PATHOMORPHOLOGICAL CHARACTERISTICS OF HEMATOGENOUS COLIBACILLARY PYELONEPHRITIS IN RATS

M. V. Starkov, É. S. Boguslavskaya, and L. I. Lisitsa

UDC 616.61-002.3-092.9-002.7(BACT.COLI)-091

The results of pathomorphological investigations of the kidneys of rats infected intravenously with Escherichia coli 24 h after ligation of the left ureter are described. The rats were sacrificed 24 and 48-72 h and 7 and 24 days after infection. The ordinary histological methods were used. Suppurative inflammation was found in the kidney in the form of diffuse infiltration of the stroma and abscesses, followed by contractions. The initial phases and the subsequent predominant development of this condition were observed in the interstitial tissues of the medulla, in the calyces, and in the collecting tubules of the kidneys.

Experimental pyelonephritis induced by injection of Escherichia coli into the blood stream after temporary ligation of the ureter is widely used in experimental research [2]. Experiments have shown [7, 8, 13] that in the stages of its course, the combination of symptoms, and the morphological picture the experimental lesion is similar to that observed in man. However, the character of the morphological changes in experimental pyelonephritis and their dynamics have been inadequately studied. Some investigators claim that the disease produced by E. coli is characterized by morphological changes in the interstitial tissue around the collecting tubules and the pelvis of the kidney [1], by contrast to staphylococcal infection when the lesions are mainly in the cortex of the kidney [4]. However, the evidence in support of this view is not conclusive. Most workers consider that in hematogenous E. coli infection, by contrast with the ascending urinary infection, the condition spreads from the periphery to the center of the kidneys [3, 10, 11]. The marked similarity of the pathomorphological changes in both types of infection has been reported [5]. The hematogenous or lymphogenous spread of infection has been shown to play an important, or even decisive, role in experimental ascending pyelonephritis [5, 12]. On the other hand, the role of urinogenous mechanisms in the development of the disease cannot be ruled out even after introduction of the pathogenic agent into the blood stream.

This paper describes the results of pathomorphological investigations of experimental pyelonephritis produced in albino rats after intravenous injection of a culture of E. coli 675.

EXPERIMENTAL METHOD

Experiments were carried out on 32 rats of both sexes weighing 150-200 g. Pyelonephritis was produced by the method described in [6, 9]. Under general ether anesthesia the left ureter was ligated. The animals were infected 24 h after ligation by injection of an 18-h culture of E. coli 675 into the caudal vein in a dose of 3×10^8 bacterial cells. The strain had undergone nine previous passages through rat kidneys. The ligature was removed from the ureter 1 h after infection. The pathomorphological investigations were carried out 24 and 48-72 h and 7 and 24 days after infection. Pieces of kidney were fixed in 10% formalin and embedded in celloidin. Histological sections were stained with hematoxylin and eosin and with picrofuchsin by Van Gieson's method. Eight experimental animals were used at each time.

S. Ordzhonikidze All-Union Scientific-Research Institite of Pharmaceutical Chemistry, Moscow. Laboratory of Pathological Anatomy, N. N. Burdenko Chief Military Hospital, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. I. Strukov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 3, pp. 111-114, March, 1973. Original article submitted February 28, 1972.

