5) Vascular lesions produced by M-SHRSP and SHRSP renal cortical extract
Yoshio Ohta, Yang Gong Ming, Tsuneyuki Suzuki, Kozo Okamoto.
Department of Pathology, Kinki University School of Medicine, Osaka-Sayama
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Introduction:

The existence of substances inducing angioneclerosis in kidney homogenate was first postulated by Winternitz et al. (Winternitz et al.: Yale J. biol. Med., 12, 623, 1940). On the other hand, we have set forth the hypotheses that there is a possibility that factors in malignant hypertension other than high blood pressure itself play a role in the occurrence of such hypertensive vascular lesions as angioneclerosis (Ohta et al.: Jpn. Heart J. 31, 543, 1990). In this study, we tried to clarify whether there are any substances in M-SHRSP and/or SHRSP renal cortex which induce vascular lesions without high blood pressures.

Materials and methods:

Renal cortex was obtained from the following three groups of rats for use in preparation of various subcellular fractions. 1) M-SHRSP and/or SHRSP with severe hypertensive vascular lesions. 2) SHR B2 rats with mild vascular lesions. 3) WKY rats with no vascular lesions. The rats were thoroughly perfused with sterile refrigerated physiological salt solution through the abdominal aorta and then nephrectomized. The renal cortex was fractionated according to a modified Nakamura et al. method. The fractions thus prepared were divided into fraction 1 containing soluble components, fractions 2 and 3 containing microsomal contents, fraction 4 containing lysosomal contents and fraction 5 containing mitochondrial contents. To examine the vascular injury for each fraction, bilateral or unilateral nephrectomies and sham operations were performed on male WKY under anesthesia. Six hours after nephrectomy, the subcellular fractions were injected intraperitoneally with 25 mg/kg protein. A Saline solution was also injected intraperitoneally as control. The rats were killed 24 hours after nephrectomy, and histopathological examinations performed. The following stains were used: H.E., PAS and Mallory-azan.

Results and discussion:

The histopathological studies revealed fibrinoid angioneclerosis in small arteries and veins when subcellular fractions were injected in bilaterally nephrectomized rats, but not in rats given saline. Fibrinoid angioneclerosis was detected as fibrinoid material depositions in blood vessels. The fibrinoid material was stained a dark reddish color with H.E. stain, was positive to PAS stain, and was stained red with Mallory-azan stain. The necrotic vascular wall was accompanied with pyknosis and karyolysis of degenerative nuclei around the cells. Angioneclerosis was noted in the mesentery, pancreas, heart and adrenals, but it was particularly frequent in the pancreas and mesentery. Among the renal cortical fractions, fraction 4 showed the greatest injury in bilaterally nephrectomized rats. Angioneclerosis in the pancreas and/or mesentery was detected more frequent in bilateral nephrectomized rats than in unilateral nephrectomized or sham operation rats. Comparing fraction 4 extracted from SHR B2 and WKY with fraction 4 extracted from M-SHRSP and/or SHRSP, the latter showed a stronger blood vessel injury effect to bilaterally nephrectomized rats. None of the fractions showed a pressor effect.

The fractions without pressor effect but with a vascular injury effect were isolated from the renal cortical extracts of M-SHRSP and/or SHRSP, SHR B2 or WKY. Compared to fraction 1-5, fraction 4 showed the greatest vascular injury effect. Furthermore, fraction 4 from M-SHRSP and/or SHRSP showed a more intensive vascular injury effect than that of SHR B2 or WKY. It is speculated that the renal cortex of M-SHRSP and/or SHRSP contains a greater amount of a vascular injury substance than for SHR B2 or WKY.