Leptomeningeal Artery Atherosclerosis Visualized by Angiography: Clinical Correlates

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SUMMARY Circumscribed atherosclerotic involvement of secondary and tertiary branches of major cerebral arteries is a common angiographic finding whose nature is rarely in question. However, widespread and severe changes are unusual, and radiologic interpretation may be more difficult. We recently cared for a patient whose angiogram demonstrated extensive involvement of leptomeningeal vessels and were prompted to review the clinical courses and autopsy findings of a number of other patients with similar angiographic findings. Our observations suggest that the radiological appearance of leptomeningeal artery atherosclerosis can be confused with that of an arteritis. Atherosclerosis of leptomeningeal arteries is strongly associated with a history of arterial hypertension and seems to parallel arterial lesions thought responsible for lacunar infarction and intraparenchymal hemorrhage.

ATHEROSCLEROTIC INVOLVEMENT of the secondary and tertiary branches of the major cerebral arteries is common. That more extensive involvement may cause small vessel angiographic arteriopathy similar to that produced by various inflammatory diseases is, however, poorly documented in the literature. In contrast to atherosclerosis of the cervical vessels or circle of Willis, and in contrast to the intraparenchymal arteriolar sclerosis not seen angiographically, leptomeningeal artery atherosclerosis visualized at angiography has incited few efforts to describe clinical correlates. We recently cared for a middle-aged patient whose clinical course and angiographic findings were, we thought, compatible with inflammatory arteriopathy. Postmortem studies, however, disclosed the presence of marked atherosclerotic involvement of the smaller surface arteries, while the larger vessels were spared. The case emphasizes the necessity, we believe, for histologic confirmation prior to initiating anti-inflammatory therapy for cerebral "vasculitis" suspected on angiographic and clinical grounds. The case, furthermore, stimulated an examination of the literature and of our previous clinical experience with angiographic findings. Our observations suggest that the radiological appearance of leptomeningeal artery atherosclerosis can be confused with that of an arteritis. Atherosclerosis of leptomeningeal arteries is strongly associated with a history of arterial hypertension and seems to parallel arterial lesions thought responsible for lacunar infarction and intraparenchymal hemorrhage.

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those leading to intraparenchymal arteriolar changes than to those causing large vessel atherosclerosis. Leptomeningeal artery atherosclerosis more often coexists with lacunar infarction and intraparenchymal hemorrhage than with occlusive disease involving the major cervical vessels or the primary cerebral arteries.

**Case Report**

A 54-year-old man (case I, table) was admitted to Hennepin County Medical Center on June 1, 1976, with acutely developing right extremity weakness and difficulty with speech. Past medical history included poorly controlled diabetes mellitus with biopsy-proven glomerulosclerosis and moderately severe hypertension despite antihypertensive therapy. He had been previously hospitalized for evaluation of renal disease and for acute glaucoma. Funduscopy during the latter hospitalization disclosed the presence of severe retinal vessel atherosclerotic changes in addition to those abnormalities more characteristic of his diabetes and hypertension. One month prior to hospitalization the patient had experienced transient right leg weakness.

At the time of admission, blood pressure was 150/100. General examination was unremarkable and peripheral pulses were palpable. Funduscopy again demonstrated abnormality of the fundal vessels. The patient was somewhat drowsy, and he was oriented only to person and place. Speech was thick, but he was able to name objects. He could perform simple calculations. He was essentially blind due to the combination of diabetic and hypertensive retinopathy as well as the effects of prior acute glaucoma. Right upper motor neuron facial paralysis was present, and there was mild right hemiparesis. The toes were bilaterally upgoing.

