able source for stroke. These findings have occasionally been observed in other cases, but unfortunately not in this one. However, our patient had no other readily identifiable source for the cerebral ischemic events and it is our conclusion that the proximal aneurysm served as a nidus for thrombosis and subsequent embolization.

Decisions regarding the treatment of patients with ischemic symptoms, who are found to have an associated intracranial aneurysm, are difficult because knowledge concerning the natural history of unruptured aneurysms presenting with cerebral ischemia is sparse. A surgical approach with aneurysm clipping has been employed with success in some cases. The rationale for this approach is apparent, because obliteration of the aneurysm removes the source of emboli as well as eliminating the risk of subsequent rupture. This would appear to be optimal therapy in patients with aneurysms larger than 7 to 10 mm. considering the low morbidity and mortality of aneurysm surgery in the elective setting. Other patients have been managed with antiplatelet drugs. Anticoagulation is not a viable option because an anticoagulated patient who goes on to rupture an aneurysm would presumably suffer greater morbidity. In the present case, medical management with low dose aspirin was instituted because the aneurysms were small and their location in the region of the cavernous sinus was felt to increase significantly the technical difficulties and risks of surgery.

References

Heparin for Lacunar Stroke in Progression

BRUCE H. DOBarkin, M.D.

SUMMARY Four patients with mild hemiparesis were treated with heparin for presumed progressing stroke. All worsened to hemiplegia with pure motor deficits and lacunar infarcts despite this medical intervention. Clinical distinction between large artery and small, penetrating vessel thrombotic disease is needed to best evaluate any benefit of anticoagulation for stroke in progression.

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ANY EFFICACY OF HEPARIN to halt or reverse the neurologic signs of acute progressing stroke could be specific for stroke subtypes with particular clinical and vascular pathological profiles. Anecdotal and controlled studies of heparin use in patients with serially evaluated and progressing hemiparesis, generally within 36 hours of onset, do not clearly distinguish whether the causative pathology is in a carotid, verteobasilar, major branch, or penetrating artery. From 20 to 60 percent of lacunar infarcts producing a pure motor deficit progress by history or serial examination in a steady, step-wise, or fluctuating pattern. We anticoagulated four patients with this lesion in an attempt to halt progression, but they continued to deteriorate until hemiplegic.

Methods
From a group of 120 consecutive patients with stroke admitted to the Daniel Freeman Hospital Medical and Rehabilitation Center, 29 suffered presumed lacunar infarcts with just motor deficits. Cerebral localization and vascular pathology for all 120 stroke patients were based on criteria established by the neurologists participating in the NINCDS Pilot Stroke Data Bank. Nine patients who progressed in the hospital according to physicians’ notes and patient confirmation were not seen by us until their deficits appeared stable. None of these patients had been anticoagulated. We did examine 5 patients serially and appreciated progression of their pure motor deficit. One had a
blood pressure of 210/130 not responsive to cautiously given antihypertensive medication for 6 hours, by which time he was plegic. Four had blood pressures quickly controlled with a diuretic to a range of 160/90 to 130/80, so we felt safe treating with heparin (table 1).

Prior to giving a bolus of 5000 units of heparin followed by a constant infusion of 1000–1200 units per hour, each patient had normal serum electrolytes, creatinine, urea nitrogen, and total protein. The hematocrit ranged from 41 to 46 percent except in case 3, where it was 34 percent. Platelet counts and prothrombin and partial thromboplastin times were normal. Case 1 had a sedimentation rate of 45 mm/hour, but subsequent evaluation for infection and collagen-vascular disease was negative.

Electrocardiograms were normal in cases 1 and 3, revealed an old inferior myocardial infarction in case 4, and during cardiac rhythm monitoring of case 2, showed a 2 hour bout of paroxysmal atrial fibrillation starting 1 hour after admission. Case 2 had an old anterior myocardial infarction, but no acute ischemic changes on electrocardiogram. Two dimensional echocardiograms in cases 1 and 2 showed no mural thrombus, valvular disease or hypokinetic ventricular walls.

The electroencephalogram was normal 1 to 3 days after hemiplegia persisted in each patient. Median nerve somatosensory evoked responses done 3 to 7 days after maximal deficit were also normal. Each patient underwent a computerized tomographic study with overlapping 8 mm sections of the brainstem and internal capsule before and after receiving contrast medium, immediately after the first neurologic evaluation and prior to initiation of heparin.

Results

Cases 1 and 4 were started on heparin after their motor deficits worsened between two examinations (table 2). Case 2 was started before any apparent deterioration, because of his paroxysmal atrial fibrillation. Case 3 was treated with heparin because of her clearcut functional worsening. She had walked into the emergency room with only subtle paresis noted by a physician, but could no longer bear weight on her left leg for gait at our first assessment. Each patient had fairly symmetric face, arm, and leg paresis graded 3/5 to 4/5 (British Medical Council scale) on initial evaluation. After adjustments, cases 1, 3, and 4 had partial thromboplastin times 2–3 times control and case 2 greater than 100 seconds at the time their deficits became profound. Three patients became hemiplegic and case 4 showed residual 2/5 shoulder and hip strength.

