Carotid Artery Disease in Patients with Retinal Artery Occlusion

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Embolization from the carotid bifurcation has been proposed as the most common cause of central retinal artery occlusion (CRAO) and branch retinal artery occlusion (BRAO). The purpose of this study was to evaluate carotid artery diseases in patients with CRAO and BRAO. Using carotid ultrasonography, 17 patients (13 males, 4 females, mean age 68.7 ± 7.1 years) with CRAO and BRAO were examined for stenotic findings and plaque morphology (homogeneous or heterogeneous) within 7 days after onset. The internal carotid artery (ICA) ipsilateral to the affected side showed a significantly higher incidence of severe carotid stenosis as compared to the non-affected side. The occurrence of heterogeneous plaques in the ICA did not differ between the affected and the non-affected side. We suspect that severe carotid stenosis in addition to heterogeneous plaques plays an important role in retinal artery occlusion.

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Key words: central retinal artery occlusion, branch retinal artery occlusion, carotid ultrasonography, homogeneous plaque, heterogeneous plaque

Introduction

It has been described that embolism from the carotid bifurcation is the most common cause of central retinal artery occlusion (CRAO) and branch retinal artery occlusion (BRAO) (1, 2). Other causes of CRAO and BRAO include cardiac disease, retinal artery thrombosis, vascular spasm, and vasculitis in addition to embolization from the carotid arteries (3, 4). Recently it has been shown that carotid ultrasonography may provide accurate information regarding both arterial lumen narrowing and plaque morphology (5, 6). The purpose of this study was to evaluate carotid atherosclerotic disease in patients with CRAO or BRAO by ultrasonography.

Materials and Methods

The clinical records of 17 consecutive patients (13 males, 4 females, mean age 68.7 ± 7.1 years) with CRAO or BRAO treated in our hospital from June 1993 to June 1995, were retrospectively reviewed. Eight patients suffered from CRAO in 8 eyes and nine experienced BRAO in 10 eyes (1 bilaterally). CRAO was diagnosed when patients experienced a sudden painless loss of vision in one eye associated with typical ophthalmoscopic findings: i.e. a pale retina, narrowing of the

retinal arteries, a swollen optic disc, and a macular cherry red spot. BRAO was diagnosed when the territory of a branch retinal artery appeared pale.

All patients were examined by a neurologist and an ophthalmologist. We reviewed cerebrovascular risk factors defined as follows: hypertension: the patient was taking antihypertensive agents and/or had a systolic blood pressure of >160 mmHg and/or a diastolic pressure of >95 mmHg; diabetes mellitus: the patient was under treatment with oral hypoglycemic agents or insulin, and/or had a fasting blood glucose level of >110 mg/dl, and/or a glycosylated hemoglobin (HbA1C) level of $>6.4\%$; hyperlipidemia: the patient was taking antihyperlipidemic agents and/or had a serum total cholesterol of >220 mg/dl and preexisting cerebrovascular or cardiac diseases (previous myocardial infarction, angina pectoris, atrial fibrillation and cardiomyopathy). The ophthalmological examination included measurement of visual acuity and the visual field, and ophthalmoscopic examination. The neurological examination was focused on transient or persistent hemispheric symptoms ipsilateral to the affected side and classified as transient ischemic attacks, minor stroke without a permanent functional neurological deficit, or major stroke with a permanent neurological deficit.

Carotid ultrasonography (Ultramark 9, Advanced Technology Laboratories, Washington, USA) was performed on each

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patient within 7 days after retinal artery occlusion. The carotid arteries of all patients were examined in longitudinal and transverse planes with anterior, lateral, and posterior approaches using B-mode imaging with color flow imaging. The common carotid artery (CCA), the carotid bifurcation, the internal carotid artery (ICA), and the external carotid artery (ECA) were studied in all patients.

Using B-mode imaging with the probe set at 5–10 MHz, a plaque was defined as an arterial wall lesion that projected into the vessel lumen. Plaques were classified as follows: 1. Homogeneous or heterogeneous; homogeneous (Fig. 1) when there was mostly medium or high level echogenicity, and heterogeneous (Fig. 2) when echogenicity was low, medium, or high.

Figure 1. Flat homogeneous plaque (arrows) at the origin of the internal carotid artery.

Figure 2. Heterogeneous plaque (arrows) with low, medium, and high echogenicity extending from the bifurcation into the internal carotid artery.

We compared plaques in the carotid artery ipsilateral to the affected side with those in the non-affected side.

Using color flow imaging to directly measure the residual lumen diameter of stenosis (7), stenotic findings were classified into normal, low-degree stenosis (reduction of 1% to 49% of the vessel diameter), high-degree stenosis (50% to 99%), and occlusion.

Magnetic resonance imaging (MRI) of the brain was performed on each patient to detect a potential cerebral infarction within 30 days after retinal artery occlusion. For a qualitative estimate of the lesion volume, a cerebral lobe was used as the unit of measurement. Thus, MRI findings were classified into five categories: normal, small and deep (infarction size <15 mm), less than half lobe, up to one lobe, and larger than one lobe. Data were statistically analyzed using the χ^2 test.

Results

Table 1 summarizes the clinical background of patients. Hypertension was found in 70.5% (12/17) of the all patients, 6 patients had diabetes mellitus and 3 had hyperlipidemia. Three patients had ischemic heart disease, 2 patients had arterial fibrillation, and one patient had hypertrophic cardiomyopathy (HCM). One patient previously experienced a major stroke ipsilateral to the affected side. Minor stroke ipsilateral to the affected side was found in two patients. The others had no ischemic cerebrovascular events.

