Urinary and Gait Disturbances as Markers for Early Multi-Infarct Dementia

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In a retrospective study of 84 outpatients with multiinfarct dementia, urinary and gait disturbances were found in 50% and 27%, respectively, and often preceded dementia and discrete stroke-like episodes by more than 5 years. Compared to patients without urinary disturbance, those with urinary dysfunction were predominantly male and more behaviorally impaired, but were similar in age, cognitive score, depression score, computerized tomography findings, and relative survival. Compared to patients without gait disturbance, those with gait abnormality had a higher Hachinski ischemic score and depression score and were more behaviorally impaired. Urinary and gait abnormalities may be markers for cerebrovascular disease and vascular dementia even in the absence of frank stroke. Damage to bifrontal outflow tracts may be the common pathophysiological mechanism underlying the behavioral and motor symptoms characteristic of vascular dementias.

(Stroke 1987;18:138-141)

MULTIINFARCT dementia (MID) is the loss of cognitive function secondary to multiple small and/or large cerebral infarcts. 1,2 A progressive illness with uniformly poor prognosis,3 MID may account for approximately 20% of all organic dementias.4 There is presently no accepted treatment for this disease, but there is some rationale for the prevention of MID via the control of risk factors for stroke and by the prophylactic administration of aspirin to patients at risk. Identification of clinical markers for early MID might allow early recognition of high-risk groups so that prophylactic treatment might prevent or delay the development of this fulminant disorder.

We therefore examined the prevalence of various risk factors for stroke and vascular disease in our patients with clinical MID. Patients with MID may have a long history of gait or urinary disturbances preceding overt dementia and discrete cerebrovascular events, and we sought to investigate this relation in a retrospective series.

Subjects and Methods

The Geriatric Evaluation Service at The Burke Rehabilitation Center in White Plains, New York, is an outpatient dementia clinic that has studied more than 700 patients over the last 6 years, as described previously.5 All patients had a complete medical, neurological, psychiatric, and neuropsychological evaluation, with laboratory work, brain computerized tomography (CT), and EEG to rule out treatable causes of dementia. Of these patients, 84 had a clinical diagnosis of MID based on the presence of typical features6 and a modified Hachinski score7 of ≥ 6. Patients thought to have a mixed dementia or a multiinfarct state coexistent with Alzheimer's disease were excluded, as were patients with dementias of other etiologies such as head trauma, alcohol abuse, or metabolic encephalopathies. Each patient's record was reviewed for 1) risk factors for and manifestations of vascular disease, 2) family history of hypertension, diabetes mellitus, coronary artery disease, myocardial infarction, and cerebrovascular accident, 3) manifestations of cerebrovascular disease such as stroke, carotid disease or surgery, and transient ischemic attacks (TIA's), 4) neurologic history and examination, 5) scores for ischemic dementia (modified Hachinski score8), cognitive impairment ("mental status quotient"), behavioral impairment (Haycox score9), and depression (Hamilton score), and 6) brain CT findings.

Subgroups with urinary and/or gait disturbances were identified. Urinary disturbance was defined as incontinence, frequency, and/or urgency; gait disturbance was defined as mild-to-severe hemiparetic, Parkinsonian, ataxic, or senile gait, i.e., a short-stepped, narrow-based, slightly spastic gait with a shuffling or "glue-footed" quality. No patient suffered from ataxia on a peripheral, afferent basis. Cognitively intact subjects (n = 36) of similar age and sex composition were studied for evidence of urinary disturbance. These subjects were referred to our clinic for evaluation of prescriptive cognitive impairment but were found to be cognitively intact on detailed neuropsychological evaluation. Differences between groups were examined using the unpaired t test and chi-square, with Yates' correction for cell sizes less than 5.

Survival curves for the patients with MID with and without urinary disturbance were based on follow-up information, including death date, obtained from caretakers by telephone interview at 6-month intervals. The cumulative proportion surviving from estimated
date of onset of dementia, based on relatives' estimates of duration of cognitive symptoms, was calculated using the actuarial method of life table analysis. Relative survival for each group was calculated by dividing actual survival at each time point by expected survival of an age-, race-, and sex-matched control group, using 1978 United States census data survival tables.

