MORPHOLOGY AND PATHOMORPHOLOGY

EXPERIMENTAL RENAL INFARCTS

COMMUNICATION II. ARTERIAL INFARCTS

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Received January 30, 1957)

A great deal of evidence has been published which shows the great importance of the tone of the coronary vessels and their collaterals in the etiology of myocardial infarct, which makes it necessary to reconsider Konheim's theory of infarction. A. V. Lebedinsky, V. I. Medvedev, and L. A. Pelmer [5] showed that a spastic condition develops in the right coronary artery following ligature of the left.

These results have been confirmed for the kidney. It has been shown that ligature of the pelvic branch of the anterior renal artery induces reflex spasm in the corresponding branch of the posterior renal artery [6, 7].

These results give reason to suppose that the reflex vasomotor changes may play an important part in the etiology of infarction. However the question of the effect of the nerve supply to the organ on infarction has not been sufficiently studied. In the present work, we report the results of an investigation into the effect of renal denervation on infarction.

EXPERIMENTAL METHODS

The experiments were carried out on 97 white rats in whom renal infarcts were induced by ligature of the pelvic branch of the posterior renal artery. An extracelomic lumbar approach to the kidney was used. In the first set of experiments, with 43 animals, the development of infarction was studied while the nerve supply to the kidney was intact. In the second set of experiments, with 32 animals, the left kidney was denervated 7-12 days prior to ligature of the vessel. For the denervation, the entering blood vessels and the upper quarter of the ureter were freed from surrounding tissue, and all nerves entering the kidney visible to the naked eye were cut. The renal vein was separated from the renal artery. Where the latter left the aorta, the arterial sheath was removed, and with it the superior and inferior renal ganglia. After this the adventitia of the above two vessels and the upper part of the ureter were treated with a 2% solution of phenol, after which the parts were washed with saline. After this, the capsule of the kidney was removed. In the third group of experiments, on 22 animals, the fibrous capsule of the kidney was removed either at the same time as, or 8-12 days before ligature of the artery. The animals were killed 40 minutes, $1^1/_2$, 3, 6, 12 and 24 hours, and 3, 7, 14, 21, and 30 days after the ligature had been made. The material was fixed in 8-10% formalin and embedded in celloidin, or else sections were cut with a freezing microtome. The sections were stained in van Gieson's hematoxylin-eosin, fuchselin for elastic fibers, with Sudan III for fat and by Goldman's method for leukocytes. In some of the animals of groups 1-3, angiograms were made for the study of the blood supply to the kidney, the vessels being perfused with a mixture of lead acetate in 3% gelatin [2]. The whole kidney was removed, and placed with the hilus upwards; it was then cut into two parts the division following the distribution of the pelvic artery. In some of the experiments stereoroentgenograms were made. The pictures were examined with a magnification of twenty times, as well as using a stereoscope.

At an early stage of the development of the infarct the morphological changes and the angiograms were the same in all the groups of experiments. In the first 12 hours after the ligature a necrotic area developed, surrounded by a hemorrhagic rim. At the beginning of this period there was a granular and watery dystrophy which was most clearly shown in the convoluted tubules, some of which perished after only 3 hours. The cells of the other regions of the tubules were preserved at first somewhat better, and the greatest resistance to the hypoxia was shown by the endothelial capillaries of the glomeruli. The angiograms showed that in the early stages the arteries in the region of the infarct are incompletely filled with the lead acetate fluid (Fig. 1, b). Under the microscope it could be seen only in some of the small blood vessels.

From the angiographs it could be seen that in both control and experimental animals there are comparatively few anastomoses between the small internal branches of the renal artery (Fig. 1).