ICA stenotic findings ipsilateral to the affected side were as follows: 6 cases of normal, 3 cases of low degree stenosis, 6 of high degree stenosis, and 3 of ICA occlusion. ICA stenotic findings ipsilateral to the non-affected side included: 7 cases of normal, 8 cases of low degree stenosis, and 1 of high degree stenosis. The ICA ipsilateral to the affected side showed significantly higher incidence of high degree stenosis as compared with ipsilateral to the non-affected side (Table 2).

There were 12 plaques of 18 ICA ipsilateral to the affected

Table 1. Mean Age, Sex, and Vascular Risk Factors

	CRAO n=8	BRAO n=9	Total n=17
Mean age	73.5±3.7	64.9±6.8	68.7±7.1
Males	7	6	13
Females	1	3	4
Hypertension	8	4	12
Diabetes mellitus	2	4	6
Hyperlipidemia	1	2	3
Minor stroke	—	2	2
Major stroke	1	—	1
Atrial fibrillation	1	1	2
Ischemic heart disease	2	1	3
HCM	—	1	1

CRAO: central retinal artery occlusion, BRAO: branch retinal artery occlusion, HCM: hypertrophic cardiomyopathy.

Table 2. Ultrasonographic Findings of Bilateral Carotid Artery in 17 Patients

Ultrasonographic finding	Affected side	Non-affected side
Normal	6	7
Stenosis <50	3	8
Stenosis ≥50	6*	1
Occlusion	3*	—
Total	18	16

*p<0.01 affected side versus non-affected side.

Table 3. Ultrasonographic Characteristics of Bilateral Internal Carotid Plaques

Echogenicity	Affected side (n=12)	Non-affected side (n=9)
Homogeneous	1	2
Heterogeneous	11	7

Table 4. MRI Findings in 17 Patients

MRI findings	Affected side	Non-affected side
Normal	15	14
Small and deep	2	2
< half lobe	1	—
< one lobe	—	—
One lobe <	—	—

side: 11 (91%) were heterogeneous plaques and 1 (9%) homogeneous plaque. Of 16 ICA of the non-affected side, there were 9 plaques: 7 (78%) heterogeneous plaques and 2 (23%) homogeneous plaques. The morphological analysis of plaques showed that occurrence of heterogeneous plaques in the ICA did not differ between the affected side and the non-affected side (Table 3).

MRI findings are summarized in Table 4. Fourteen (82%) patients as normal and 2 patients as small and deep and one patient as less than one-half lobe. The patients with small and deep infarction had no neurological symptoms. The patient with less than one-half lobe infarction had persistent hemispheric symptoms ipsilateral to the affected side.

Discussion

Carotid arterial disease has been shown to be a significant contributing factor in the development of retinal ischemic syndrome (1–4). B-mode ultrasonography allows the characterization of the structure of carotid plaques (5, 6). Plaques with homogeneous echogenicity consist of homogeneous fibrous tissue (5, 8). Plaques with heterogeneous echogenicity corre-

spond to hemorrhagic plaques with a mixed histology, including cellular infiltrates, cholesterol, and necrotic material (5, 8). It is important to distinguish between homogeneous and heterogeneous plaques. Several studies have shown a correlation between the presence of heterogeneous plaques and the frequency of cerebral complications (9, 10). Muller et al reported that ulcerated and heterogeneous plaques increases the risk for embolization in patients with CRAO or BRAO (11). In this study, we found that patients with ICA ipsilateral to the affected side showed a significantly higher incidence of severe carotid stenosis compared to that ipsilateral to the non-affected side. But the occurrence of heterogeneous plaques was high in both the affected and the non-affected sides. These findings indicated that severe carotid stenosis in addition to heterogeneous plaques played a more important role in retinal artery occlusion. Thus severe carotid stenosis seems to be an important cause of retinal ischemia.

In this study, 14 (82%) out of 17 patients showed normal MRI findings. We suspected the size of emboli related to retinal artery ischemia was smaller than that of emboli causing cerebral ischemia. Using transcranial Doppler ultrasonography it is possible to detect asymptomatic cerebral emboli in patients with carotid stenosis (12, 13). It has been demonstrated that microspheres of less than 105 µm in diameter injected into the common carotid artery of rabbits cause no overt neurological dysfunction (14).

In some patients neurological events including transients ischemic attacks, amaurosis fugax, and cerebrovascular accidents occur prior to, concurrent with, and subsequent to CRAO. O'Farrel and Fitzgerald reported that of 144 patients with retinal ischemia, 37 (26%) had cerebrovascular ischemic events in the follow-up period (2–7 years) (15). Douglas et al reported that carotid endarterectomy in CRAO patients significantly reduced cerebrovascular ischemic events (16). The patients with CRAO develop a high incidence of subsequent ipsilateral hemispheric strokes. Thus patients with CRAO should be routinely investigated by ultrasound examination of the carotid artery not only due to a high risk of recurrent ocular ischemia but also at for the risk of developing cerebral infarction, so that the appropriate treatment, either carotid endarterectomy or antiplatelet medication, can be indicated.

The frequency of retinal ischemia due to cardiogenic embolism is unknown. In the present, we found six patients with no carotid artery disease ipsilateral to the affected side. Of the six patients, three had cardiac diseases as the possible source of embolism. Thus, in patients with retinal ischemic syndrome and no carotid artery disease ipsilateral to the affected side, it may be important to investigate the presence of cardiac disease.

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