Letters to the Editor

Pentoxifylline Alters the Natural Course of Acute Nonhemorrhagic Stroke

To the Editor:

Recently Hsu et al reported the results of a placebo-controlled, double-blind trial in patients with acute nonhemorrhagic stroke using pentoxifylline.1 The authors state that although pharmacologic effects were present during the first few days, the clinical benefits were small and not sustained.

This study shows a change in the natural course of stroke using pentoxifylline infusion therapy in contrast to a placebo group. To our knowledge, this is the first time that an improvement has been demonstrated in the acute phase of stroke using a rheologically active drug.

Consciousness, motor and cranial nerve functions, and total neurologic deficit scores improved significantly in the patients treated with pentoxifylline infusion. These variables deteriorated in the placebo group during the first 2 days, which partially reflects the very early entry of the patients (within 12 hours after onset of symptoms) into the trial. The significant differences between placebo and pentoxifylline therapy could not be maintained in the subsequent oral treatment period (after 3 days), although initial improvements due to pentoxifylline were sustained. These findings may be related to the different pentoxifylline plasma levels following the intravenous or oral route of administration.

We recommend further clinical investigations to substantiate the role of pentoxifylline infusion treatment in acute cerebral ischemia.

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The following is in response:

To the Editor:

We thank Drs. Ott, Chandra, and Hartmann for their thoughtful comments about our observations of pentoxifylline’s effects on acute stroke. We discussed the potential differences in pentoxifylline pharmacokinetics between intravenous and oral routes in the unabridged version of our paper, available from NAPS (c/o Microfiche Publications, PO Box 3513, Grand Central Station, New York, NY 10163-3513 [NAPS Document No. 04557, 54 pages]) and others.2

Furthermore, the pharmacokinetic differences between administering pentoxifylline intravenously and by controlled-release tablet have been studied by the clinical trial sponsor. While the multicenter controlled trial in acute stroke was ongoing, a study of the pharmacokinetics of the stroke trial intravenous regimen was carried out in 15 healthy volunteers. Summary comparisons of mean drug and metabolite steady-state plasma concentrations between intravenous administration (1,200 mg/day, 24-hour continuous infusion) and controlled-release tablet (400 mg t.i.d.) are shown in Table 1.

Clearly, the plasma concentrations of pentoxifylline and metabolite I are about 3 times higher during intravenous dosing compared to oral administration. The pentoxifylline metabolites are all considered to be hemorheologically active. It is possible that the higher concentrations of pentoxifylline and metabolite I present during intravenous dosing may produce more pharmacologic effects than an equal dose administered orally. If so, greater pharmacologic effects might account for the significant differences between drug and placebo noted during intravenous dosing for the first 3 days after stroke.

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Reference


Neurosarcoidosis and Stroke

To the Editor:

Brown et al1 recently reviewed the issue of sarcoidosis and stroke. Given the relatively common occurrence of vascular disease and microscopic infarction in neuropathologic studies of sarcoidosis involving the brain,2 the paucity of stroke cases is surprising. It is often difficult to substantiate the diagnosis of central nervous system (CNS) sarcoidosis and define the underlying pathophysiology of stroke syndromes. We report a case of CNS sarcoidosis presenting with stroke and an incidental suprasellar mass.

A 38-year-old white male with sarcoidosis was admitted with acute onset of left hemiparesis following a 2-week history of transient ischemic attacks. The patient had had biopsy-proven sarcoidosis since age 25 with ocular, skin, lymph node, and pulmonary involvement. He required corticosteroid treatment for control of his systemic disease and was taking triamcinolone (4 mg twice daily) at the time his neurologic symptoms developed. On admission, the patient related a history of 10 minutes of left
Letters to the Editor

FIGURE 1. Cerebral angiography showing a tapering stenosis of the right anterior cerebral artery (arrow).

hemiparesis on two occasions. A third episode led to persistent weakness.

Physical examination revealed a blood pressure of 134/88 mm Hg. The pupils were equal and reactive with no afferent pupillary defect. Visual fields were normal. There was grade 3/5 strength of the left arm and leg with associated hyperreflexia. Primary and cortical sensory modalities were intact.

Cranial computed tomography (CT) with and without contrast revealed a 12-mm enhancing suprasellar mass. Angiography demonstrated a tapering stenosis of the A1 segment of the right anterior cerebral artery (Figure 1). Magnetic resonance imaging showed that the suprasellar mass abutted the internal carotid and anterior cerebral arteries. A small area of increased signal intensity on the T2-weighted image was seen in the posterior limb of the right internal capsule.

Cerebrospinal fluid analysis demonstrated a sterile fluid with a total protein of 89 mg/dl, glucose of 60 mg/dl, IgG index of 0.79 (normal, 0.34–0.66), and angiotensin converting enzyme of 0.47 U/l (normal, <0.61). There were 118 WBC/mm³, with 64% polymorphonuclear cells and 36% mononuclear cells. Additional studies included a Westergren sedimentation rate of 37 mm/hr (normal, 0–8) and cholesterol of 240 mg/dl. Thyroid, prolactin, and testosterone hormone levels were normal. Twenty-four hour Holter monitoring was normal, and two-dimensional echocardiography revealed moderate concentric left ventricular hypertrophy with apical hypokinesis.

We made the diagnosis of neurosarcoidosis and started the patient on prednisone (40 mg daily). The left hemiparesis resolved within 4 weeks. Over the next several months, the prednisone dose was gradually decreased. Serial cranial CT scans confirmed a progressive decrease in the size of the suprasellar mass. Cranial CT at 12 months, with the patient taking prednisone (6 mg daily), showed only residual enhancing tissue in the suprasellar area. The patient has had no further stroke symptomatology.

The diagnosis of CNS sarcoidosis in our patient was based on the presence of biopsy-proven systemic sarcoidosis, the response of the intracranial mass to corticosteroid therapy over a 1-year period, and angiographic findings consistent with vasculopathy. Several different mechanisms can be responsible for stroke in this patient: small-vessel granulomatous vasculitis; cardiogenic embolus; or large-vessel inflammation resulting in artery-to-artery embolization, stenosis, or occlusion. In our patient, with a granulomatous mass in close proximity to the internal carotid and anterior cerebral arteries and angiographic evidence of disease of the A1 segment of the right anterior cerebral artery, the likelihood of rostral internal carotid artery or middle cerebral artery inflammation is very real.

In summary, our patient demonstrates that multiple mechanisms may be responsible for stroke in neurosarcoidosis.

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References


The following is in response:

To the Editor:
The case report by Corse and Stern exemplifies the problems posed by the development of stroke in patients with neurosarcoidosis. Although stroke is an uncommon complication of this disease, it often develops as the presentation of previously unexpected intracranial sarcoidosis. There is difficulty in ascribing the infarct to the effect of granulomatous angiitis. Steroid therapy was accompanied by a decrease in the size of the parascellar mass, but it is problematic whether this treatment was of benefit in altering the natural history of the functional deficit resulting from the infarct. Indeed, the clinical deficit did not necessarily correspond to the small lacunar lesion demonstrated by computed tomography scanning. Large-vessel disease, although present in the region of the mass, was not associated with arterial territory infarction. Positron emission tomography or single photon emission computed tomography scanning may be useful in correlating the arterial lesions with the functional deficit in such patients.

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