EDITORIAL

Acute Retinal Arterial Ischemia: An Emergency Often Ignored

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ETINAL ARTERIAL ISCHEMIA, WHETHER TRANSIENT or permanent, is a form of anterior circulation ischemic stroke caused by decreased blood flow in the ophthalmic branches of the internal carotid artery. Transient ischemic attack (TIA), including transient monocular visual loss (so-called retinal TIA or amaurosis fugax), is well known to be a prodromal syndrome of ischemic stroke. Indeed, a TIA is a medical emergency associated with a high risk of early ischemic stroke and other cardiovascular events. Among patients with TIA, 10% to 15% have a stroke within 90 days, with approximately half occurring within 48 hours.² Individuals who have had a TIA and survive the initial high-risk period have a 10-year stroke risk of approximately 19% and a combined 10-year stroke, myocardial infarction, or vascular death risk of 43% (4% per year). These findings highlight the need for the urgent referral of patients with TIA and acute ocular and cerebrovascular events so that they can access expert evaluations and immediate treatment.

The current trend is to consider TIA and acute ischemic stroke on the same spectrum of serious conditions involving brain and eye ischemia, just as angina and acute myocardial infarction are part of the continuum of acute coronary syndromes.^{3–7} Therefore, it is not surprising that the definition of TIA has evolved from a purely time-based definition to a tissue-based definition. Until recently, patients with spontaneously reversible acute visual loss or neurologic deficits were considered to have a TIA if the deficit lasted less than 24 hours.^{3,6} The new definition of TIA includes the absence of ischemia on funduscopic examination and on brain magnetic resonance imaging (MRI) performed with diffusion-weighted imaging, and describes TIA as "a transient episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischemia without acute infarction." This newly proposed definition of TIA by the American Heart Association implies that a brain MRI with diffusion-weighted imaging be performed immediately on all patients with suspected TIA, including patients with apparently isolated retinal ischemia.

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Over the past decade, a great deal of data has emerged in the neurologic and emergency medicine literature regarding the need to evaluate and manage immediately and aggressively all patients with acute cerebral and ocular ischemia. This has resulted in major international guidelines from the American Heart Association, 5,6 National Stroke Association, 4 and numerous other international organizations.7 These guidelines recommend that all patients with presumed retinal ischemia (whether transient or permanent) undergo urgent brain imaging and etiologic testing similar to patients with cerebral ischemia. According to these guidelines, patients with abnormal diffusion-weighted MRI are diagnosed as having an acute stroke (and admitted to the hospital and managed accordingly) regardless of their initial clinical presentation, whereas those with normal MRI results usually are evaluated within 24 hours in a dedicated TIA clinic, an emergency department observation unit, or a stroke center.²⁻⁷ This is not routinely performed currently in the United States, where a large majority of patients with acute retinal arterial ischemia are never sent to the emergency department or a stroke neurologist for immediate evaluation.8 Additionally, most health professionals and the public consider retinal TIAs benign with a low risk of subsequent stroke. This is incorrect, and such belief only delays the evaluation of patients with visual loss as the main symptom of retinal or cerebral ischemia. A study from 1995 emphasized that the average time of delay from the onset of TIA to treatment was much longer for patients with retinal TIAs than for patients with cerebral TIAs (48.5 vs 15.2 days).¹⁰ The same was observed recently in a series of patients with carotid stenosis whose surgery was delayed when the symptom was a retinal TIA.¹¹ The North American Symptomatic Carotid Endarterectomy Trial showed a high-risk of recurrent TIAs or stroke after a first retinal TIA, with up to 24.2% of retinal TIA patients having had a stroke at 3 years. 12 However, because this risk was still lower than that for patients who had a cerebral TIA, emphasis was placed on the relatively "good" prognosis of retinal TIAs compared with cerebral TIAs, contributing to the misconception that retinal TIAs are relatively benign.

Following the most recent guidelines from the American Heart Association, a study from Boston published in 2012 showed that retinal arterial ischemia (both transient and permanent) carries the same overall poor vascular prognosis as cerebral ischemia.¹³ The authors evaluated

129 patients with permanent or transient retinal ischemia similarly to acute ischemic stroke patients and showed that 1 of every 4 patients with acute retinal ischemia had acute brain infarctions on diffusion-weighted imaging. The probability of abnormal MRI results was higher in embolic versus nonembolic retinal ischemia (28% vs 8%) and in permanent visual loss patients versus retinal TIA patients (33% vs 18%). All patients with abnormal diffusion-weighted imaging (even when neurologically asymptomatic) were managed as having had a stroke according to the newest guidelines. These infarctions typically were small and often multiple, frequently occurred in the hemisphere ipsilateral to the involved eye, and tended to remain asymptomatic. Importantly, these infarctions indicated a high risk of having a major cause of retinal TIA, and therefore were associated with a worse prognosis. The authors emphasized the need for emergent workup and treatment of all patients with acute retinal ischemia in a specialized center. However, although this important study was published in a major neurology journal, it has remained largely unnoticed by eye care providers. In this issue of the Journal, Lee and associates report strikingly similar results in a cohort of 33 Korean patients with central retinal artery occlusion and branch retinal artery occlusion. 14 All patients underwent diffusion-weighted MRI of the brain within 7 days of visual loss. Acute cerebral infarctions were observed on MRI in 8 (24.2%) patients (5 of the 18 central retinal artery occlusion patients and 3 of the 15 branch retinal artery occlusion patients). These infarctions were always small and multiple, were ipsilateral to the involved eyes, and occurred in the same vascular territories. The presence of diffusion-weighted MRI abnormalities was correlated strongly with positive workup results for a major cause of

stroke such as a source of emboli, reinforcing the usefulness of immediate MRI in patients with retinal ischemia, even when apparently neurologically asymptomatic.

The management of retinal arterial occlusions and true vascular transient visual loss varies greatly depending on where and to whom they first present. Despite the lack of acute definite treatment for most patients with central retinal artery occlusion and branch retinal artery occlusion, such patients, as well as those with recent transient visual loss, must be seen immediately by an ophthalmologist (to rule out ocular causes of transient monocular visual loss and giant cell arteritis), before being referred emergently to a specialized center equipped with a stroke unit and expert physicians (most often to an observation unit affiliated with an emergency department where all necessary tests (including immediate brain MRI) and treatments can be performed 24/7). Outpatient testing or referral to the patients' primary care physician only delay appropriate management. Not surprisingly, one study from 2010 found that only 40% of 2975 patients with stroke or TIA used emergency medical services. Patients with visual changes were much less likely to call 911 than those with weakness, confusion, speech deficit, or dizziness. The article by Lee and associates confirms that patients with visual loss should be managed similarly to those with cerebral ischemia.¹⁴ Increased awareness of the dangers of retinal TIAs and permanent retinal ischemia should change the practice of eye care providers. The development of local networks prompting collaboration among optometrists, ophthalmologists, and stroke neurologists should facilitate such evaluations, whether in a rapid-access TIA clinic, an emergency department observation unit, or with hospitalization, depending on local resources.

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