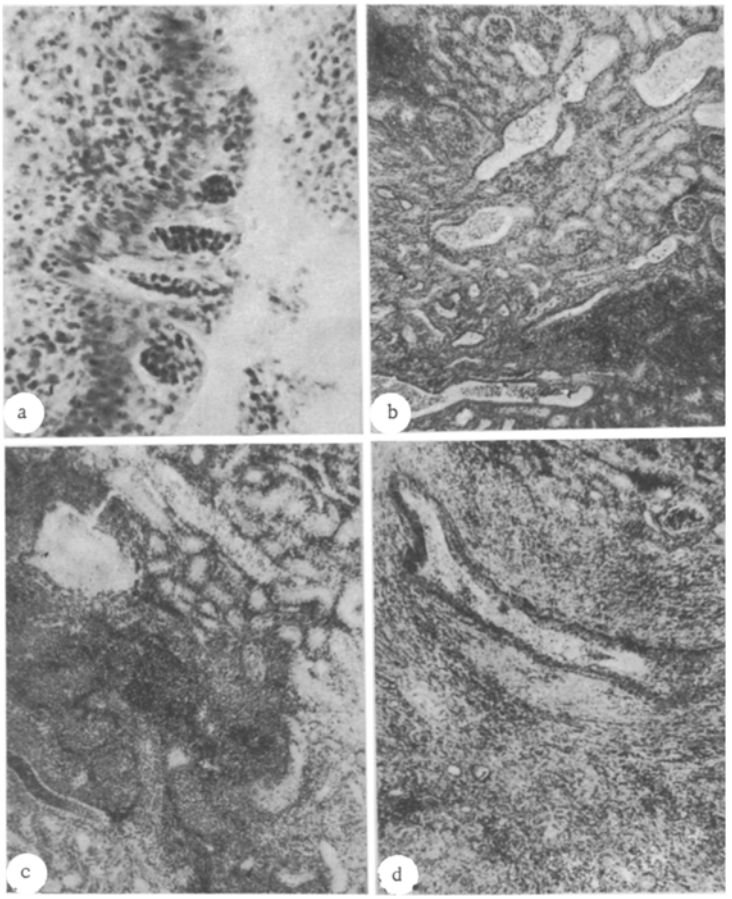

Fig. 1. Changes in kidney tissue in colibacillary pyelonephritis in rats: a) purulent exudate in lumen of renal calyx. Suppurative and lymphocytic infiltration of epithelium and subepithelial layer. Autopsy after 72 h. Hematoxylin-eosin, 600 ×; b) diffuse suppurative inflammation in interstitial tissues of renal cortex. Clusters of leukocytes in lumen of tubules. Autopsy after 7 days, hematoxylin-eosin, 100 ×; c) abscess formation in renal medulla. Many tubules filled with purulent exudate. Autopsy after 7 days. Hematoxylin-eosin, 100 ×, d) marked destruction and sclerosis of renal parenchyma superposed on diffuse suppurative infiltration of all layers. Atrophy of glomeruli and tubules. Autopsy after 24 days Hematoxylin-eosin, 100 ×.

EXPERIMENTAL RESULTS

Under the microscope the left kidney of the rats 24 h after infection was slightly enlarged and congested, and sometimes solitary subcapsular abscesses had developed. The number of abscesses in the kidney of the rats was increased after 48-72 h. Some of the abscesses joined to form larger, irregularly shaped areas of suppuration. By the 7th day the pathological changes were more marked: multiple large abscesses with ill-defined outlines had developed and the lumen of the calyces of the kidney was filled with purulent urine. By the end of the experiment multiple abscesses scattered over the whole surface of the kidney, frequently with areas of necrosis, were found.

Histological investigation of the rat kidneys in the early stage showed slight microfocal infiltration of the stroma with lymphocytes in some animals, mainly in the medulla, together with congestion of the glomeruli with swelling of the capillary endothelial cells and cloudy swelling of the epithelium of the first-order tubules. Solitary polymorphs and small foci of lymphocytic infiltration could be seen in the epithelium

of the calyces. Similar foci were also found in the subepithelial layer. Besides these changes, more marked features of hemostasis could be seen in other animals of this group, especially in the renal capillaries and veins, together with focal infiltration of the epithelium and subepithelial layer with polymorphs. In some rats solitary small abscesses with the initial phase of organization of the pyogenic membrane were visible in the medulla and beneath the capsule of the kidneys. In the center of the abscesses, as a rule, large colonies of bacteria and advanced necrobiotic and necrotic changes in the kidney cells were found.

After 48–72 h of the experiment, diffuse infiltration with lymphocytes and polymorphs, together with numerous colonies of bacteria of different sizes were observed in the interstitial tissues of the kidneys, especially in the medulla, both in the stroma and in the lumen of the collecting tubules. Large abscesses with a wide band of young granulation tissue were formed around individual colonies. Clearly outlined foci of leukocytic infiltration were formed in the epithelium of the calyces. Diffuse infiltration with polymorphs was also observed in the subepithelial layer (Fig. 1a). The lumen of many calyces was filled with purulent masses containing numerous, frequently calcified, colonies of bacteria. Congestion was well-marked in the glomerular capillaries and the renal arterioles and veins of different caliber, while marked degenerative changes were seen in the epithelium of the tubules.

