The Impact of Atherosclerotic Factors on Cerebral Aneurysm Is Location Dependent: Aneurysms in Stroke Patients and Healthy Controls

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Previous studies have indicated that cerebrovascular diseases (CVDs) seem to increase the occurrence of unruptured intracranial aneurysms (UIAs). However, this maybe explained by the fact that CVDs and UIAs share common risk factors, such as hypertension (HT) and smoking. To clarify the impact of atherosclerotic risk factors on cerebral aneurysmal formation, we explored the incidence of UIAs and their locations in healthy controls and patients with CVD, who frequently have atherosclerotic risk factors. This study included consecutive 283 asymptomatic healthy adults and 173 acute stroke patients, from patients diagnosed with acute cerebral hemorrhage or cerebral infarction and admitted to our hospital. The incidence, maximum diameter, and location of UIAs were evaluated, and we also investigated the following factors: age, gender, current smoking, HT, diabetes mellitus (DM), and dyslipidemia. UIAs were found in 19 of the total 456 subjects (4.2%), 11 of 283 healthy subjects (3.9%), and 8 of 173 stroke patients (4.6%). These differences are not statically significant. The incidence of middle cerebral artery (MCA) aneurysms was significantly higher in the CVD patients than in the healthy controls ($P = .03$), and the incidence of paraclinoid aneurysms was significantly higher in the healthy controls than in the CVD patients ($P = .03$). Moreover, higher incidences of HTs and CVDs in the MCA aneurysms than in the other locations of UIAs were observed. These results indicate that the impact of atherosclerotic factors on cerebral aneurysmal formation depends on their location and that there is a stronger impact on MCA aneurysms than on paraclinoid aneurysms. **Key Words:** Cerebral aneurysms—location—atherosclerotic factor—stroke.

Many studies have investigated risk factors for unruptured aneurysms.[1-5] These risk factors have been generally divided into 2 categories: congenital or inherited defects weakening the arterial wall and atherosclerotic factors. Female sex, positive family history for subarachnoid hemorrhages, previous history of unruptured intracranial aneurysms (UIAs), and polycystic kidney disease are all nonmodifiable risk factors for UIAs.[5] In contrast, hypertension (HT) and smoking are well-established modifiable risk factors; the evidence for other possible modifiable risk factors, such as dyslipidemia, diabetes mellitus (DM), and excessive alcohol use are limited and sometimes conflicting.[1,2,4,5]

UIAs are incidentally found when a brain MRA is performed in asymptomatic healthy volunteers[6,7]; UIAs in stroke patients are also incidentally detected.[2,5,6,8-10] Some previous studies indicated that cerebrovascular diseases (CVDs) seem to increase the occurrence of UIAs.[5,11] However, the relationship between UIAs in CVD patients and in healthy subjects still remains unclear. As far as we know, only 1 report evaluates

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whether UIAs are more frequent in CVD patients than in healthy controls.[6] They found no statistical differences in frequency of UIAs and their locations between the 2 groups. In their report, however, the incidence of internal carotid artery (ICA) aneurysms was found to be 47% in healthy controls and 28% in stroke patients, although this difference is insignificant. This may suggest that non-modifiable factors have stronger effects on ICA aneurysmal formation than arteriosclerotic risk factors and that those atherosclerotic factors have stronger effects on other UIA locations. Thus, it maybe possible that each risk factor has a different effect on each aneurysmal formation, because of its unique location.

To clarify the impact of atherosclerotic risk factors on cerebral aneurysmal formation, we explored the incidence of UIAs and their locations in healthy controls and patients with CVD, who frequently have atherosclerotic risk factors.

Patients and Methods

Patients

This study included consecutive 283 asymptomatic healthy adults (153 males and 130 females) and 173 acute stroke patients (111 males and 62 females) between April 2012 and March 2013. The present study was approved by the Ethics Committee of Kushiro Rousai Hospital.

A total of 283 asymptomatic healthy adults (the healthy group) underwent a physical check-up, including brain MRI and MRA in our hospital, during the study period. In Japan, "Brain Dock," a formalized screening system for asymptomatic brain diseases are popular and all these asymptomatic adults voluntarily paid and applied for brain dock at our hospital. Therefore, most of the subjects lived in the vicinity, and they volunteered for the examinations without any investigator's prejudiced selection.

Thus, there was nothing in their medical history that could bias the detection of UIAs. The healthy subjects who had experienced an magnetic resonance angiography (MRA) within 3 years or who had a past history of CVD were excluded.

A total of 173 patients (the CVD group) were diagnosed with an acute intracerebral hemorrhage (ICH) or a cerebral infarction and were admitted to our hospital during the period. The patients were subclassified into cardiac embolism, noncardiac cerebral infarction, and ICH. For all patients, magnetic resonance imaging (MRI) and MRAs were routinely performed within 2 weeks from onset. Those who could not undergo an MRI or an MRA, such as patients with pacemakers or those with severe damage and who died after discharge, were excluded from this study. Also excluded were patients with a past history of CVD or whose UIAs were found by previous examination. Consequently, there were no prejudiced selection criteria to detect UIAs in the stroke patients' clinical history.

Methods

Clinical data were collected from the patients' medical records. In this study, the authors used the following factors: age, gender, current smoking habit, HT (systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg) or current treatment status, DM (hemoglobin $A1_C \geqq 6.5$) or currently treatment status, and dyslipidemia (serum low-density lipoprotein cholesterol >140 mg/dL) or current treatment status.

UIAs were diagnosed by a 3-dimensional time-of-flight MRA. The incidence, maximum diameter, and location of each UIA were evaluated. In this study, aneurysms longer than 3 mm were defined as UIAs. Aneurysmal locations were classified as follows: (1) intracranial–paraclinoid ICA aneurysm; (2) distal portion from posterior communicating artery bifurcation of ICA aneurysm, including internal carotid artery–posterior communicating artery aneurysm and internal carotid artery–anterior choroidal artery aneurysm; (3) middle cerebral artery (MCA) aneurysm; (4) anterior cerebral artery aneurysm, including anterior communicating artery and distal anterior cerebral artery aneurysms; and (5) posterior fossa aneurysms.

Statistics

All data are expressed as mean ± standard deviation. Clinical variables—including age, gender, aneurysm size, location, smoking habit, HT, DM, and dyslipidemia—were compared by use of χ^2 test or unpaired t test as appropriate. Multivariate logistic regression analysis was performed to determine whether the incidence of UIAs was associated with the clinical variables with a P value of $<.1$ in univariate analysis. Differences with a P value of $<.05$ were considered statistically significant.

Results

Clinical Data and Incidence of UIAs

Characteristics of the patients and incidence of UIAs in this study are represented in Table 1. The mean age of all subjects was 63.1 ± 12.8; the mean age for the healthy subjects was 58.3 ± 10.6; the mean age for the stroke patients was 71.2 ± 9.5; the percentage of males was higher in stroke patients than in healthy subjects. There are significant differences in age and gender between the 2 groups. Moreover, history of HT and DM and smoking habit were more frequently observed in the stroke patients than in the healthy subjects (67.1%, 30.6%, and 30.1% in the stroke patients vs. 23.7%, 9.2%, and 18.0% in the healthy subjects, respectively) with significant differences. Thus, there were significant differences in risk factors between the 2 groups.

UIAs were found in 19 of the total 456 subjects (4.2%), 11 of the 283 healthy subjects (3.9%), and 8 of the 173 stroke patients (4.6%). In the stroke patients, UIAs were recognized in 0 of 51 (0%) with cardiac embolisms, 3 of