Diagnostic Classification of Stroke, Especially Lacunes

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Evolution and Testing of the Lacunar Hypothesis" by Bamford and Warlow in this issue of Stroke reviews many important aspects of these unique pathologic vascular lesions. I concur with the authors' emphasis on the need to maintain homogeneity in the classification of stroke conditions, specifically lacunes. A stroke classification scheme would ideally be based on 1) risk factor profile such as hypertension, cardiac disease, and diabetes mellitus; 2) clinical features such as transient ischemic attacks (TIAs), time of onset of deficit, pattern of evolution of the deficit, and abnormal neurologic findings; 3) neuroimaging studies such as computed tomography (CT) and magnetic resonance imaging (MRI); 4) vascular anatomy determined by noninvasive carotid studies and angiography; 5) functional studies such as single-photon emission computed tomography (SPECT), positron emission tomography (PET), and xenon blood flow; 6) natural history such as clinical course and level of recovery; and 7) pathologic anatomy. This scheme of stroke classification would make it possible to devise therapeutic trials involving homogeneous groups of patients and would reduce the risk of two types of errors. One type of error occurs when a specific therapy is reported to be effective because the treated stroke population contained many patients with a benign natural history who would have done well even if they had received no specific treatment. The second type of error occurs when a therapy is reported to be ineffective because the treated stroke population was so large and diverse that one or more homogeneous subgroups in which the treatment was effective were not identified.

Many reports have described the "lacunar syndromes" as having nonischemic or even nonvascular etiologies including intracerebral hemorrhage, subdural hematoma, neoplasm, and infectious-inflammatory conditions. The list of nonischemic etiologies continues to proliferate, demonstrating the need for careful neurodiagnostic evaluation of each patient. It is crucial to exclude patients with nonischemic etiologies to determine accurately the natural history of cerebral lacunes of ischemic etiology. The potential for misdiagnosis has become less of a problem with CT and MRI, but lacunes are still best delineated on autopsy rather than with neuroimaging studies. Lumbar puncture in the evaluation of stroke patients has become neglected in this neuroimaging era. However, with our changing spectrum of neurologic illnesses including neurosyphilis, neurocysticercosis, vasculitis secondary to bacterial meningitis, and now acquired immunodeficiency syndrome, cerebrospinal fluid analysis has become especially important.

The most common lacunar syndrome caused by a nonischemic etiology is "pure motor hemiparesis." There are wide variations in the definition of this condition, with the most common patterns of motor weakness syndromes being face-arm-leg or arm-leg with facial sparing. The clinician must exclude patients with additional findings such as denial symptoms indicative of a parietal lesion, language dysfunction, hemianesthesia, homonymous hemianopsia, or atypical motor distribution. It would be most unusual for cortical ischemia to cause lacunar syndromes. When neuroimaging studies show a cortical infarct in a patient with a clinical lacunar syndrome, it is probable that the "lacunar syndrome" is caused by a small deep infarct not visualized by the neuroimaging studies; the cortical infarct is an epiphenomenon or a manifestation of cerebral infarction rather than the cause of the lacunar syndrome. It is important to recognize the limitations of CT/MRI in determining the age of a cortical infarct or a cerebral lacune. In certain cases, the diagnosis of "ischemic infarct of indeterminate age" is the best that can be established by neuroimaging studies. It is also important to stress that CT/MRI are not adequate strategies to study the pathologic process that underlines lacunes but are only convenient ways to study the clinical effects of lesions of varying sizes and locations. A strategy for therapeutic intervention in patients with lacunes depends on a knowledge of the underlying vascular pathophysiologic disturbance.

Most patients with lacunar stroke have been reported to have systemic arterial hypertension and/or diabetes mellitus although CT studies have
recently reported a lower incidence of hypertension than previously thought. Hypertension and chronic hypertensive vascular change may define a specific subgroup that differs from other patients with lacunes. Assessment of the patient’s clinical characteristics, such as length and duration of the hypertension, type of antihypertensive medication used, and the presence of chronic hypertensive vascular disease, may differentiate these patients. It is important to assess the presence of the signs of chronic hypertensive vascular disease including hypertensive retinopathy determined by clinical examination, funduscopy, and fluorescein angiography; left ventricular hypertrophy determined by electrocardiography or echocardiography; and cardiomegaly determined by chest radiography. Diabetes mellitus is a risk factor for small-vessel, arteriolar disease and thereby possibly for lacunar stroke. Our preliminary data indicate that diabetes associated with hypertension is a major risk factor but maybe not an independent risk factor for lacunar infarction. The roles of hypertension, diabetes, and chronic hypertensive vascular disease in lacunar stroke will be determined by the findings of the large stroke data banks.

It has been reported that TIA’s precede 20% of lacunar strokes compared with a 50% incidence for large-vessel, atherosclerotic disease. If we consider microatheroma with embolism to be a major mechanism of arteriolar occlusion in lacunes, the incidence of TIA is expected to be closer to that of atherosclerotic disease. Bamford and Warlow indicated that potential cardioembolic sources are uncommon in patients with lacunar stroke. In patients with CT-documented basal ganglia infarcts due to cardiac embolism, the clinical deficit was more extensive than would be expected with lacunes, and CT showed a “giant” or “mega-lacune.” These giant lacunes may differ from the smaller ones seen in hypertensive patients without a potential cardiac source of embolus or atherosclerotic disease. It is important to define these different types of patients with lacunes to determine appropriate management strategies.

