科学论文

抗磷脂抗体：一种风险因素，影响系统性红斑狼疮和‘原发’抗磷脂抗体综合征

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摘要 七例有系统性红斑狼疮的弥漫性视网膜血管疾病被发现在84例连续患者中，这些患者曾在St Thomas’s Hospital接受狼疮关节炎诊。1985年至1987年间，六例患者系统性红斑狼疮（SLE）中，其中一例被诊断为‘原发抗磷脂抗体综合征’，从视网膜血管疾病影响到各种血管。这为视网膜血管疾病8%的发病率提供了证据，这在SLE患者中，其发病率显著高于0.5-2.0%。四例患者除SLE外，还患有其他系统性疾病，支持了过去文献中对于视网膜血管疾病和中枢神经系统疾病的关联。此外，原发抗磷脂抗体综合征的特征明显存在。这些发现表明SLE患者和高滴度抗磷脂抗体患者，存在更高的发展出弥漫性视网膜血管疾病的风险。

关键词：抗磷脂抗体，抗凝血，视网膜动脉/静脉血栓

眼底表现系统性红斑狼疮（SLE）包括结膜炎，Sjögren综合征，视网膜炎，视网膜炎。1-7视网膜炎一般包括有棉球样剥脱，或视网膜炎，视网膜炎。安全情况下，视网膜血管疾病的发展可能伴有视网膜小动脉梗塞，导致视网膜纤维层梗塞。3视网膜血管疾病发病率从3%到29%不等，视病患人数而定。

对比之下，更常见但更严重的视网膜血管疾病是弥漫性视网膜血管疾病。其过程一般为弥漫性视网膜血管疾病。Ascheron等人

接受发表21 July 1988。
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<th>Patient No</th>
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<th>Age (years)</th>
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<td>53</td>
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*APL=antiphospholipid; aCL=anticardiolipin; SLE=systemic lupus erythematosus; MI=mitral incompetence.
†IgG aCL: high=>80 GPL units, medium=20-80 GPL units, low=5-20 GPL units; IgM aCL: high=>50 MPL units, medium=6-50 MPL units, low=3-6 MPL units.
bodies, we identified seven patients with occlusive ocular vascular disease. These seven patients had previously undergone a full ophthalmological examination. Table 1 records their main clinical and serological characteristics. The anticardiolipin antibodies were estimated by an assay as described by Gharavi et al. 8

Results

Of the 84 patients in the study, seven patients suffered from occlusive ocular vascular disease (six had SLE and one had primary antiphospholipid syndrome). Thus the prevalence of occlusive ocular vascular disease was 8% in this subgroup of patients with raised antiphospholipid antibodies. Table 1 records the ocular lesions of these patients.

Four of these patients also had cerebrovascular disease (three had SLE, one had primary antiphospholipid syndrome). Thus three of six patients (50%) with SLE and occlusive ocular vascular disease had cerebrovascular disease. Table 1 records the neurological lesions of these patients.

Six of the patients recorded displayed additional features of the antiphospholipid syndrome.

Discussion

The 8% prevalence of occlusive ocular vascular disease in the subgroup of patients we studied is significantly higher than the 0.5–2.0% previously reported in SLE. 1 This study also supports the finding in SLE of a strong association between occlusive ocular vascular disease and central nervous system involvement. 2

The subject of occlusive ocular vascular disease in SLE was extensively reviewed recently by Jabs et al, who documented 11 of their own patients and reviewed the studies of 21 patients previously published. 2 Of their own patients, seven had severe generalised retinal vaso-occlusive disease, while four had more focal vascular occlusions (central retinal artery occlusion (one), branch retinal artery occlusions (two), and central retinal vein occlusion (one)). They found that eight of their 11 patients (73%) also suffered from central nervous system lupus, which was a significantly higher prevalence than in the other publications reviewed, where the figure was 37%. No reference to antiphospholipid antibodies was made in their paper, though one of their patients was subsequently found to have antiphospholipid antibodies on testing by our laboratory. This patient had recurrent deep vein thromboses, pulmonary emboli, transient ischaemic attacks, hemiparesis, and thrombocytopenia.

The antiphospholipid antibodies (antibodies to cardiolipin, the ‘lupus anticoagulant’, and the antibodies responsible for the false positive serological test for syphilis—Venereal Disease Research Laboratory (VDRL) test) have been associated with arterial and venous thrombosis occurring at various sites. 9 This association, originally called the ‘anticardiolipin syndrome’ 10 and subsequently referred to as the antiphospholipid syndrome, has been expanded to include recurrent fetal loss, a variety of neurological syndromes, and thrombocytopenia. 11 Livedo reticularis has also been associated. 12 13 In comparison with the general SLE population an increased prevalence of heart valve lesions, particularly affecting the mitral and aortic valves, has recently been recorded in patients with these antibodies. 14–16 In addition, there have been case reports where the association appears to be prominent. 17 18 This subject has recently been extensively reviewed. 19 The antiphospholipid syndrome may manifest as a primary entity in the absence of any specific autoimmune disease 20–22 but is more commonly seen in association with SLE, or lupus-like disease (where less than four of the 1982 American Rheumatism Association criteria for the classification of SLE are met). 23

In a previous study of an unselected group of 40 patients with occlusive ocular vascular disease and no underlying connective tissue disease antiphospholipid antibodies were not found. 24 There have been few reports linking occlusive ocular vascular disease with antiphospholipid antibodies in SLE. The two patients reported by Hall et al, both of whom demonstrated the lupus anticoagulant, represented the first definitive documentation of this association. 25 One of their patients had thrombocytopenia. One patient recorded by Silverman et al, with a central retinal vein occlusion complicating SLE, had a prolonged partial thromboplastin time, suggesting the presence of the lupus anticoagulant. 26 The patient recorded by Ford et al also suffered a retinal artery occlusion. 17 Retinal vein thrombosis is also mentioned in several reviews on the lupus anticoagulant. 27–29 A recent interesting paper described a woman with Sneddon’s syndrome, who developed a central retinal artery occlusion in association with antibodies to phosphatidyl-ethanolamine. 30 Sneddon’s syndrome comprises livedo reticularis, variable cerebrovascular symptoms, and labile hypertension. 31 The original patients described by Sneddon did not show any evidence of autoimmune disease, though immunological testing was limited in 1965. In a recent study from our unit, 32 however, three of 35 patients with cerebrovascular disease and livedo reticularis were found to have antiphospholipid antibodies in the absence of SLE, and would conform to the same group of patients as described by Sneddon.
We therefore conclude that patients with SLE and raised levels of anticardiolipin antibodies have a higher risk of developing occlusive ocular vascular disease than previously reported. In our group of patients features of the antiphospholipid syndrome were frequently present and in addition there was a high prevalence of central nervous system disease, particularly stroke.

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