Case Report

Neuroimaging Demonstration of Evolving Small Vessel Ischemic Injury in Cerebral Amyloid Angiopathy

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Background and Purpose—Cerebral amyloid angiopathy is a small to medium vasculopathy most commonly associated with symptomatic intracerebral hemorrhage and microbleeds.

Summary of Case—We present a patient with cerebral microbleeds and likely amyloid angiopathy with evolving ischemic lesions visualized on diffusion-weighted imaging.

Conclusions—This case captures with serial MRI the evolving and dynamic nature of cerebral amyloid angiopathy and particularly illustrates the subclinical, yet progressive, ischemic aspects of this vasculopathic process. (Stroke. 2009;40:e675-e677.)

Key Words: amyloid angiopathy n cerebrovascular disease

Cerebral amyloid angiopathy (CAA) is a small to medium vasculopathy involving deposition of β-amyloid within the vessel wall of the brain and the leptomeninges. Amyloid deposition occurs predominantly in the cortical vessels, leading to effacement of the smooth muscle cells and, ultimately, weakening of the tunica media and adventitia, often resulting in symptomatic intracerebral hemorrhage. Gradient-echo MRI studies frequently demonstrate a pattern of lobar microbleeds in patients with CAA.1 In addition, small vessel ischemic disease has also been described to frequently occur in the setting of CAA but has been less well-characterized.2 We present a case that captures with serial MRI the evolving and dynamic nature of CAA and, in particular, illustrates the subclinical, yet progressive, ischemic aspects of this vasculopathic process.

Clinical Summary
A 61-year-old man with hypertension and chronic renal insufficiency presented with acute left face, arm, and leg weakness. No seizure activity was noted. On presentation, his blood pressure was 224/116 mm Hg. He was alert, awake, and able to follow simple commands. He had a right gaze preference, left central seventh cranial nerve palsy, and left hemiparesis with no ataxia. His total NIHSS score was 14. Baseline MRI demonstrated an acute right frontal hematoma in the setting of multiple cortical lobar microbleeds with right hemisphere parieto-occipital predominance, as well as a chronic left parietal hematoma (Figure 1). Of note, no deep microbleeds were observed. The entire diffusion-weighted imaging was negative for any ischemic lesions remote from the hematoma. MRA showed no significant intracranial or extracranial stenosis. Basic laboratory studies were remarkable only for hyperlipidemia (total cholesterol, 221; low-density lipoprotein, 143). Complete blood count and coagulation studies were within normal limits. The patient was enrolled in a natural history, serial MR imaging, observational study approved by the institutional review board. All images were acquired on a 3.0-T clinical MRI scanner. The MRI protocol included gradient-recalled echo, diffusion-weighted imaging/apparent diffusion coefficient, fluid-attenuation inversion recovery, contrast-enhanced MRA (baseline study only), and T1-weighted sequences. The imaging studies were performed at baseline and days 2, 4, 30, and 90.

These follow-up imaging studies showed several areas of new ischemia over time on diffusion-weighted imaging, including a new right frontal ischemic lesion at day 2, and a new right temporal lesion at day 30 (Figures 2 and 3). Subsequent work-up to rule out other etiologies included negative urinary toxicology screen, negative hypercoagulable work-up, as well as negative transthoracic and transesophageal echocardiograms. Statin therapy was initiated during the acute hospital admission and antiplatelet therapy was initiated 1 month after presentation.

Discussion
Cerebral amyloid angiopathy is estimated to be responsible for ≈5% to 20% of nontraumatic intracerebral hemorrhages and 30% of lobar hemorrhages.3 Whereas CAA may be asymptomatic, a classic clinical presentation is lobar hemorrhage, often recurrent or multifocal, in an elderly individual. Less commonly, patients may present with TIA or other
ischemic stroke-like episodes, seizures, or dementia involving a spectrum of cognitive decline.4

In the past decade, neuroimaging studies, particularly MRI, have played an increasingly important role in the diagnosis and understanding of the pathophysiology of CAA.5 Specifically, gradient-recalled echo sequences have documented the occurrence, frequency, and distribution of microbleeds. Multiple lobar microbleeds, particularly in the absence of deep microbleeds and an alternative cause (eg, hypertension, CADASIL), are now considered a radiological hallmark of CAA.1

An additional MRI technique, diffusion-weighted imaging, has offered the ability to identify ischemic lesions. These may be clinically symptomatic ischemic strokes, or small ischemic lesions that do not reach the threshold of clinical symptomatology. Some researchers have identified a more definitive relationship between lacunar stroke and microbleeds, with clinico-radiographic data suggesting a potential association at the level of the microvasculature. However, these findings are not specific to CAA.6

In fact, the frequency and continuum of ischemic events in CAA has not been fully characterized and is likely underappreciated. This may be attributable to a combination of factors, including the more slowly progressive and less severe (or asymptomatic) nature of small vessel ischemic events, in contrast to the more dramatic presentation of lobar hemorrhage. One recent article7 documented diffusion-weighted imaging lesions in 15% of living CAA patients. Our report complements this work by demonstrating a temporal evolution and time course of lesion development. In this recent CAA study, the presence of diffusion-weighted imaging lesions was not associated with the severity of white matter disease. Despite the fact that numerous studies have demonstrated an important association between CAA and leukoaraiosis, the nature of this association is not well-understood.8 However, the data available to date do suggest that small vessel ischemia, including both cortical and subcortical events, contributes to dementia and cognitive decline in CAA.9,10

Our patient presented with a classical neuroimaging picture of CAA—lobar hemorrhage in the setting of multiple lobar microbleeds with an occipital predominance. This appearance is consistent with probable CAA by the Boston Criteria for diagnosis of CAA-related hemorrhage in that additional work-up did not reveal any alternative etiology for lobar hemorrhage (eg, coagulopathy, tumor, malformation, vasculitis).11 By performing serial diffusion-weighted imaging studies at later time points, we were able to document the occurrence of ongoing clinically silent ischemic events that would have gone otherwise undiagnosed.

It is possible that hypertension and hyperlipidemia contributed to the underlying arteriopathy despite the imaging appearance consistent with CAA. Classically, the imaging appearance of primary intracerebral hemorrhage has been dichotomized into hypertensive and CAA classifications. However, it seems likely that multiple disease processes influence the development of cerebral arteriopathy in many patients. Further research is needed to refine our understanding of intracerebral hemorrhage risk factors and their complex interplay; it may be important to reframe our thinking from 2 dichotomous etiologies (CAA vs hypertension) to embrace a spectrum of causative factors.

Whereas no primary treatment is presently available for CAA, the prevalence and frequency of clinical and subclinical ischemic events may play an important role in determining secondary prevention strategies in the setting of acute CAA-related intracerebral hemorrhage, particularly when additional vascular risk factors are present. Further studies are needed to understand the role of antiplatelet therapy and other
treatment approaches in these circumstances, and to determine whether risk of new intracerebral hemorrhage outweighs risk of ongoing ischemic events.

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Disclosures
None.

References
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