
Multiple Transient Ischemic Attacks, Lupus Anticoagulant and Verrucous Endocarditis

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SUMMARY A young adult with lupus anticoagulant and systemic lupus erythematosus had onset of multiple transient ischemic attacks four years after a major left hemispheric infarct. The symptoms were stereotyped, recurred several times daily over three years and ceased when aspirin was added to steroid therapy. It is speculated that her symptoms were due to recurrent embolism from the heart in the presence of a thrombotic state.

LUPUS ANTICOAGULANTS are immunoglobulins of either the IgG or IgM class which interfere with phospholipid-dependent coagulation tests, without inhibiting the in-vivo activity of specific coagulation factors. 1 2 Though in laboratory tests the lupus anticoagulant prolongs the partial thromboplastin time, the seeming paradox is that its presence in the patient’s circulation appears to be associated not with bleeding but with a tendency to thrombosis. 3–5 It is frequently associated with both false positive serologic tests for syphilis and mild thrombocytopenia (possibly due to antibody activity against phospholipid antigen in the platelet membrane). It is most frequently found in patients with S.L.E., but occasionally in others. Most associated thrombotic episodes have affected the venous side of the circulation and deep venous thrombosis, pulmonary embolism, cerebral venous thrombosis and axillary vein thrombosis have all been described. 4–6 There have been several recent reports of cerebral ischemia in patients with lupus anticoagulant, both with and without S.L.E. 5–8 Most reported patients had cerebral infarction, but a few had several transient ischemic attacks. Reported effective treatments include corticosteroids, antiplatelet agents and anticoagulants. Preliminary evidence suggests that lupus anticoagulants inhibit prostacyclin production by arterial walls, possibly by interfering with the release of arachidonic acid from the cell membranes. 9

Case Report
The patient was a 26 year old right-handed female who was referred in November, 1983 because of multiple transient ischemic attacks. In 1976 she was admitted to another hospital following sudden onset of a right hemiplegia and aphasia. She had recently resumed oral contraceptives, which had been stopped 6 months earlier following an episode of phlebitis. Examination on admission revealed the following: Blood pressure 130/80. Pulse 80 per minute and regular. Respiratory rate 12 per minute and regular. No cardiac murmur was detected. Examination of her central nervous system showed a right he-
miparessis and an aphasia, characterized as mainly expressive. At that time repeated ANA, rheumatoid factor and cryoglobulins were negative. The patient had a false positive VDRL and was found to be anergic. Her P.T.T. was found to be abnormal on repeated testing, with no factor deficiencies. Selective left carotid angiography was performed on the day of admission and was reported as showing occlusion of the superior division of the middle cerebral artery, about 5 mm after its origin. She had an extremely long hospital course complicated by unexplained fever, abdominal pain, a pleural effusion and acrocyanosis. Several echocardiograms in hospital were normal. She was discharged without a definite diagnosis. At 1 year she could walk almost normally, but had a spastic right upper limb without any useful function and a mild dysnomic aphasia.

She was subsequently well until 1980 when she started having episodes of amaurosis fugax affecting only the left eye. They continued for the next three years at a frequency of between 2 to 5 times per 24 hours and were usually of less than 30 seconds duration. These took the form of a complete blacking out of vision, occasionally with residual small central field preservation, or an inferior altitudinal defect. In addition since that time she had approximately two episodes of vertigo per month lasting from 1 to 3 minutes and these were not related to postural change and occurred independently of the amaurosis. She had several episodes of paresthesia affecting either upper limb lasting a few seconds on each occasion and one episode of transient dysphagia lasting 2 to 3 minutes.

Examination revealed a pulse of 100 per minute, with a regular rhythm. Blood pressure was 146/90 in the right arm and 130/98 in the left arm. The pulse upstroke was normal. There was a grade 3/6 ejection systolic murmur at the base of the heart radiating up the neck and a grade 2/6 early diastolic blowing murmur at the left sternal border. There was no evidence of cardiacomegaly. Neurological examination revealed the old right hemiparesis and a mild dysnomic aphasia. General physical examination was otherwise normal.

