so that thickening as the sole abnormality is uncommon. Analysis of data from multiple studies [10] show that mitral regurgitation is the most common hemodynamic dysfunction, occurring in 22% and 26% of all patients with PAPS and SLE, respectively. Aortic regurgitation is less common, occurring in 6% and 10%, respectively. Mitral and aortic stenosis are uncommon, and usually accompany valvular regurgitation. Involvement of right-sided valves is also uncommon, and probably reflects pulmonary hypertension secondary to mitral or aortic regurgitation. In many cases, two or more valves are involved.

The valvular abnormalities associated with aPL may resemble those seen in cases of rheumatic fever. However, several echocardiographic differences have been observed. In APS-related cases, valve thickening is generally diffuse, and when localized thickening is noted, it involves the leaflets' midportion or base. Chordal thickening, fusion, and calcification is rarely seen and, when present, is not prominent. In contrast, valve thickening is typically confined to the leaflets' tips in rheumatic fever, and chordal thickening, fusion, and leaflet calcification is prominent in these cases [10] (Table 5.1).

Vegetations

Early reports of the link between aPL and SLE vegetations – the so-called "Libman–Sacks endocarditis" – date back to the mid-1980s when isolated reports of the association started appearing in the literature [2, 3]. Several echocardiographic studies with larger numbers of patients confirmed that SLE patients possessing aPL have a significantly higher prevalence of vegetations, particularly on the mitral valve, than those without [4–6,13]. Information on the histological appearance of these lesions in patients with aPL derives from anecdotal reports of individual cases and systematic studies are clearly lacking.

Pathogenesis

The pathogenesis of valvular abnormalities in APS is not entirely clear. It has been postulated that in APS the aPL directly cause valvular or endothelial injury unrelated to clinical severity of the disease. Ziporen et al [1] have shown positive staining for human immunoglobulins and for complement compounds in the subendothelial ribbon-like layer along the surface of the leaflets and cups. Amital et