Relationship between Hypertension and Cerebrovascular Lesions in Stroke-prone Spontaneously Hypertensive Rats

Akinobu NAGAOKA, Akio SHINO, and Hisashi IWATSUKA

High blood pressure plays an important role in the development of malignant hypertension in patients and experimental animals. The stroke-prone spontaneously hypertensive rats (SHRSP), regarded as a useful animal for human malignant hypertension, also showed a severe hypertension which was followed by the onset of cerebrovascular lesions (stroke, cerebral hemorrhage and/or infarction). However, we recently reported that genetic factors besides hypertension were very important for the onset of stroke in the SHRSP (Nagaoka, Iwatsuka, Suzuoki, and Okamoto Am J Physiol 230: 1354, 1976). In the present study, we have further examined whether other factors in addition to the high blood pressure are required to induce the hypertensive vascular lesions.

Antihypertensive therapies or experimental hypertensive manipulations were performed to attenuate or aggravate the development of hypertension in the SHRSP of 10 weeks of age. In the therapeutic experiment, hydralazine or reserpine dose-dependently inhibited salt-accelerated elevation of blood pressure. The onset of stroke was also dose-dependently inhibited by either antihypertensive drug. These results are in agreement with the hypothesis that high arterial pressure is responsible for arteriolar damage in severe hypertension.

However, an evidence for dissociation between hypertension and onset of stroke was obtained from the experiments of hypertensive challenges. Grollman type of renal hypertensive procedure and adrenal enucleation, as well as the salt-loading, exaggerated hypertension (240–260 mmHg) and cerebrovascular lesions in the SHRSP. The final incidences of stroke were 90% in the 3 groups of SHRSP. On the other hand, administration of glucocorticoid (dexamethasone) or thyroid hormone (thyroxine) to the SHRSP resulted in the elevation of arterial pressure to the levels higher than 270 mmHg, but the cerebral lesions were not aggravated in the both groups of rats. Furthermore, administration of deoxycorticosterone acetate and salt to the adrenalectomized SHRSP also caused tremendously severe hypertension over 280 mmHg without the cerebral lesions. In these latter 3 groups, the final incidences of stroke were 0–10%.

Histological observation was performed on all groups. Intensive renal vascular changes such as arteriolosclerotic or proliferative changes were always noted in the SHRSP with the cerebral lesions irrespective of type of treatments. In the SHRSP without the cerebral lesions, there were slight or mild renal vascular changes in spite of severe hypertension. Furthermore, our preliminary experiment demonstrated that the development of cerebral lesions followed the development of renal vascular changes under the salt-loaded conditions.

From the Biological Research Laboratories, Central Research Division, Takeda Chemical Industries, Osaka.

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These evidences suggest that 1) the development of stroke in the SHRSP is not dependent on high blood pressure per se, and 2) a combination of hypertension and some renal factor in relation to severe renal vascular changes is of great importance for the onset of cerebrovascular lesions.