MORPHOLOGY OF THE PANCREATICORENAL SYNDROME

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Renal failure is a frequent and serious complication of acute pancreatitis and is attended by high mortality [4, 6-10, 16]. Milder forms of renal lesions are found much more often and are observed in 50-80% of all cases of pancreatitis [14]. This has led some workers to distinguish concepts such as "pancreatic nephropathy" [12] and "pancreaticorenal syndrome" [6, 15]. However, the specificity and pathogenetic mechanisms of kidney lesions in acute pancreatitis have not yet been adequately explained.

The investigation described below was accordingly devoted to a study of changes in the kidneys at different stages of development of experimental pancreatitis in order to discover the morphological substrate of the various manifestations of renal failure.

EXPERIMENTAL METHOD

Experiments were carried out on 56 noninbred male albino rats weighing 180-200 g in which pancreatitis was induced by cooling the pancreas with ethyl chloride [5]. The animals were decapitated 5 and 60 min, 3, 6, 12, and 24 h, and 3 and 7 days after injury to the organ. The kidneys were fixed in 10% Lillie's buffered formalin and embedded in paraffin wax. Paraffin sections 4 μ thick were stained with hematoxylin and eosin, for fibrin by the Gram—Weigert and Mallory (phosphomolybdic acid—hematoxylin) methods, and by the PAS reaction. Starting with animals used after a period of 3 h, some of the animals from each series were given an intravenous injection of ink 30 min before decapitation as an indicator of vascular permeability, in a dose of 0.25 ml/100 g body weight.

EXPERIMENTAL RESULTS

Only mild congestion in the microcirculation of the kidneys was observed 5 min after cooling of the pancreas. By the 60th minute of the experiment many of the renal structures still remained intact, although the congestion was more widespread in character, stases were observed in the cortical capillaries, single microthrombi were present, and the walls of the arterioles and of certain arteries were permeated with plasma. The cytoplasm of the epithelium in the proximal part was rather swollen in some places, with pinching off of the apical part of the cytoplasm into the lumen of the tubule. Changes in the kidneys increased in severity as the pathological process in the pancreas progressed. For instance, by 3 h of the experiment two-thirds of the mass of the pancreas was in a state of necrobiosis, saturated with hemorrhagic exudate, whereas the rest was occupied with "vitreous" edema. Plaques of steatonecrosis were found in the omentum and mesentery, and up to 5 ml of bloodstained effusion was present in the peritoneal cavity. In the kidneys at this stage congestion, stasis in the capillaries, especially in the juxtamedullary zone, and disseminated microthrombosis were observed, including in the glomerular capillaries (Fig. 1). Evidence of increased vascular permeability in the kidneys was given by the outflow of ink into the mesangium, deposition of ink particles in the capillary walls of the cortex and in the stroma, and also the appearance of a small quantity of protein-containing exudate in the cavity of the glomerular capsule and of perivascular edema. Degenerative changes in the epithelium of the proximal portion of the nephron increased in severity: Swelling of the cytoplasm was observed everywhere, accompanied by the presence of eosinophilic granules and of vacuolation; the cell

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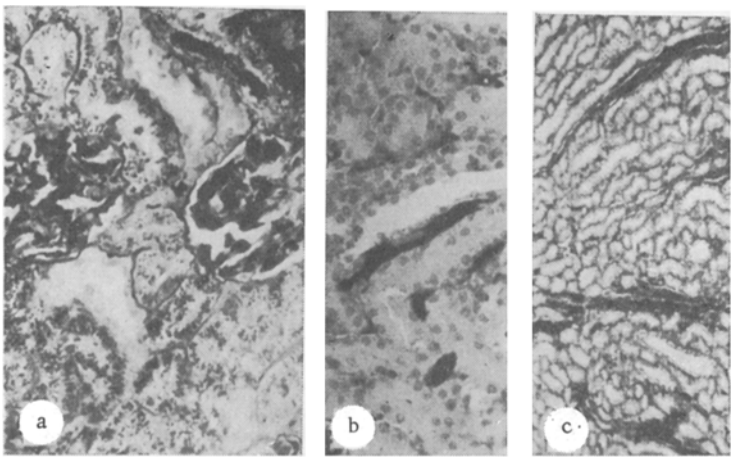

Fig. 1. Rat kidney in stage of formation of hemorrhagic pancreonecrosis (3 h). a) Microthrombi in glomerular capillaries; b) microthrombi in capillaries of renal cortex; c) microthrombosis of capillaries in juxtamedullary zone. Gram—Weigert stain. Magnification: a and b) 120 ×, c) 30 ×.

