A Radiologic Study of Dynamic Processes in Lacunar Dementia

Yasufumi Tanaka, MD, Osamu Tanaka, MD, Yoshikuni Mizuno, MD, and Mitsuo Yoshida, MD

Using magnetic resonance imaging and digitized brain computed tomography, we evaluated 33 elderly patients with documented lacunar stroke and divided them into three groups (non-demented, n=15; borderline, n=9; and demented, n=9) by neuropsychological assessments and DSM III criteria. We evaluated the extent of white matter lesions and the degree of atrophy of specific anatomic structures, such as the corpus callosum, using magnetic resonance imaging and quantified the volumes of the ventricles, the subarachnoid spaces, and the brain parenchyma using digitized brain computed tomography. Our results show that both borderline and demented patients had significantly more extensive white matter lesions than non-demented patients, indicating a significant relation between the extent of white matter lesions and intellectual decline. In addition, borderline and demented patients had significantly larger ventricles and more brain atrophy than non-demented patients; demented patients also had significantly larger subarachnoid spaces than non-demented patients and more brain atrophy than borderline patients. Our findings suggest that in most patients with lacunar stroke, periventricular and subcortical white matter lesions with subsequent white matter atrophy first induce ventricular enlargement, followed by generalized brain atrophy, resulting in dementia. (Stroke 1989;20:1488-1493)

Vascular dementia and dementia of the Alzheimer type are two main types of dementia. Vascular dementia can be divided into three major subgroups: multiple discrete strokes following thrombotic or embolic occlusion of large cerebral arteries (multi-infarct dementia); multiple, small, deep subcortical lacunar infarcts, mostly located in the anterior and middle cerebral artery distributions (the lacunar state or lacunar dementia); and subcortical arteriosclerotic encephalopathy (Binswanger's disease) attributed to arteriosclerosis of the long penetrating cerebral arteries, arterioles, and capillaries. However, it is very difficult to distinguish the lacunar state type from the Binswanger type of vascular dementia on the basis of clinical or radiographic features, and some investigators claim that the clinical and the pathologic features of these disorders are identical.

Recently, with the advent of high-resolution computed tomography (CT) and magnetic resonance imaging (MRI), periventricular white matter lesions traditionally associated with Binswanger's disease are being recognized with increasing frequency. Several studies indicate that these lesions are more common in the elderly and in hypertensive individuals. However, the association of these lesions with intellectual impairment remains uncertain.

We performed MRI on 33 elderly patients with lacunar stroke to determine whether there is a relation between white matter lesions and intellectual impairment. Using digitized brain CT, we also quantified the volumes of the ventricles, the subarachnoid spaces, and the brain parenchyma.

Subjects and Methods

We studied 33 patients who had a history of lacunar stroke, a clinical picture consistent with one of the classic lacunar syndromes described by Fisher, and CT and/or MRI evidence of lacunar infarcts that appeared responsible for the symptoms. All patients had an ischemic score of >7 according to Hachinski et al. All 33 patients had >6 years of education and no history of alcohol or drug abuse; renal, hepatic, or pulmonary disease; or heart failure.

For controls, we studied 10 men and two women with no history of neurologic disorders or alcoholism in the same manner as the patient group, except that MRI was not performed. The mean±SEM age and years of education of the controls was 67.4±4.3
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Results

Patients were classified as demented if they satisfied all DSM III criteria for dementia and if they performed abnormally on both assessment instruments (a score of ≤23 on the MMSE and identification of three categories on the WCST). Patients who did not satisfy all DSM III criteria for dementia but who had abnormal scores on one assessment instrument were identified as borderline. Non-demented patients were those who failed to meet DSM III criteria and who scored within the normal range on both assessment instruments. In our series of 33 patients, nine were demented, nine were borderline, and 15 were non-demented. No significant differences were found between the controls and any patient group with respect to mean age or years of education, or between patient groups with respect to mean age, sex, mean years of education, or the presence of risk factors for stroke such as hypertension and diabetes mellitus (Table 1).

On MRI, both borderline and demented patients showed significantly more extensive white matter lesions (Figure 3) than non-demented patients. In addition, demented patients had significantly more extensive atrophy of the corpus callosum than non-demented or borderline patients (Figure 3).