Laboratory data: Hemoglobin 132 grams/litre, W.B.C. 5,800, Sed. rate 38 mm/hour, Platelet count 142,000 (normal 150,000–400,000). The ANA was positive at a titer of 1/80, with a speckled pattern. VDRL was non-reactive. Serum protein electrophoresis showed diffuse hypergammaglobulinemia. Anti-DNA antibodies were normal. The C50 complement level was 12 × 10^6 units/litre (normal range 20–40). PTT 33 seconds (normal range 22–26). Assays for clotting factors VIII, IX and XII were normal. Incubation with normal plasma showed the presence of an inhibitor and the platelet neutralization test was positive, confirming the presence of a lupus anticoagulant. Platelets showed increased aggregation. A Doppler examination of the carotids was normal. An echocardiogram showed fluttering of the mitral valve in diastole, consistent with aortic regurgitation and there was thickening of the endocardium in the sub-mitral valve area and of the anterior mitral valve leaflet (fig. 1). She initially refused cerebral angiography.

A diagnosis of S.L.E., with lupus anticoagulant was made and she was started on treatment with Prednisone 30 mgs daily. After 2 weeks her symptoms persisted unchanged and Aspirin 650 mgs b.i.d. was added to her regime. Within 3 days there was complete cessation of her amaurosis fugax, vertigo and upper limb paresthesia. Within 6 weeks her sed. rate dropped to 10 mm/hour, her PTT to 26 seconds and her C50 complement increased to 18 units/litre. In May 1984 she was hospitalized because of undiagnosed abdominal pain which rapidly cleared. At this time she had digital intra-arterial bilateral carotid and left vertebral angiography which was normal. One year later her neurological symptoms have not recurred and she continues to take Prednisone 15 mgs daily and Aspirin 650 mgs b.i.d.

Comment

The diagnosis of S.L.E. was clearly established in this patient following her recent presentation. She had a lupus anticoagulant and this had been present in 1976, at the time of her initial stroke, when she had also been taking oral contraceptives. There was currently clinical and echocardiographic evidence of cardiac disease, consistent with the presence of verrucous endocarditis, particularly affecting the aortic and mitral valves. Since 1980 she had hundreds of episodes of amaurosis fugax affecting the left eye but not the right, with less frequent episodes of vertigo and paresthesia. These did not stop after several weeks of Prednisone 30 mgs daily, but ceased within 3 days after the addition of aspirin to her regime.

The mechanism of her recent T.I.A.'s is uncertain. Digital intra-arterial angiography performed several months after initial consultation showed no evidence of a vasculitis but did not exclude one which had responded to treatment, or which affected predominantly smaller vessels. Similar symptoms, however, have not previously been described in association with vasculitis. They have been reported in patients with rheumatic valvular heart disease, particularly aortic valve dis-

**Figure 1.** 2D Echocardiogram: Long axis view of the mitral valve. The arrow indicates a thickening of the anterior mitral valve leaflet, consistent with verrucous endocarditis.
Cerebral Amyloid Angiopathy Associated With Giant Cell Arteritis: A Case Report

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SUMMARY A case of cerebral amyloid angiopathy associated with granulomatous arteritis is presented with description of the microscopic, immunocytochemical and ultrastructural features. The amyloid proved to be of the AL-type, with failure to show reactivity with anti-AA, anti-prealbumin and anti-albumin. Antisera against SAP and IgG (AF) did show reactivity. Hence the immunologic characteristics of this amyloid differ from those of other known conditions and may therefore represent a new form of amyloid.

The role of granulomatous arteritis in this case remains speculative.

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Case Report

A 66 year old male was referred to the Health Sciences Centre, Winnipeg, with a 4 week history of circumferential headache associated with nausea, vomiting, and unsteady gait with a tendency to list to the left. A computerized tomogram of the brain undertaken at a peripheral hospital revealed a 1.8 cm. mass in the right temporo-parietal region with marked surrounding edema. He was also found to have diabetes mellitus for which he received insulin, 20 units daily. His past medical history included transthyretine death and "lupus" anticoagulant; Detection of immunoglobulins interfering with prostacyclin formation. Lancet 1: 244–246, 1981


References


CEREBRAL AMYLOID ANGIOPATHY (CAA) is seen in association with many conditions, such as Alzheimer's disease, dementia pugilistica, adult mongolism, vascular malformations, generalized amyloidosis, radiation necrosis, hereditary cerebral hemorrhage and a multiple sclerosis-type demyelinating disorder. It is also noted within a significant proportion of aging brains. It is now recognized that CAA can occur without associated disease. Apart from the familial cases of CAA, there have been several reports of sporadic CAA associated with intracerebral hemorrhage. We report a patient with CAA and giant cell arteritis, an association not previously documented.

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