Routine admission laboratory data, including hemogram, electrolytes, other chemistries, and coagulation profile, were normal except for a fasting blood sugar of 184 mg/dl and a BUN of 23 mg/dl. Erythrocyte sedimentation rate was 13 mm per hour, and VDRL was nonreactive. Initial computerized tomography (CT) was normal as were a contrast-enhanced repeat CT study and a radionuclide scan later in the hospitalization. Lumbar puncture yielded clear cerebrospinal fluid under normal pressure and containing 120 mg/dl of protein, a normal concentration of sugar, and no white cells. A left carotid angiogram was performed (figs. 1 and 2), and the study demonstrated extensive leptomeningeal artery changes characterized by smooth concentric narrowing involving numerous branches of the anterior and middle cerebral arteries. The carotid bifurcation, internal carotid artery, carotid siphon and horizontal portion of the middle cerebral artery were not radiologically involved. When serological studies and a testicular biopsy failed to demonstrate a systemic vasculitis, clinical and angiographic findings were interpreted as consistent with so-called "granulomatous angiitis." The patient was begun on Prednisone, 100 mg daily. Over the following month he became more alert, and motor signs almost disappeared. He continued, however, to manifest impaired mentation with intermittent confusion. Management of his diabetes mellitus and hypertension was significantly complicated by corticosteroid therapy, which was gradually tapered and eventually discontinued. The patient was hospitalized several months later when elective leptomeningeal biopsy was planned. Because of the patient's poor medical status and, further, because the decision had already been made to discontinue corticosteroids, a less aggressive diagnostic approach was pursued.
FIGURE 2: Photographic enlargement of Figure 1, showing the severe “beading” of the pericallosal and callosal marginal branches of the anterior cerebral artery.

The patient was admitted for the last time on February 8, 1977, with a 3-day history of slurred speech and increasing confusion. Blood pressure at the time of admission was 172/120. The patient was alert but disoriented, and he manifested verbal perseveration. Right-sided hyperreflexia and bilateral toe signs were present. Six days following admission the patient became increasingly lethargic, and shortly thereafter he developed a flaccid left hemiplegia. CT scanning showed ventricular enlargement. He remained lethargic with profound pseudobulbar dysfunction and bilateral hemipareses until his death on March 12, 1977.

Autopsy Findings

The autopsy was limited to examination of the brain. The cerebral gyri were normal in size, configuration and consistency. There was mild atherosclerotic involvement of the large arteries at the base of the brain with severe focal involvement of small leptomeningeal arteries, particularly distal branches (fig. 3). Severe involvement was noted at the origin of the perforating branches of the basilar artery, and the right superior cerebellar artery was occluded. Infarcts were noted in the basal ganglia and internal capsule, bilaterally; that on the left appeared older than the lesion on the right (fig. 4). Scattered old infarcts were also present in the frontal white matter, the right hippocampus, thalamus and in the right cerebellar hemisphere in the distribution of the superior cerebellar artery. In the pons there were multiple old infarcts. The optic nerves and the lateral geniculate bodies were atrophied.

Microscopic examination confirmed the widespread atherosclerotic involvement of medium-sized and small leptomeningeal arteries (fig. 5). Thickening of the walls of small arteries and arterioles was also noted, consistent with a diagnosis of arteriolar sclerosis. The involvement of the medium-sized arteries consisted of focal fibroatheromatous changes in the intima, while the media and elastic tissues were often well preserved. Scattered small infarcts were noted in the hippocampus and thalamus. Extensive recent and old infarction was noted in the basis pontis. There was secondary degeneration of the pyramids in the medulla, bilaterally. The optic nerves and tracts showed severe degeneration.

Discussion

The case demonstrates that the angiographic findings of atherosclerotic involvement of leptomeningeal vessels can mimic those of inflammatory vascular disease. Angiographic findings in cerebral vasculitis, including granulomatous angiitis, are not uniformly described, but the diffuse occurrence and regular concentric appearance of the narrowings in our case are thought to be characteristic of inflammatory involvement and highly atypical for atherosclerosis. Furthermore, the absence of radiologically detectable disease of the extracranial carotid vessels and circle of Willis argues against an atherosclerotic basis for the leptomeningeal artery abnormalities. The clinical features of cerebral vasculitis are protean, though subacute multifocal symptomatology is most characteristic. The signs and symptoms, CSF findings, as well as the clinical course of our patient’s illness would be consistent with a vasculitis involving the brain. Thus, definitive diagnosis in such a clinical setting with the associated

FIGURE 3: Small branches of the left middle cerebral artery over the left parietal and temporal lobes show numerous small atherosclerotic plaques (arrows).
Numerous plaques (arrows) are present in the branches of the left middle cerebral artery in the Sylvian fissure and of the anterior cerebral arteries. There are several lacunar infarcts in the thalamus.

