Cerebrovascular Disease in Type 2 Diabetic Patients Without Hypertension

To the Editor:

The close relationship between diabetes mellitus and arteriosclerosis of the cerebral arteries has recently been reported. However, in these studies, the subjects included older patients with hypertension, which itself is a significant risk factor for arteriosclerosis of the cerebral arteries.1–3 Thus, previous studies on the effect of diabetes on the development of sclerosis were confounded by hypertension and aging. Therefore, we examined relatively young patients with diabetes mellitus who did not have hypertension in order to clarify the influence of diabetes mellitus itself on the development of sclerosis of the cerebral arteries.

The subjects included 30 patients with type 2 diabetes mellitus (DM). The subjects with DM did not have hypertension (systolic blood pressure <140 mm Hg, diastolic blood pressure <90 mm Hg) and had no history of cerebral infarction, diabetic retinopathy, diabetic neuropathy, or diabetic nephropathy. Among the 30 diabetic patients, 4 were being treated with insulin injections, 10 with oral hypoglycemic agents, and 16 with dietary therapy alone. The control group (C) consisted of 20 healthy adults without a history of diabetes, hypertension, or cerebral infarction. There were no significant differences in age (DM: 50.1±7.0 years versus C: 49.7±6.7 years), sex (DM: 21 males/9 females versus C: 11 males/9 females), systolic blood pressure (DM: 120±11 mm Hg versus C: 117±10 mm Hg) between the DM and control groups. The diastolic blood pressure was significantly lower in the DM group than in the control group (DM: 72±8 mm Hg versus C: 77±5 mm Hg; P<0.05). There were no significant differences in total cholesterol (DM: 197±24 mg/dl versus C: 218±41 mg/dl), triglyceride (DM: 88±41 mg/dl versus C: 110±61 mg/dl), nor high-density lipoprotein cholesterol levels (DM: 59±17 mg/dl versus C: 67±23 mg/dl) between the DM and C groups. The fasting plasma glucose was significantly higher in the DM group than in the control group (DM: 147±38 mg/dl versus C: 89±9 mg/dl; P<0.05). The hemoglobin A1c was significantly higher in the DM group than in the control group (DM: 7.2±1.6% versus C: 5.1±0.4%; P<0.05) (Mann-Whitney U test).

Lacunar lesions (LA) were depicted as a low-signal area on T1-weighted images and as a high-signal area on T2-weighted images of MRI (field strength, 1.5 T; CV, General Electric). Such areas with the largest diameter exceeding 3 mm were considered to represent LA.4 As to atherosclerosis (AS), subjects with positive findings on either magnetic resonance angiography (MRA) or ultrasonographic scanning of the intracranial and extracranial arteries or both were identified as having AS. Images of arteries in the head and neck were obtained by MRA. A reduction in the diameter of an artery by >25% was considered to indicate stenosis. On ultrasonographic scanning, the common and the internal carotid artery were observed on both the left and right sides. We measured the intima-media thickness (IMT) and the thickness of the plaque. An IMT of >1.0 mm was considered to indicate significant thickening.5,6 Plaques with a diameter of >1.0 mm were considered to be a significant finding.5 Fisher’s exact probability test was used for incidence analyses of LA and AS.

LA were found in 12 subjects (40%) of the DM group and 2 subjects (10.0%) of the control group. The incidence of LA was significantly higher in the DM group than in the control group (P<0.05). AS were found in 11 subjects (36.7%) of the DM group and 2 subjects (10.0%) of the control group. The incidence of AS was significantly higher in the DM group than in the control group (P<0.05).

Our results indicate that the incidence of LA and AS were significantly higher in relatively young diabetic patients without hypertension than in the control group (P<0.05). These findings suggest that diabetes mellitus itself contributes to the development of sclerotic lesions in cerebral arteries.

Koji Nagata, MD
Eun Sasaki, MD
Koshi Goda, MD
Naomune Yamamoto, MD
Masakazu Sugino, MD
Toshiaki Hanafusa, MD
First Department of Internal Medicine
Osaka Medical College
Osaka, Japan


Response

We read with great interest the study of Nagata et al concerning the influence of diabetes mellitus on the development of sclerosis of the cerebral arteries. The authors studied a group of patients with uncomplicated diabetes mellitus type 2 and a group of control subjects comparable for age and sex. The 2 groups of subjects were studied by means of MRI to assess the presence of silent lacunar lesions and by means of magnetic resonance angiography and ultrasonographic scanning of the intracranial and extracranial arteries to assess the presence of atherosclerosis. Moreover, sonographic examination was also performed to measure carotid artery intima-media thickness (IMT) and to evaluate carotid plaques. Authors found that either the incidence of lacunar lesions or the incidence of atherosclerosis was significantly higher in the diabetic group than in the control group. These findings suggest that diabetes mellitus itself (even in relatively young subjects without hypertension and any other diabetic organ damage) contributes to the development of sclerotic lesion in cerebral arteries. Both silent lacunar lesions and increased carotid artery intima media thickness has been found independent risk factors for stroke in older population. Thus, the study of Nagata et al outlines an important role of diabetes as an independent risk factor for the development of atherosclerosis. In our study concerning carotid artery IMT evaluation in lacunar versus nonlacunar infarcts, we did not find increased carotid artery IMT values in the subtype of first-ever symptomatic lacunar infarcts. However, we think that a comparison with our previous study is difficult. In fact, we evaluated first-ever stroke patients, not homogeneous for vascular stroke risks, in order to investigate whether common carotid artery IMT measurements may help to identify different subtypes of ischemic stroke patients. Moreover, we did not look at the presence of possible coexistent, previous, silent lacunar lesions in the 2 groups (namely lacunar
versus nonlacunar) of patients. Nagata et al looked at the relationship between diabetes, as a vascular risk factor, and the presence of silent lacunar lesions and cerebral atherosclerosis. However, stroke patients were not included in their study. It has been hypothesized that 2 types of lacunar infarcts with different prognosis could be distinguished, namely those with silent lacunar lesions and those without such lesions. Two types of underlying small-vessel pathology could underlie these lesions, although they might not be mutually exclusive. In addition, de Jong et al recently found that patients with a single symptomatic lacunar stroke had better prognosis over time than those with concomitant silent lacunar lesions. We think that a prospective study on the evaluation of carotid artery IMT in lacunar patients with a single symptomatic lacunar stroke and those with concomitant silent lacunar lesions might add further insights on this issue.

**Letizia M. Cupini, MD**
*Clinica Neurologica, Ospedale S. Eugenio, Rome, Italy*

**Fabrizio Vernieri, MD**
*Dipartimento di Neuroscienze, AfaR, Ospedale Fatebenefratelli, Isola Tiberina, Rome, Italy*


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Koji Nagata, Eun Sasaki, Koshi Goda, Naomune Yamamoto, Masakazu Sugino, Toshiaki Hanafusa, Kazuhiro Yamamoto and Isamu Narabayashi

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