Prevention of Stroke in Patients With Systemic Lupus Erythematosus

To the Editor:

In the paper by Futrell and Millikan,1 the authors recommend anticoagulant therapy as the most effective preventive treatment for patients with systemic lupus erythematosus (SLE) who have had a stroke, transient ischemic attack, or cardiac valvular disease. They postulate that since cardiac emboli are the cause of strokes in SLE patients, they are best prevented by anticoagulants. We would like to argue this conclusion and suggest another etiologic factor in the pathogenesis of stroke in SLE patients, which might also favor other modes of treatments.

One of the mechanisms invoked in the pathogenesis of central nervous system lupus is deposition of immune complexes in the choroid plexus in a manner similar to that occurring in the glomerular basement membrane.2 The suggestion that cerebral lupus may be due to a cross-reactivity of human brain antigens with circulating antibodies, which gain access to the central nervous system after damage to the choroid plexus by antigen/antibody-mediated disease,3,4 was followed by other immunologic hypotheses involving cross-reactivity with neurons themselves.5 Recently, Briley and colleagues6 reported 25 patients with elevated anticardiolipin antibody levels and associated neurological symptoms, 15 of them with SLE or a lupus-like syndrome and eight with positive lupus anticoagulant. They speculated that cross-reactivity anticardiolipin antibody or lupus anticoagulant with platelets or endothelium might be responsible for thrombosis. Although they did not find a consistent trend in their various treatment results, including anticoagulants, they emphasize that three patients who received plasmapheresis and immunosuppressive therapy appeared to respond in temporal relation to the therapy.

Futrell and Millikan1 treated with anticoagulants only seven patients with SLE and transient ischemic attacks or stroke, and only one of these revealed that the source of stroke was cardiac. They also evaluated lupus anticoagulant in only eight of 13 patients with SLE and stroke. Based on these findings, we consider their recommendation to treat with anticoagulants the SLE patients who have had a stroke, transient ischemic attack, or cardiac valvular disease not entirely valid. Moreover, since anticoagulant therapy does not correct the fibrinolytic defect in SLE, we suggest evaluating both anticardiolipin antibodies and lupus anticoagulant in patients with SLE and stroke, since patients with anticardiolipin antibody may not exhibit lupus anticoagulant.7 We also recommend considering immunosuppressive therapy in these patients.

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The following is in response:

To the Editor:

Stroke is only one of many types of neurological disease in patients with systemic lupus erythematosus (SLE), and combining all of them into "central nervous system lupus" as do Achiron and Sarova-Pinhas is misleading. The need for careful classification of the types of nervous system involvement in SLE is being increasingly recognized.1

The references used by Achiron and Sarova-Pinhas do not support their hypothesis that the deposition of immune complexes in the choroid produces nervous system pathology. Atkins et al2 specifically state that this immune complex deposition was seen in all patients with SLE, whether or not they had nervous system involvement. They concluded that these deposits are not specific for nervous system involvement in SLE and also suggest that circulating antibodies to neuronal elements may cause "cerebral lupus." Although Bluestein et al4 postulate that anti-neuronal antibodies may cause some types of nervous system disease, they conclude that focal cerebral ischemia is caused by focal pathology in cerebral vessels. The use of immunosuppressive medication in the study of Briley et al6 cannot be applied to our patients since they were treating patients with diffuse encephalopathy rather than patients with focal cerebral ischemia or infarction. It is also not known how many patients in their study actually had SLE.

Our hypothesis that the major cause of stroke in SLE is from cardiogenic emboli is based on the frequent valvular disease in our patients2 and is supported by a major autopsy study.4 Achiron and Sarova-Pinhas consider our suggestion that anticoagulants be used to prevent stroke in SLE invalid because only seven patients were treated with anticoagulants. The suggestion to anticoagulate patients with SLE following a stroke or a transient ischemic attack was not based solely on these patients, but also on 1) three studies7–9 in the literature suggesting that anticoagulant seemed effective in preventing stroke, 2) reports that anticoagulant is the treatment of choice for the prevention of systemic thrombosis in patients with SLE,10,11 3) the autopsy documentation of cardiogenic embolus as a major cause of stroke in SLE, and 4) the need to correct the balance between fibrin formation and lysis. A. Achiron and Sarova-Pinhas incorrectly state that "eighth of the 13 stroke patients" were tested for lupus anticoagulant. Our Table 2 (Reference 5) shows that 10 of the 14 group A stroke patients were tested for lupus anticoagulant. The other four stroke patients were studied retrospectively and could not be tested for lupus anticoagulant. Of the 10 stroke patients who were tested, only four had lupus anticoagulant. Thus, lupus anticoagulant testing alone fails to predict stroke risk in SLE.

We agree that anticardiolipin antibody and lupus anticoagulant should be evaluated in all stroke patients with SLE, but the partial retrospective nature of our study and the fact that anticardiolipin antibody assays were not available at the time of the stroke in most of our patients made this impossible. It is important to point out that the role of lupus anticoagulant or anticardiolipin antibody in the production of thrombosis in patients with SLE has not been determined, and Laskin and Solonika12 state that the predictive
value of the anticardiolipin antibody is too questionable to be a
criterion upon which to base any therapeutic decision. Meyer et
al.\(^1\) compared anticardiolipin subtypes in patients with SLE and
syphilis and concluded that IgG anticardiolipin may be an epiphe-
nomenon and is probably not implicated in the pathogenesis of the
thrombotic diathesis seen in SLE. This controversial area has not
yet been adequately studied. The suggestion of Achiron and
Sarova-Pinhas that these patients be treated with immunosuppres-
sion is startling in view of the serious complications of immuno-
suppression and the absence of evidence that such therapy would
reduce the risk of cardiogenic emboli in patients with SLE.

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