Results
The mean age (± SEM) of the patients with MID was 76.0 ± 0.9 years. There were 47 males and 37 females. Common risk factors for vascular disease included hypertension (55%), smoking history (46%), diabetes mellitus (27%), symptomatic cardiac disease (25%), peripheral vascular disease (21%), and myocardial infarction (16%). Complete family histories were available in 61 patients; 46% of these had a family history of cardiovascular disease, and 16% of hypertensive disease. Discrete episodes compatible with stroke occurred in 56% of the patients, and 24% had TIA's. Only 8 patients (9.5%) had documented carotid disease (bruits on examination and/or Doppler/angiographic studies) or endarterectomy.

Urinary and gait disturbances frequently preceded overt dementia by more than 5 years. Urinary disturbances were present in 42 patients (50%). In 10 of 42 patients (24%), urinary symptoms predated the clinical diagnosis of MID by 5 years or more. At least 16 of 42 (38%) had urinary symptoms predating a discrete stroke-like episode. Gait disturbances were found in 23 patients (27%), of which 14 (61%) had gait disturbances preceding overt dementia by 2 years or more, and 15 (65%) also had urinary symptoms.

Among the patients nearly three times as many men (n = 24) as women (n = 11) had abnormal urinary function. Even though 20 of these men had been diagnosed with benign prostatic hypertrophy, urinary symptoms persisted after prostatectomy. Four female patients had urinary tract infections. Eighteen patients, or 21% of all patients with MID, had urinary symptoms not explained by urological disease. Half of these patients belonged to the group with urologic complaints prior to a discrete stroke-like episode.

Of 36 cognitively intact controls (mean age 72 ± 2, male:female 24:12) 2 had a history of urinary complaints. Men (n = 9) outnumbered women (n = 3) by 3:1. Five of the 9 men had prostatectomies and were asymptomatic at evaluation or had prostatic enlargement on examination. The other 4 had a history of diuretic use or urinary tract infections explaining their symptom of urinary urgency. The 3 women had histories of multiple urinary tract infections. Thus, all urinary symptoms in cognitively intact controls could be explained by urological disease.

Compared to patients with MID without urinary dysfunction, those with urinary dysfunction were predominantly male and more behaviorally impaired but were similar in age, cognitive score, depression score, and head CT findings. Their past medical history was significant for at least one of the following: hypertension, symptomatic cardiac disease, smoking, or diabetes mellitus. Compared to patients without gait disturbance, those with gait abnormalities had higher ischemic and depression scores and were more behaviorally impaired (Tables 1 and 2). CT scans were systematically reviewed for periventricular changes, but these were found in only 1 patient with both urinary and gait abnormalities. This patient had periventricular white matter hypodensities, suggesting multiple white matter strokes.

Relative survival was similar in patients with or without urinary disturbance (Figure 1). In both groups, survival was higher than expected, relative to controls, until 5–8 years after the estimated date of onset of dementia, when relative survival decreased in both groups (Figure 1).

Discussion
Our patients with MID had many of the risk factors associated with stroke. The Framingham Study cited age, hypertension, symptomatic cardiac disease, and
diabetes mellitus as leading contributors to stroke.11,12 More than half our patients had major episodes compatible with stroke, 55% had hypertension, and approximately 25% had symptomatic cardiac disease, diabetes mellitus, or TIA's. Since MID is thought to be caused by multiple large and/or small infarcts,12 it is expected that stroke and MID share common risk factors.

Urinary dysfunction often surfaced in the neurologic history many years before the diagnosis of MID or prior to a documented cerebrovascular accident. Urinary abnormalities were seen in 30% of women and 66% of men with MID. In contrast, only 25% of cognitively intact female controls and 37.5% of cognitively intact male controls had urinary abnormalities. Although the groups of women with and without MID did not differ significantly in percent of urinary disturbance, nearly all the demented women had no explanation for the urinary disturbance, whereas the cognitively intact women had urinary tract infections. Over 20% of the patients with MID, but no cognitively intact controls, had urinary symptoms unexplained by urologic disease. Gait disturbance was seen in 28% of the patients with MID, often 1–2 years before the diagnosis of overt dementia. There was no sex difference. One half of the patients with gait disturbance had concurrent urinary disturbance.