Computerized tomography showed no lesion at the time of the first neurologic evaluation. Three patients developed lacunes limited to the posterior limb of the contralateral internal capsule. Case 3 had normal serial scans (table 3).

Carotid doppler and ultrasound studies in each patient revealed an intimal calcified plaque in cases 2, 3, and 4, but no intraluminal stenosis. Selective three vessel cerebral angiography, performed because of her youth and elevated sedimentation rate, was normal in case 1. Digital intravenous angiography in cases, 2, 3, and 4 revealed normal bifurcation, carotid siphon, proximal middle cerebral, and vertebrobasilar vessels except for a 25 percent stenosis of the proximal internal carotid ipsilateral to the lacune in case 3. The studies were performed within one week of admission.

All patients showed slight recovery of strength 2 to 4 weeks after onset of hemiplegia and all became ambulatory with an assistive device during a 4 to 7 week rehabilitation effort. Only case 4 developed full functional use of his affected hand.

Discussion

We based the diagnosis of a capsular lacune on a pure motor deficit in hypertensive patients with normal electroencephalograms and somatosensory evoked responses, no apparent occlusive disease in the carotid, vertebrobasilar or middle cerebral stem by angiography, and presence of a capsular lesion on CT scan or absence of any CT lesion. We could not have made the diagnosis of a progressing lacunar infarct with certainty when we started each heparin infusion. We tend to manage all patients with non-hemorrhagic stroke in progression with heparin when worsening of a neurologic deficit appears secondary to increasing ischemia, not to edema or medical complications. But we initially suspected a lacunar syndrome in our four patients based on facial weakness and hemiparesis without visual, sensory, coordination, language or cranial nerve abnormalities, a normal CT ruling out hemorrhage, and carotid doppler and ultrasound examinations that ruled out a greater than 30 percent intraluminal stenosis.

We presume that focal, small vessel disease was the anatomical substrate, probably involving the lateral lenticulostriate branches of the middle cerebral artery or perforating branches of the anterior choroidal artery in cases 1, 2, and 4 and possibly a basilar penetrator in case 3 where repeated CT scans were normal.
TABLE 3  Capsular Lacune Seen on CT Scan

<table>
<thead>
<tr>
<th>Case</th>
<th>Admission</th>
<th>Day 3</th>
<th>Day 14</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

sel stenoses by lipohyalinosis or very localized atheromatous plaque, sometimes associated with a microthrombosis or platelet-fibrin mass. He and others suggested that anticoagulation might prevent occlusion of the residual lumen in some patients. Embolization from heart, carotid artery or adjacent major cerebral or basilar artery could also possibly occlude a penetrator.

Treatment with heparin for stroke in progression is based on dissimilar studies that are about 20 years old, antedating the CT scan and not usually identifying angiographically the presumably stenotic vessel. Anecdotal experience with high grade, large arterial stenoses also suggests apparent usefulness. Milliken states, “Each study points to fewer patients progressing when receiving anticoagulants, compared to those not getting such therapy.” Heparin reacts with antithrombin III to prevent clotting, creates a supranegative charge on a vessel wall, reduces the rigidity of fibrinogen, inhibits platelet accumulation, and alters the activity of many enzymes. Different commercial preparations show different activities in coagulation tests. With all of these potential interactions, heparin might affect the process of thrombosis differently in the 30–100 u residual lumen of a penetrating vessel than in the 1–2 mm residual lumen of a large artery.

Hemorrhage into a lacune, especially in a hypertensive patient, is a potential hazard of anticoagulation. It is not known whether the risk is any greater here than with large vessel thromboses or with cardiac emboli, where hemorrhage into an infarct is uncommon. And it is not clear what, if any, induced fall in blood pressure to make anticoagulation seem safe to a physician may lead to iatrogenic hypoperfusion through a penetrator.

Prospective studies of progressing stroke should determine the underlying vascular pathology as best as clinically possible, so we can learn whether some subgroups of stroke patients benefit from anticoagulation more than others. Our series is too small to suggest that heparin never prevents progression of a lacunar stroke. Such cases are difficult to capture. Lacunar infarcts represent 10–20 percent of all strokes. About 20 percent of these patients may worsen in their motor deficits after hospitalization under neurologic observation. So perhaps only 2–4 percent of all stroke patients might present with lacunar stroke in progression for randomized study with anticoagulation or any other intervention. We need a continuing clinical effort to generate data on the natural history of stroke with therapeutic interventions aimed at more certain etiologies.

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