Digitized brain CT showed that both borderline and demented patients had significantly larger ventricles than non-demented patients. In addition, demented patients had significantly larger subarachnoid spaces than non-demented patients. Furthermore, brain atrophy was significantly more marked in borderline than in non-demented patients and in demented than in borderline patients (Figure 3).

Discussion

The association of white matter lesions with intellectual impairment is controversial. Some investigators have suggested a close correlation, whereas others have found no difference in the severity of white matter lesions between non-demented and demented patients. Our results support the former view in that both borderline and demented patients had significantly more extensive white matter lesions than non-demented patients. Such differing results may be due to methodologic problems that occur in the assessment of intellectual function or in the grading of white matter lesions.

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On digitized brain CT, we also found that both borderline and demented patients had significantly
FIGURE 1. Examples of white matter lesions on magnetic resonance imaging (spin-echo sequence). Grade 1: linear areas of high intensity along margin of ventricles; Grade 2: narrow halo of high intensity surrounding lateral ventricles, with discrete, patchy, high-intensity areas in subcortical white matter beside or above lateral ventricles; Grade 3: more extensive, confluent foci forming multiple large patches of high intensity in subcortical white matter beside and above lateral ventricles; and Grade 4: marked thick, irregular bands completely encasing lateral ventricles.

enlarged ventricles and significantly more extensive brain atrophy than nondemented patients. In addition, demented patients had significantly larger subarachnoid spaces than nondemented patients and significantly more extensive brain atrophy than borderline patients.

FIGURE 2. Examples of atrophy of corpus callosum on magnetic resonance imaging (inversion-recovery sequence). Grade 1, normal size or mild atrophy; Grade 2, moderate atrophy; and Grade 3, severe atrophy.
TABLE 1. Clinical Profiles of 33 Patients With Lacunar Stroke

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Taken together, these findings suggest that, in most patients with lacunar stroke, periventricular and subcortical white matter lesions play a significant role in the progression of intellectual decline and that white matter atrophy, secondary to white matter lesions, first induces ventricular enlargement, then generalized brain atrophy, resulting in dementia.

However, we also noticed that some demented patients did not have these typical radiographic changes but, rather, had relatively mild periventricular white matter lesions and/or brain atrophy. In such demented patients, the most salient finding on MRI was atrophy of the corpus callosum. However, the role of this structure in cognition is controversial. Callosectomy does not produce a clini-
cal state of dementia⁴³-⁴⁶ so that it is unlikely that callosal atrophy is the primary cause of vascular dementia. Rather, atrophy of the corpus callosum is probably a secondary change due to lesions in the cerebral hemispheres.

All of our demented patients exhibited more or less extensive subcortical white matter lesions immediately above the lateral ventricles. This subcortical white matter region probably corresponds to that underlying the cingulate gyrus. Since this region is close to the corpus callosum, lesions here, even if not too widespread, would cause more extensive callosal atrophy than lesions in other areas. Based on an autopsy study on 700 patients with documented ischemic strokes, Kameyama⁴⁷ indicated that patients with lesions involving the white matter underlying the cingulate gyrus and the anterior corpus callosum were significantly more demented than patients without such lesions. This suggests that involvement of specific anatomic structures, such as the cingulate gyrus and the underlying white matter, play an important role in the progression of intellectual deterioration.

A relation between callosal degeneration and dementia has also been reported in patients with multiple sclerosis.⁴⁸,⁴⁹ Thus, the presence of callosal atrophy as well as white matter lesions on MRI should alert physicians to the possibility of dementia, especially in patients with lesions in the deep white matter.

Finally, white matter changes similar to those in our patients, designated “leuko-araiosis” by Hachinski et al.,⁵⁰ have also been described recently in patients with dementia of the Alzheimer type.¹⁸,²¹,²²,²³,²⁸,³⁹,⁵¹-⁵⁵ although the lesions were not as pronounced as those in vascular dementia.³⁸,³⁹ The pathogenesis and clinical significance of these lesions remain uncertain.⁵² Recently, Steigart et al.⁵³ indicated a highly significant trend for the association of leukoaraiosis with increased dementia scores in cases of early Alzheimer’s disease. These patients may also show atrophy of the corpus callosum. Further accumulation of relevant data is necessary to clarify these points.

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Key Words • dementia, multi-infarct • lacunar infarction • magnetic resonance imaging
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