The problem of the sensorimotor lacunar stroke syndrome requires clarification. If the term “lacune” is used to describe small deep infarctions due to occlusion of a single penetrating vessel, it is unlikely that sensorimotor stroke is usually due to a lacune. The lenticulostriate vessels supplying the internal capsule are branches of the middle cerebral artery, whereas the thalamoperforating vessels are branches of the posterior cerebral artery. The blood supplies to the internal capsule and thalamus are therefore usually separate. With variations in the blood supply to those regions, it is possible, but uncommon, for sensorimotor stroke to be caused by a lacunar infarct. In many of our patients with sensorimotor stroke, neuroimaging studies have shown giant lacunes, which are more likely due to cardiac sources of embolus or atherosclerotic disease. It seems likely that the underlying arteriopathy of most cases of sensorimotor stroke is different from that of lacunar stroke syndromes due to arteriolar disease. Studies that include many patients with sensorimotor syndromes as examples of lacunar infarcts are likely to have a heterogeneous population and thus reduced accuracy of data concerning the natural history of lacunar stroke.

Hypertension is a major risk factor for stroke because it predisposes patients to intracranial hemorrhage and accelerates atherosclerosis to cause ischemic stroke. Lacunar infarction is believed to result from chronic hypertensive disease affecting the arterioles that are 50–400 μm in diameter located in specific deep brain regions. The arteriolar lesions most commonly seen in patients with lacunes are microatheroma and lipohyalinosis. If microatheroma is the predominant vascular lesion, it is probable that atherosclerotic disease initially involves large vessels and later the small vessels, possibly by artery-to-artery embolus. If lipohyalinosis is the underlying pathologic vascular lesion, a qualitatively different type of arteriopathy is involved in the pathogenesis of lacunes. It has been noted by Fisher that the severity of atherosclerosis in extracranial and intracranial vessels parallels the number of lacunes. In a review of lacunar stroke, Miller reported the incidence of extracranial carotid stenosis in selected patients with lacunes, but the results varied widely depending on selection criteria. In patients with giant lacunes, the incidence of extracranial carotid angiographic abnormalities or detection of cardiac sources of embolus would be increased. These patients with giant lacunes should therefore be investigated for potential cardiac sources of embolus or have angiography to detect possible surgically correctable carotid disease, but these studies are not warranted for subgroups of patients with hypertension and chronic hypertensive vascular disease. The clinical features of these lacunar subgroups must be recognized before treatment strategies for reduction of cerebrovascular complications can be planned.

In the Oxfordshire Community Stroke Project, a recurrent stroke occurred within 12 months in 11.8% of the patients with lacunar infarction; this rate is similar to that for other stroke disorders. There is no information indicating whether these recurrent strokes were lacunes or other types of ischemic stroke.

We studied 16 patients with CT evidence of a single lacune who were asymptomatic for cerebrovascular disease. During 36 months, these patients had a high incidence of cerebrovascular and cardiovascular disease. Seven developed a clinical lacunar stroke syndrome in a distribution different from the initial asymptomatic lesion, three developed a cerebral hemispheric stroke, two had a myocardial infarction, and one died suddenly of an unknown cause. These patients had systemic arterial hypertension with a high incidence of chronic hypertensive vascular complications (75% had cardiographic...
evidence of left ventricular hypertrophy, 63% had radiographic cardiomegaly, and 63% had clinical hypertensive retinopathy). The lacunes were located in the internal capsule, corona radiata, basal ganglia, or thalamus; were <12 mm in size; and were seen on a single 10-mm tissue section. We hypothesize that these lacunes were due to a hypertensive small-vessel arteriopathy. No patient had TIAs, which are more common with atherosclerotic disease. Since it is not known whether antiplatelet treatment would be beneficial in altering the natural history of lacunar stroke, further studies may be warranted to determine if antiplatelet treatment or other stroke prevention therapies are recommended in these or other patients with lacunes.

In other patients, neuroimaging (CT/MRI) evidence of lacunes indicate cerebral infarction with transient signs (CITS). These patients have angiographically demonstrable carotid artery atherosclerotic disease, and the location of the lacune adequately explains the clinical stroke features. It is important to study such patients with SPECT or PET to determine the exact mechanism of the impaired neurologic function. If the carotid lesion is the underlying cause of the neurologic disorder, it is likely that the cortical and subcortical regions will show an abnormality. However, CT/MRI studies might show only a lacunar lesion because of the adequacy of the collateral supply of blood to the cerebral hemispheres compared with the subcortical region, which contains mostly end-arteries. In one report of patients with CITS, only three of five were hypertensive; two were normotensive. In these patients with lacunes, it would be important to determine if treatment should include carotid endarterectomy, anticoagulants, or antiplatelet medication. The unanswered question is whether the angiographically detected carotid lesion directly caused the clinical deficit and the underlying lacune or whether it represents only atherosclerotic disease. In the latter case, the underlying causal arteriopathy of the clinical deficit may involve the small (50–400 μm) vessels. The natural history of clinical outcome and stroke recurrence in patients with CITS must be ascertained to determine if they differ from those with other forms of ischemic stroke.

With the development of multicenter stroke data banks and increasing use of SPECT and PET, we hope to have a better understanding of the entity classified as lacunar infarction. However, until neurologic investigators have a probe or a technique to visualize small intracranial vessels, the underlying arteriopathy of lacunar infarction will remain elusive. Without autopsy confirmation of lacunar stroke, the actual pathologic features of the "holes in the brain" visualized by CT/MRI will continue to elude us.

References

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