Caffeine and Stroke

To the Editor:

Several investigators have recently shown that rodents chronically given caffeine develop upregulation of adenosine receptors and tolerate brain ischemia better than rodents not given caffeine.\(^4\) The upregulation results from caffeine's action as a competitive antagonist of adenosine. These findings provide further evidence for a neuroprotective effect of adenosine in the setting of brain ischemia.

Rudolphi et al\(^1\) conclude their article by saying that "An epidemiologic study of caffeine intake and stroke may prove quite interesting." Is not the investigation in humans by Grobbee et al\(^4\) such a study? They reported that chronic caffeine intake by men was inversely related to the risk of fatal and nonfatal stroke and that the trend for the association was statistically significant. The trick is to drink plenty of coffee and tea to upregulate adenosine receptors, but somehow to avoid caffeine-containing beverages once the stroke begins so that caffeine does not block adenosine from exerting its beneficial effect.

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References


Ischemic Stroke As the Sole Manifestation of Human Immunodeficiency Virus Infection

To the Editor:

It seems that patients with acquired immunodeficiency syndrome (AIDS) may be at risk for cerebrovascular diseases. These diseases appear in nine of 124 patients (7%) in one series.\(^1\) Twelve patients with cerebral infarction were identified in another series from approximately 1,600 patients with AIDS.\(^2\) In these patients, stroke was associated with opportunistic infections, human immunodeficiency virus (HIV)-related vasculitis, thromboembolism, or nonbacterial thrombotic endocarditis.\(^3\)

Young patients with stroke constitute a heterogeneous group. Recent reports suggest that an elevated number of these patients with stroke or transient ischemic attacks had antiphospholipid antibodies.\(^4\) These antibodies are a group of circulating autoantibodies that are strongly linked with immune-mediated thrombotic events. The most extensively studied antiphospholipid antibodies have been the lupus anticoagulant and anticardiolipin antibodies,\(^5\) which are seen primarily in patients with systemic lupus erythematosus, other autoimmune diseases, and a variety of seemingly unrelated disorders, including HIV infection.\(^6\) Patients with the HIV infection may develop antiphospholipid antibodies, and this linking may explain the elevated rate of ischemic stroke in this population.\(^7\)

We describe a young patient whose first and only manifestation of HIV infection was an ischemic stroke. A 32-year-old previously healthy man suddenly developed weakness in his right side and slurred speech. His medical history was significant for intravenous drug abuse (heroin) until 3 years before, hepatitis B surface antigen negative hepatitis, and left saphenous vein thrombophlebitis 5 years before that was related to intravenous drug injections. He smoked 20 cigarettes daily, but had no history of hypertension, diabetes, cardiac disease, or migraine. General and neurological examination revealed mild right facial paresis, mild right hemiparesis, and dysarthria.

Laboratory studies, including complete blood count, automated serum chemistries, prothrombin and activated partial thromboplastin time (aPTT), quantitative serum immunoglobulins, antinuclear antibodies, anti-DNA assay, rheumatoid factor (latex), Westergren erythrocyte sedimentation rate, serum complement, antithrombin III, proteins C and S activity, drug screening, and Venereal Disease Research Laboratory (VDRL) serology for syphilis were all normal or negative. Serum protein electrophoresis showed elevated gammaglobulins. Cerebrospinal fluid (CSF) was acellular with glucose of 38 mg/dl and protein of 62 mg/dl; VDRL serology was negative, and no oligoclonal bands were found. Serology for HIV (Western blot) was positive in both serum and CSF. Anticardiolipin antibodies (IgG aCL ELISA) were 112.2 units GPL. Repeated normal aPTT determinations ruled out the presence of lupus anticoagulants. Cardiac investigations (two-dimensional echocardiography, electrocardiography, and chest x-ray film) were normal. Head computed tomography and magnetic resonance imaging showed an ischemic area in the left temporal lobe. Four-vessel conventional cerebral angiography was normal.

The patient had an excellent clinical recovery and was asymptomatic on aspirin (325 mg/day) for 8 months. Recent measurement of anticardiolipin antibodies was 65 units GPL and, since new OKT4 determination was 100, zidovudine was started at this time. Patients with acquired immunodeficiency syndrome appear to be at increased risk for stroke.\(^2\) Cerebrovascular events in adult patients with AIDS occur with an incidence of 7–19%.\(^8\) In these series, both hemorrhages and ischemic infarcts were included, and most of the strokes were secondary to other diseases.\(^9\) According to the recent report of Engstrom et al,\(^2\) stroke is 40 times more likely to occur in persons <45 years of age who are infected with HIV. He identifies four patients with cryptococcal meningitis and one patient with herpes zoster–related vasculitis as the cause of the stroke suffered by his patients. In the remaining patients, the mechanism is unknown, although references to rule out neurosyphilis do not appear. He concluded that the pathogenesis of AIDS-related infarction is not clear and that the observed microscopic vascular changes seem not to have a specific etiology. According to the Walter Reed classification system,\(^9\) our patient was in stage I at the time of the ischemic event (he is now in stage III). Because he was no longer an intravenous drug user, we exclude drugs as a risk factor for stroke. Opportunistic infection and cardiac causes can also be ruled out by laboratory studies. HIV-related vasculitis seems improbable because of acellular CSF examination and normal four-vessel angiography. Only the pres-
ence of anticardiolipin antibodies in the setting of HIV infection remains as a risk factor for cerebrovascular disease.

We think that the presence of anticardiolipin antibodies is not merely casual, as stated by Brey et al. Several potential mechanisms of thrombosis induced by the antiphospholipid antibodies have been reported, although a unifying pathogenesis is lacking. On the other hand, there was evidence of reduced cerebral blood flow in the early stages of HIV infection.

The cause of ischemic stroke in young people is not usually determined, even after thorough studies are performed. We believe that HIV infection must be included in the differential diagnosis of young persons who have stroke of unknown origin.

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