The early symptomatology of urinary and gait disturbance in these patients with clinically diagnosed MID is reminiscent of that found in most patients with normal pressure hydrocephalus and in up to one third of patients with subcortical arteriosclerotic encephalopathy orBinswanger's disease.13 The latter is linked to systemic hypertension and thought to be caused by white matter hypoperfusion secondary to local vasculopathy.14 The possibility of non-CT-imaged damage to periventricular corticospinal fibers can be raised. Only 1 patient displayed periventricular white matter hypodensities on CT scan. Although ventriculomegaly in most CT scans was not out of proportion to cortical atrophy, the CT scans were performed at the time of evaluation for overt dementia. It is possible that CT scans done earlier in the course might have revealed ventricular enlargement without cortical atrophy, suggesting early damage to periventricular bifrontal outflow tracts. It is equally possible that later scans might reveal periventricular white matter hypodensities, or that magnetic resonance imaging (MRI) may be a more sensitive way to detect periventricular abnormalities in these patients. In fact, a recent study of demented patients with subcortical ischemia documented white matter abnormalities on MRI.15 What, if any, overlap exists between these particular MID patients and those with the recently described symmetrical white matter disorder in dementia of the Alzheimer's type16 is unclear at present. Follow-up with postmortem data may prove enlightening.

Since only half of our patients had discrete stroke-like episodes, these patients meeting clinical criteria for MID may actually be suffering from periventricular leukoencephalopathy on a vascular basis, or from dementia caused by vascular disease by mechanisms that are not yet known. Thus, the term “vascular dementia” might be preferred to MID pending autopsy confirmation. In fact, a recent study in Finland found that only 8 of 19 patients with MID diagnosed by careful clinical criteria had infarcts at autopsy. The 11 patients without infarcts did not have pathological changes of Alzheimer's disease or other recognizable etiology for the dementia.17

Patients with urinary dysfunction in vascular dementia were more behaviorally impaired, and the patients with vascular dementia with gait dysfunction were more behaviorally impaired and more depressed than their counterparts without urinary or gait symptoms. The Haycox scores were predictably higher in patients with gait or urinary symptoms, given that the behavior scores include ratings for ambulatory status and bowel-bladder function. The higher ischemic score in patients with gait deficits again lent support to the link between gait disturbance and vascular factors. In fact, groups with urinary or gait disturbance suffered from at least one risk factor for stroke among hypertension, symptomatic cardiac disease, smoking, or diabetes mellitus, in declining frequency. Taken together, these findings suggest that ischemic damage to periventricular bifrontal outflow tracts may be a common pathophysiological mechanism underlying both the behavioral disturbance and the motor symptoms characteristic of vascular dementia. The emo-
tional lability and "pseudobulbar state" described in MID are not characteristic of Alzheimer-type dementia, which is usually devoid of motor findings until relatively late in the course. 18

Relative survival, compared to age-, sex-, and race-matched controls, was similar in patients with or without urinary disturbances. In fact, survival in both groups was higher than in population-based controls (relative survival > 1.0) until 5 years after the estimated date of onset of cognitive symptoms, perhaps indicating that vascular dementia has a very long natural history and is compatible with prolonged survival. Since history of gait and urinary disturbance may precede overt dementia by more than 5 years, the actual course of this disorder may be very long indeed. Clinical markers of early vascular dementia would therefore be particularly useful diagnostically and perhaps therapeutically.

Patients with a history of stroke, hypertension, and other markers of vascular disease such as symptomatic cardiac disease, smoking, or diabetes, may be at high risk to develop vascular dementia. Urinary and gait disturbances may be earlier and more sensitive markers for vascular dementia than even actual strokes, particularly in men. We recognize that this retrospective study does not discern how many patients with urinary and gait disturbances go on to develop MID. Prospective studies of urinary and gait disturbances as early markers for vascular dementia, and of the relative importance of vascular risk factors in developing dementia, are needed and are underway. Nevertheless, early recognition of urinary or gait abnormalities, especially in subjects with prominent markers of vascular disease, may help to identify groups at high risk not only for stroke but also for vascular dementia, whether on the basis of multiple infarcts or periventricular leukoencephalopathy. Aggressive control of hypertension and cardiac disease, the discontinuation of smoking, and perhaps prophylactic use of antplatelet agents in these vulnerable groups might delay, if not prevent, the development of vascular dementia.

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Key Words • multi-infarct dementia • vascular dementia • subcortical ischemia • Binswanger’s disease
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*Stroke*. 1987;18:138-141
doi: 10.1161/01.STR.18.1.138

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/18/1/138

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