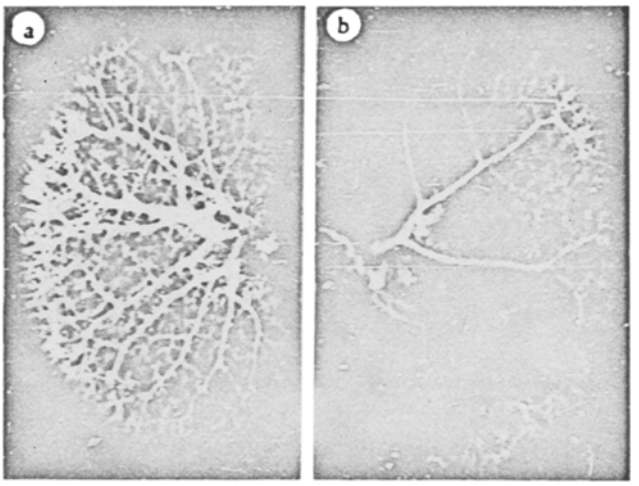

Fig. 1. Angiogram. a) Right (healthy) kidney; b) left denervated kidney. In the region of the infarct the arteries have not been filled with the contrasting substance. Anastomoses between the vessels can be seen. Length of experiment 24 hours. Enlargement on printing $3^{1}/_{2}$ times.

On account of the paucity of collaterals [6, 7], the denervation, which prevents the development of spasticity in the anterior pelvic artery from occurring after ligature of the pelvic branch of the posterior renal artery, and which therefore increases the blood supply to the ischemic zone, had comparatively little effect on the development of the infarct. For the same reason, on account of the limited potential development of the extrarenal collaterals, their removal with the capsule of the kidney had no great effect on the process of infarction.

At later stages, definite differences were shown between the innervated and denervated kidneys. Investigation of the infarct in the denervated kidney showed: (1) an increased inflammatory reaction, with exudate; the band of leukocytes around the edge of the infarct was broader and contained a larger number of leukocytes (Fig. 2, a and b); (2) there was an increased amount of new connective tissue around and in the infarct; (3) the process of transformation of the granulation into fibrous tissue to form a capsule around the infarct with layers penetrating into it proceeds more rapidly, being approximately one week in advance of the corresponding process in the control animals.

Similar but less well-marked changes were shown in the experiments with decapsulated kidneys.

We have found no publications describing the effect of denervation and decapsulation of the kidney on the development of the inflammatory reaction round an infarct. However, our findings confirm those of D. E. Alpern [1], V. G. Eliseev [3], and other workers who found an increased inflammatory reaction following section of the sympathetic nerves or denervation of the tissue, and who also found an increased permeability of the blood vessels

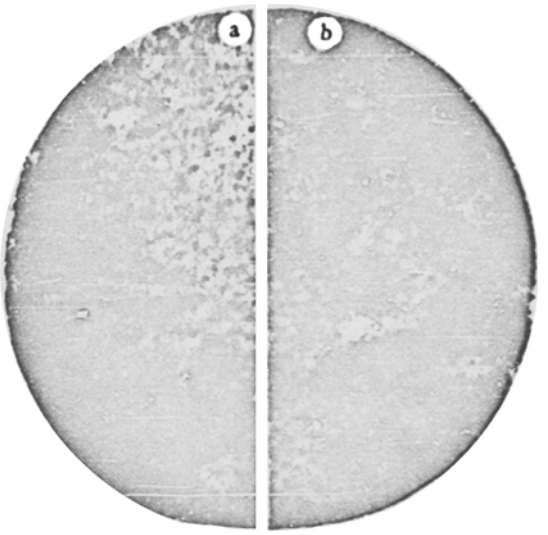

Fig. 2. Band of leukocytes around periphery of infarct in experiment lasting 24 hours.
a) Innervation intact; b) denervated kidney, stain hematoxylin-eosin, Magnification, eye piece 10 objective 20.

after denervation. B. I. Lavrentyev [4] showed that the nervous system regulates the degree of cellular differentiation. We may suppose, therefore, that denervation may increase proliferation of connective tissue, as we in fact observed in our experiments.

Decapsulation itself, which at the present time is considered by many workers to be a partial denervation, had a similar but less strong influence on the reactive inflammatory process and the organization of the infarct.

SUMMARY

The development of infarction after ligature of the posterior pelvic artery of a denervated and decapsulated kidney and of a normal kidney with intact innervation was compared. No difference in the development of infarctions in both kidneys could be noted at an early stage, but later on reactive inflammation, growth of connective tissue and cicatrization were enhanced in the denervated kidney.

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