Special Article

Cerebral Atherosclerosis of Japanese*

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IT has been clarified by epidemiological survey as well as pathological study that cerebrovascular disease in Japan is the major cause of death and the incidence of cerebral thrombosis is much higher than that of cerebral hemorrhage. On the other hand, the death rate due to arteriosclerotic heart disease is much lower in Japan compared with that in most of the western countries.

Several reports, including ours, demonstrated that severity of atherosclerosis of Japanese aorta and coronary artery obtained at hospital or medico-legal autopsy was remarkably lower when compared to Caucasians materials. It is difficult to understand why in Japanese the incidence of cerebral thrombosis is higher and the incidence of coronary heart disease is lower compared to those in Europeans and/or Americans. Very few studies have been conducted on the severity of cerebral atherosclerosis of Japanese in a large number of cases. Only Resch et al¹⁾ had conducted a cooperative study in which the macroscopic severity of cerebral atherosclerosis in a Japanese and a Minnesota population was determined in a hospital-autopsy study. They pointed out a possible ethnic difference in severity of cerebral atherosclerosis between a Japanese and a Minnesota autopsy population in the direction of greater involvement in the Japanese cases.

In the present report, we attempt to report the macroscopic severity as well as lipids contents of Japanese intracranial cerebral artery and also to describe a specific character of acid mucopolysaccharides in the cerebral artery. Since the extracranial neck vessels and the clinical findings were not obtained in the present study, the relationship between the clinical evidence of strokes and atherosclerosis of the intra- and extracranial arteries is not discussed here.

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During a period of 2 years, 1965–1966, 717 cerebral arteries, males and females, were obtained from the unexpected, and, sudden death cases. Systematic grading of the macroscopic severity of cerebral atherosclerosis was

Fig. 1. Macroscopic severity of cerebral atherosclerosis in Japanese with age.

Fig. 2. Frequency and location of early mild cerebral atherosclerosis. The number demonstrated at the 28 sites represents the total number of the cases with mild or early cerebral atherosclerosis.

Fig. 3. Frequency and location of +4 lesion of cerebral atherosclerosis. The number demonstrated at the 28 sites of cerebral arteries represents the total number of cases with +4 lesions.

performed by the method described by Gore et al²⁾ for total of 717 and/or Baker et al³⁾ for 423 out of 717 cases.

Cerebral atherosclerosis of Japanese was seen as early as in the 2nd decade and increased in severity with age, particularly at the 6th decade in females as shown in Fig. 1. The prevalence of localization of mild and/or severe cerebral atherosclerosis was studied.

The site of early mild lesion in Japanese appears to be the same (Fig. 2), but the sites of severe cerebral atherosclerosis not the same as the previous investigation⁴⁾ on Caucasians (Fig. 3). The common sites of the severe cerebral atherosclerosis causing marked lumen narrowing were the peripheral portion of the middle cerebral, proximal portion of the posterior cerebral, vertebral arteries and their fusing site at basilar artery, but the internal carotid artery and proximal portion of the middle cerebral arteries were rather less frequent site. When macroscopic severity of cerebral atherosclerosis is determined by the different investigators, the geographic comparison of severity of cerebral atherosclerosis would be liable to introduce some errors. So, we determined the amount of lipids in order to evaluate these macroscopic results by chemical means.

Figs. 4 and 5 demonstrated an increase of contents of total lipids and cholesterol of Japanese cerebral arteries with age. The solid line represents

Fig. 4. Relationship between total lipids of Japanese cerebral arteries and age ($r=0.516$).

the mean value of lipids concentration with various decades of the individual cerebral arteries obtained from 258 cases. The dashed line also represents lipids concentration by single determination of the pooled cerebral artery at each decade obtained from 364 cases. Both lines for the total cholesterol and total lipids contents of Japanese cerebral arteries coincide well each other and appear to show slightly higher concentration at 7th decade and steeper increase with age than the dotted lines for the South African Whites which were obtained by Dr. Meyer et al.⁵⁾

Although the exact comparison of the amount of various lipids between the present study and the others is impossible, the steepness of rise of lipids contents with an increase of age were compared between our cases and South African Whites. In South African Whites, esterified cholesterol of the cerebral artery increased from approximately 3 mg at the 2nd, 3rd, and 4th decade to 11 mg per Gm of dried tissues at the 7th, and in our cases it increased from 3

Fig. 5. Relationship between total cholesterol of Japanese cerebral arteries and age ($r=0.495$).

to 18 mg per Gm of dried tissues. Similar trend was also found concerning total lipids and free cholesterol. The trend may indicate that the increase of lipids with age in Japanese cerebral artery is not low and rather higher compared with Caucasians.

Previously we reported on lower content of hyaluronic acid and chondroitin sulfate A/C in the intracranial artery compared with those in aorta and coronary artery.^{6),7)} In the present study, an attempt was made to dissociate change of acid mucopolysaccharides (AMPS) in atherosclerosis from that in the simple aging. The cerebral arteries of 364 cases were pooled being divided by decades, and, each decade into the grossly normal site and the lesion site. These tissues were surveyed for AMPS analysis. The fractionation and quan-

titative determination of total and various types of AMPS were carried out by a slight modification of Schmidt's method.⁸⁾

In Fig. 6 it was demonstrated that the total AMPS increased with an increase of age both in the normal and the lesions. In the lesions, heparan sulfate decreased and chondroitin sulfate A/C and B increased. However, in the normal, the relative proportion of various types of AMPS remained almost constant. This finding on AMPS may suggest a metabolic change of arterial wall in atherosclerosis which may be different from a change by simple aging. From this study, it became clear that contents of hyaluronic acid of the cerebral artery was approximately one tenth of that of the aorta.

In summary, severity of cerebral atherosclerosis in Japanese appears to be slightly higher or same in terms of macroscopic grading and lipid contents compared with those in Caucasians reported by others.

A decrease of heparan sulfate concentration and an increase of chondroitin sulfate A/C and B concentration in the atherosclerotic tissue, seems

Fig. 6. Acid mucopolysaccharides of Japanese cerebral arteries with age or atherosclerosis.

to be in contrast to the findings in the grossly normal tissues with simple aging.

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