Progression of Carotid Atherosclerosis in Japanese Patients with Coronary Artery Disease

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Abstract. The authors investigated the relationship between the progression of carotid atherosclerosis and the severity of coronary artery disease (CAD). The two-year follow-ups of extracranial carotid atherosclerosis in 50 patients with CAD were evaluated by B-mode high-resolution ultrasonography. The summed maximal thickness of carotid plaques increased by 3.2 to 10.1 mm (mean 1.06 mm, SD 2.42 mm). The extent of coronary atherosclerosis (p < 0.02) and the serum total cholesterol level (p < 0.01) were different between the progressing group (n = 20) and the nonprogressing group (n = 25) with carotid atherosclerosis. Carotid disease progression was significantly higher in patients with three-vessel coronary disease than in those without significant coronary disease (p < 0.005). Age, serum triglyceride, high-density lipoprotein-cholesterol, pack-years of smoking, % smokers, % hypertensives, and % diabetics were not different between the two groups. It was concluded that the severity of CAD was one of the strong predictors for carotid disease progression in patients with CAD.

Introduction

It has been reported that mortality from ischemic heart disease in Japan is low compared with that in the United States and, conversely, mortality from stroke is higher in Japan [1]. It has also been reported that severe cerebral vascular lesions in Japanese were located intracranially, whereas those present in Americans occurred extracranially [2,3]. With lifestyle changes in Japanese, the incidence of all strokes in Japan appears to have decreased and the incidence of coronary artery disease (CAD) has increased [4]. Carotid artery plaque has been recognized as important as a source of cerebrovascular events [5]. And a significantly higher incidence of cerebrovascular events has been reported in a group with progression of carotid plaques [6].

Some studies have reported sequential changes of carotid plaques and revealed several risk factors for progression. A thirty-month follow-up study of 38 patients suggested that coronary atherosclerosis and elevated low-density lipoproteins (LDL) and fibrinogen may be predicting factors for progression of carotid stenosis [7]. In another study, cigarette smoking, diabetes mellitus, and age were proposed to be the major factors associated with progression of disease [8]. A two-year follow-up study using intimal-medial thickness measurement suggested that age, serum LDL-cholesterol concentration, pack-years of smoking, blood leucocyte count, and platelet aggregability were strong predictors for progression of atherosclerosis [9]. A strong association between the extent of carotid atherosclerosis and coronary atherosclerosis has been demonstrated [10–13]. One follow-up study reported a relationship between CAD and carotid plaque progression [7]. There is no definitive study that has demonstrated the changing aspects of coronary and intraextracranial carotid atherosclerosis in a Japanese population. Extracranial carotid atherosclerosis could have recently increased in the Japanese population. It is meaningful to investigate the progression of extracranial carotid atherosclerosis in Japanese with CAD.

To investigate the relationship between the progression of carotid atherosclerosis and the severity of coronary atherosclerosis, we evaluated the two-year follow-up of carotid lesions in 50 Japanese patients with CAD by using high-resolution ultrasonography.
Methods

Ninety-two consecutive Japanese patients with CAD (angina and/or postmyocardial infarction), aged thirty-nine to seventy-six, were evaluated. There were 63 men and 29 women. No one had a stroke or a transient ischemic attack. All patients signed an informed consent approved by the Osaka Rosai Hospital Ethical Committee.

From January to March 1989 selective coronary angiography was performed by the percutaneous technique using either Judkins or multipurpose catheters for all 92 patients. In succession, an ultrasonographic assessment of carotid arteries was carried out until a week after the coronary angiography.

The baseline examination included measurement of height, weight and blood pressure, serum cholesterol, triglyceride, and high-density lipoprotein (HDL) cholesterol concentration and assessment of smoking pattern with a self-administered questionnaire. All 92 patients who had undergone carotid ultrasonography from January to March 1989 were invited to a two-year reexamination. Of the patients invited, 2 had died, 5 had migrated, 6 refused to participate, and 29 could not be contacted. The remaining 34 men and 16 women were included in this study.

Treatment of the patients admitted to our follow-up was left to the discretion of the referring physician.

All carotid B-mode imaging was performed with a 7.5 MHz transducer having an axial resolution of <0.4 mm. Patients were examined in the supine position and each carotid system was imaged in anterior oblique, lateral, and posterior oblique planes. For this study, readings were made from just above the clavicle to the internal carotid artery 15 mm above the flow divider. Atheromatous plaques were identified as echogenic lesions showing localized thickening of arterial wall. Where echogenic plaques were identified, the view that displayed the greatest axial thickness of the lesion was recorded on Polaroid films. If multiple plaques were identified at the reading site, the records for both plaques were taken. The greatest axial thickness of each plaque was measured with a ruler on each Polaroid reproduction. To obtain a "plaque score" for each patient, these measurements for each patient were summed (Fig. 1). Follow-up scans were performed according to the same procedures. Examiners were informed of the location and the plane of the plaque previously identified, but readers were blinded as to the result of the first measurement. To evaluate the progression of carotid atherosclerosis, "delta plaque score" was obtained by subtracting the baseline plaque score from the follow-up plaque score.

According to the delta plaque score, patients were divided into three groups: progressing group, nonprogressing group, and regressing group. Twelve paired ultrasound examinations were done twenty-four ± sixteen days apart in 12 patients with atheromatous plaques. The mean differences in plaque score between these 12 paired images was 0.19 ± 0.22 mm. The nonprogressing group was defined in the standard deviation. A line from 0 mm baseline plaque score to the two-year follow-up plaque score was significantly higher than the baseline plaque score (p < 0.01).

Twelve patients had no coronary branch with 75% or consistently above 95 mm Hg or a history of arterial hypertension treated with antihypertensive drugs. Diabetes mellitus was diagnosed on the therapeutic history with oral hypoglycemic agents or insulin, and/or the fasting blood glucose level exceeding 110 mg/dL, and/or the glycosylated hemoglobin (HbA1c) level exceeding 6.4%. Serum total cholesterol, triglyceride, and HDL-cholesterol level were determined on blood drawn after an overnight fast. Pack-years of smoking was calculated according to self-administered questionnaire.

Data were analyzed by paired or unpaired t test and by chi-square test. The extent of carotid plaque progression was related to Gensini's score of coronary atherosclerosis in univariate analysis by linear regression.

Results

The baseline plaque score ranged from 0 to 7.0 mm (1.60 ± 1.94 mm) (mean ± SD) and the two-year follow-up plaque score from 0 to 13.1 mm (2.67 ± 3.16 mm) (Fig. 2). The increase of plaque score over two years (delta plaque score) ranged from 3.2 to 10.1 mm with a mean of 1.06 mm and a standard deviation of 2.42 mm. The paired t test showed that the two-year follow-up plaque score was significantly higher than the baseline plaque score (p < 0.01).

According to the classification by delta plaque score, the progressing group included 20 patients, the nonprogressing group included 25, and the regressing group included 5.

Table 1 lists background profiles in the progressing and nonprogressing groups. Because of the small number of the regressing group, these variables were not listed for the regressing group. The two groups were not different except for serum total cholesterol level (p < 0.01) and coronary status. Both Gensini's score and CAG score were significantly higher in progressing group than in nonprogressing group (p < 0.02). These variables were also not examined for the regressing group because of the small number of patients.

Sixteen patients had no coronary branch with 75% or