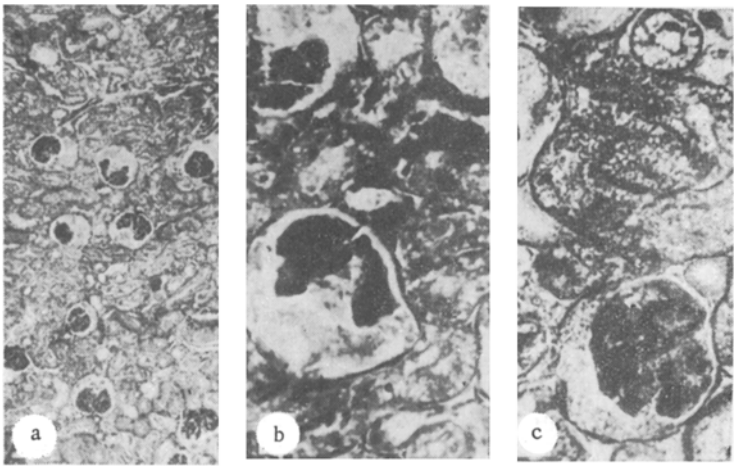

Fig. 2. Rat kidney in stage of parenchymatous necrosis of the pancreas (24 h). a) Protein-containing exudate in cavity of capsule. Hematoxylin—eosin, 30 ×; b) detail, 120 ×; c) exudate gives fibrin-positive reaction to Mallory's stain, 120 ×.

boundaries were indistinctly outlined and in some cases were obliterated. Marked congestion, with diapedetic hemorrhages in the cortex, was observed in the kidneys 6 h after the beginning of the experiment. Small arteries in all layers of the kidney were seeped with plasma and had deposits of fibrin in their walls. Fibrin also was deposited on membranes of the glomerular capillaries and in the mesangium. After 12 h the changes described above were joined by foci of tubulorhexis. The severest changes in the kidneys were found after 24 h, against a background of necrosis of the pancreatic parenchyma with hemorrhages, massive foci of fatty necrosis, and a generalized increase in vascular permeability [1]. These changes were manifested as marked edema of the paranephric cellular tissue and capsule of the kidney, swelling of the laminae of the glomerular capsule, and edema of the stroma of the pyramids. Inside the cavity of the glomerular capsule there was an abundant protein-containing exudate with globular fibrin-positive reaction, displacing the capillary loops of the glomeruli (Fig. 2). Cells of the glomerular capsule became cubical in shape. Deposition of fibrin- and PAS-positive material was found on the membranes of the glomerular capillaries, in the mesangium, and in the parietal lamina of Shumlyanskii's capsule. Individual necrotic glomeruli could be seen. Severe degenerative changes were present in the epithelium of the proximal portion, where the hypochromic nuclei were poorly outlined, the cytoplasm was filled with fine gran-

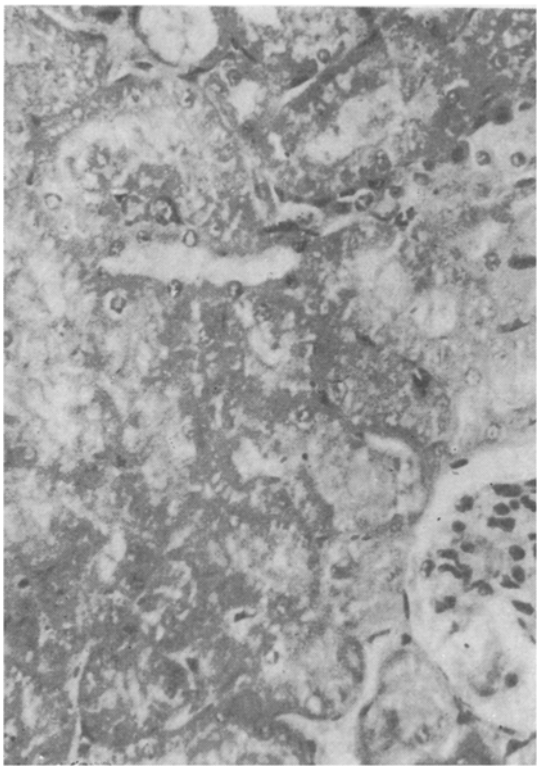

Fig. 3. Focus of tubular necrosis 24 h after injury to the pancreas. Hematoxyin-eosin, 280 ×.

ules or vacuoles, and the brush border was fragmented. Besides foci of tubulorhexis, areas of tubular necrosis were found (Fig. 3). The walls of the arteries were seeped with plasma and showed fibrinoid changes and marked perivascular edema. The 24-hourly diuresis in this stage was 15.3 ± 0.5 ml compared with 25.0 ± 0.5 ml in the control ($P < 0.001$).