Angiographic "beading" of leptomeningeal arteries depends on leptomeningeal biopsy because of the overlapping clinical and radiologic features of inflammatory and atherosclerotic arteriopathy. The importance of establishing the correct antemortem diagnosis is magnified by the strikingly different management strategies appropriate for the 2 entities. The recent literature reflects increasing enthusiasm for the efficacy of corticosteroids in granulomatous angiitis, an inflammatory vascular disease confined to the central nervous system.9-13 On the other hand, corticosteroids are known to exacerbate both hypertension and diabetes.

With the objective of determining the clinical and pathological significance of angiographic leptomeningeal artery atherosclerosis, we reviewed the clinical records and autopsy material of 3 similar cases (table). Previous radiologic studies1 have shown that leptomeningeal vessel atherosclerosis is common in stroke patients, but the entity is rarely thought to be clinically germane and is not uniformly noted in the official radiologic interpretations. Consequently, cases were identified by personal recollection and, therefore, tended to be the most memorable and probably most severe, though none manifested the multiplicity of involvement of case I. It should be pointed out that our selection process was both retrospective and incomplete, but it did yield a group of patients whose only known shared feature was a radiologic abnormality. We were interested in determining whether common clinical or pathological features might be identified among these otherwise dissimilar patients.

Our findings suggest that in and of itself, leptomeningeal artery atherosclerosis is of no direct clinical consequence. Though pathological evidence of atherosclerotic occlusion of these small vessels is available,14 most studies of intracranial occlusive disease suggest that embolism is the more important mechanism in vessels of this size.16, 18 In patient I, as well as in the others, we found no evidence of occlusion of the leptomeningeal arteries despite the extensive nature of the atherosclerosis. On the other hand, we found lacunar infarctions in the basal ganglia of 3 of our patients. The fourth patient sustained a hypertensive intraparenchymal hemorrhage.

It may be that leptomeningeal artery atherosclerosis demonstrated angiographically and the vasculopathy which underlies lacunar infarction or intraparenchymal hemorrhage share a common pathogenic mechanism, namely hypertension. We found that all our patients were hypertensive. An association between leptomeningeal artery atherosclerosis and hypertension has been noted before.17-19 In that it leads to characteristic changes in the intraparenchymal arteries and arterioles, hypertension has been closely linked to lacunar infarction17, 20-22 and intraparenchymal hemorrhage.23-27 Indeed, the association between lacunar infarction and leptomeningeal artery atherosclerosis has been noted in a series of brains examined by Fisher.17 In approximately 50 percent of the brains with lacunar infarction, surface vessel atherosclerosis was noted.

Two of our patients had diabetes mellitus which might also be a common pathogenetic mechanism shared by leptomeningeal artery atherosclerosis and the vessel involvement responsible for lacunar infarction. An increased incidence of lacunar infarction has been noted in patients with diabetes mellitus, even when the contribution of hypertension is neutralized.28 However, diabetic patients appear to have a reduced incidence of intraparenchymal hemorrhage.
Finally, we found a paucity of atherosclerosis in the vessels of the circle of Willis and in the extracranial carotid arteries despite the extensive intracranial small vessel involvement of our patients. This somewhat surprising disparity between intraparenchymal and large artery changes has been noted previously. While there is an association between large vessel atherosclerosis and hypertension, an even stronger association exists between arteriolar level disease and hypertension. It may be possible to draw a distinction between those cerebrovascular disorders which are closely linked to hypertension — leptomeningeal artery atherosclerosis and intraparenchymal artery disease, such as segmental arterial disorganization and microaneurysm formation — and those that are weakly associated, namely atherosclerosis of the extracranial carotid vessels and circle of Willis. Like hypertension, hyperlipoproteinemia may also be associated differently with large and small vessel disease; one recent study showed an increased incidence of hyperlipoproteinemia in extracranial atherosclerotic disease compared to its occurrence in "intracranial small-vessel" disease.

In summary, analysis of the clinical and pathological features of a group of patients with angiographic leptomeningeal artery atherosclerosis suggests that such involvement may be another sequela of hypertension and/or diabetes mellitus. The involvement does not appear to produce a characteristic clinical syndrome in and of itself, but there may be utility in recognizing the entity because it appears to be allied with other hypertensive cerebrovascular sequelae such as lacunar infarction and intraparenchymal hypertensive hemorrhage. Furthermore, in its angiographic appearance it may suggest cerebral inflammatory arteriopathy and should be excluded before corticosteroid treatment for the latter is initiated.

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