Seven days after infection marked infiltration of the interstitial tissue with purulent exudate was observed in the kidney, where it was superposed on congestion in the blood vessels and edema of the interstitial tissue (Fig. 1b), and also in the epithelium and subepithelial zone of the calyces and individual glomeruli, with the formation of numerous abscesses in different stages of ripeness, located in both the cortex and the medulla. Some abscesses had a ripe pyogenic membrane, while in others it was only just beginning to be formed. Here and there in the renal parenchyma, outside the abscesses, proliferation of granulation tissue with marked destruction of the renal tissue could be seen. Groups and sometimes large collections of polymorphs filled the lumen of many renal tubules. These clusters were particularly frequent in the collecting tubules (Fig. 1c).

The structure of the kidneys of the experimental animals killed 24 days after infection was sometimes so changed as to be unrecognizable on account of the marked diffuse sclerosis of the parenchyma and thinning of all the layers. In many areas there was atrophy of the glomeruli (Fig. 1d). Side by side with marked proliferation of fibrous tissue and suppurative infiltration, groups of hypoplastic glomeruli and degenerated tubules could be seen, the lumen of which as a rule was filled with polymorphs. The very numerous and large abscesses located both in the subcapsular zone and in the depth of the kidney were surrounded by well-developed layers of connective tissue and a zone of fibroblasts. The centers of the abscesses were necrotic, and they contained numerous foci and deposits of calcium salts. The epithelium of the calyces also showed severe degeneration as the result of the diffuse suppurative inflammation, and in many places it was necrotic with the formation of erosions and ulcers. In the lumen of the calyces a purulent exudate mixed with erythrocytes and calcified colonies of bacteria could be seen.

The pathomorphological changes in the kidney after intravenous infection of rats with E. coli and temporary ligation of the left ureter thus exhibit the character of suppurative inflammation, becoming more severe with longer periods of observation, and also becoming uniform in type in all the animals of each separate group. In many animals, at various stages of the experiment more severe inflammatory changes were observed in the pelvis, the collecting tubules, and the interstitial tissues of the renal medulla, a characteristic feature of ascending pyelonephritis. With an increase in the duration of the experiment the suppuration spread throughout the parenchyma, leading to destruction, fibrosis, and contraction of the organ.

LITERATURE CITED

1. I. G. Bachurina, Clinical and Experimental Investigation of Pyelonephritis. Candidate's Dissertation, Voronezh (1966).
2. É. A. Rudzit and L. I. Lisitsa, Farmakol. i Toksikol., No. 2, 246 (1971).
3. V. S. Ryabinskii, The Pathogenesis of Acute and Chronic Pyelonephritis. Candidate's Dissertation, Moscow (1963).
4. L. B. Guze, in: First International Congress of Nephrology. Abstracts, Amsterdam (1960), pp. 43 and 56.
5. R. H. Heptinstall, Nephron, 1, 73 (1964).
6. E. H. Lepper, J. Path. Bact., 24, 192 (1921).

7. W. R. McCabe and G. G. Jackson, in: Biology of Pyelonephritis, Boston (1960), p. 39.
8. V. Prat, D. Benesova, and F. Cervinka, Chekhoslovatsk. Med. Obozr., No. 4, 241 (1959).
9. V. Prat, D. Benesova, L. Pavkova, et al., Acta Med. Scand., 165, 305 (1959).
10. V. Prat, L. Konickova, M. Hatala, et al., Brit. J. Exp. Path., 49, 60 (1968).
11. J. P. Sanford, B. W. Hunter, and P. Donaldson, J. Exp. Med., 116, 285 (1962).
12. E. Vivaldi, R. Cotran, D. P. Zangwill, et al., Proc. Soc. Exp. Biol. (New York), 102, 242 (1959).
13. H. M. Weyrauch, M. L. Resenberg, A. D. Amar, et al., J. Urol. (Baltimore), 78, 532 (1957).