On the 3rd day of the experiment, when the acute inflammatory and necrotic changes had subsided and repair processes were developing in the pancreas [2] the structure of the tubular system of the kidneys was considerably restored to normal, but exudate was still present in some of the glomeruli. The microcirculatory disturbances also were less sharply defined. Restoration of the structure of the kidney was almost complete on the 7th day, when encapsulation of the necrotic focus in the pancreas was achieved. The 24-hourly diuresis also was back to normal at this time: 22.4 ± 1.8 ml compared with 25.0 ± 0.5 ml in the control ($P > 0.2$).

Early and significant changes thus develop in the kidneys in the state of formation of hemorrhagic pancreatic necrosis (after 3 h). These changes, in the form of microcirculatory disorders, disseminated microthrombosis, and focal destruction of the apical zones of the epithelium of the proximal tubules, correspond to the picture of "shock kidney" [3, 12], and they are undoubtedly due both to the general toxic action and to the local action of pancreatic enzymes excreted by the kidneys. The microthrombosis, characteristic of this stage, evidently plays an important role in the pathogenesis of the subsequent renal lesions. The infrequent discovery of microthrombosis in experimental studies and autopsy material [11, 13] can evidently be attributed to the fact that intravascular clots are liquified on recovery from shock. In the stage of "parenchymatous" necrosis of the pancreas, the high blood enzyme level is accompanied by poisoning by pancreatic tissue breakdown products, leading to the development of exudative glomerulitis and focal tubular and glomerular necrosis. It is against this background that the maximal decrease in the 24-hourly diuresis takes place. Encapsulation of the pathological focus in the pancreas leads to relative recovery of the structure and of some of the functional parameters of the kidneys.

Consequently, in acute pancreatic necrosis the kidneys undergo a series of successive changes the manifestations of which depend on the character and stage of the pathological process in the pancreas, and which must be regarded as links of a common pathogenetic chain.

LITERATURE CITED

1. R. A. Burnazyan, A. S. Kanayan, and V. I. Megrabyan, Byull. Éksp. Biol. Med., No. 3, 288 (1981).
2. A. S. Kanayan and P. S. Simavoryan, Byull. Éksp. Biol. Med., No. 11, 548 (1978).
3. N. K. Permyakov, Principles of Resuscitation Pathology [in Russian], Moscow (1979).
4. V. Pozdnyakov, Vrach. Delo, No. 1, 77 (1964).
5. P. S. Simavoryan, "Some aspects of the pathophysiology of pancreatitis," Doctoral Dissertation, Erevan (1973).
6. V. V. Chaplinskii and A. I. Gnatyshak, Acute Pancreatitis [in Russian], Moscow (1972).
7. H. Damman, Med. Klin., 73, 1029 (1978).
8. C. Frey, Am. J. Surg., 109, 747 (1965).
9. D. Gordon and R. Y. Calne, Br. Med. J., 3, 801 (1972).
10. M. Jacobs, J. Daggett, J. Civetta, et al., Ann. Surg., 185, 43 (1977).
11. H. Kwaan, M. Anderson, and L. Gramatica, Surgery, 69, 663 (1971).
12. H. Otto, Med. Klin., 60, 1848 (1965).
13. G. Simon and J. Giacobino, Lancet, 2, 669 (1970).
14. H. Sommer and H. Kasper, Med. Klin., 70, 645 (1975).
15. G. Wense and R. Kühlmayer, Klin. Med., 22, 370 (1967).
16. M. Werner, D. Hayes, C. Lucas, et al., Am. J. Surg., 127, 185 (1974).

MORPHOLOGICAL CHANGES IN THE PANCREAS AFTER TOTAL OCCLUSION OF ITS DUCT SYSTEM BY SYNTHETIC POLYMER MATERIAL

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Surgical treatment of chronic pancreatitis is an urgent and difficult problem. The main aim of treatment is to relieve pain and prevent recurrence of the disease. These aims are achieved at present by extensive resection of the organ and by total pancreatectomy. However, endocrine disturbances arising after total pancreatectomy are difficult to control and there is thus a need for development of a safer and less traumatic method of treatment of chronic pancreatitis.

Observations on patients with advanced forms of chronic pancreatitis show that progression of atrophy of the exocrine parenchyma of the pancreas can lead to weakening and disappearance of the distressing pain so characteristic of this disease [3]. At the same time the results of experimental investigations have shown that in some cases atrophy of the exocrine parenchyma of the pancreas can be produced by ligation of its efferent ducts [2, 4].

However, even a little experience of the use of this method under both experimental and clinical conditions has shown that complete occlusion of the pancreatic ducts is extremely difficult to achieve by ligation because of technical difficulties in the performance of the operation and the risk of development of postoperative complications (aggravation of intraductal hypertension, failure of the ligature with the formation of pancreatic fistulas, and so on).

Accordingly attempts are currently being made to improve the method of occlusion of the pancreatic ducts by their total plugging with synthetic polymers [5, 6]. An extremely im-

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