MITOSES IN THE TUBULAR EPITHELIUM OF ALLOGRAFTED HUMAN KIDNEYS

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In the early stages (until 1 month) cells dividing by mitosis were found in the tubular epithelium of allografted human kidneys. Mitoses were located in the proximal and distal convoluted tubules of the nephrons. They exceeded in number 100/cm^2 of the section. Most of the dividing cells were in prophase and in metaphase. Pathological mitoses (colchicine-like metaphases, metaphases with deletions of chromosomes) were rarely seen. The results were compared with information on mitosis in the epithelium of the renal tubules in acute renal failure and data in the literature on regeneration of the renal epithelium in rodents.

Data on the histological structure of allografted kidneys of man and some experimental animals are described in the literature. Most attention has been paid to the description of the morphological substrate of the reaction of rejection of the grafted organ [8, 11, 12, 15, 17]. The development of infiltration by lymphocytes and plasma cells and distinctive changes in the walls of the blood vessels and epithelium of the renal tubules have been observed in allografted kidneys. Meanwhile, not enough attention has been paid to the investigation of regeneration in transplanted kidneys.

This paper deals with mitosis in the tubular epithelium of allografted human kidneys at various times after the operation.

EXPERIMENTAL METHOD

Allografted human kidneys, remaining in the recipient's body for between 2 days and 14 months after transplantation, were used as the test objects. Pieces removed from various parts of the kidney were fixed in 10% neutral formalin or Carnoy's mixture, embedded in paraffin wax, and cut into sections 3-7 μ in thickness. Mitoses in the various parts of the nephrons were identified in sections stained with hematoxylin-eosin and by Van Gieson's method or treated by Feulgen's method. The number of mitoses was counted in each case in 5-10 sections in an area of about 1 cm^2. The ratio between the phases of mitosis was studied and a quantitative description of the mitoses was given by Alov's system [2] in the modification suggested by one of us (V.N.B. [3]).

EXPERIMENTAL RESULTS

Mitoses in the epithelium of the renal tubules were most numerous in allografts which had remained in the recipient's body for a comparatively short time (under 1 month). A description of 2 cases in which the mitotic activity of the tubular epithelium was greatest is given below.

Patient N. (Removal of graft because of rupture on 10th day after operation.) Microscopic examination of sections of the transplanted kidney showed a subcapsular hematoma, necrosis of the fibrous capsule, and necrobiotic changes in the subcapsular zone. The deeper areas of the cortex preserved an almost normal histological structure (presence of a brush border in the epithelium of the proximal convoluted tubules,

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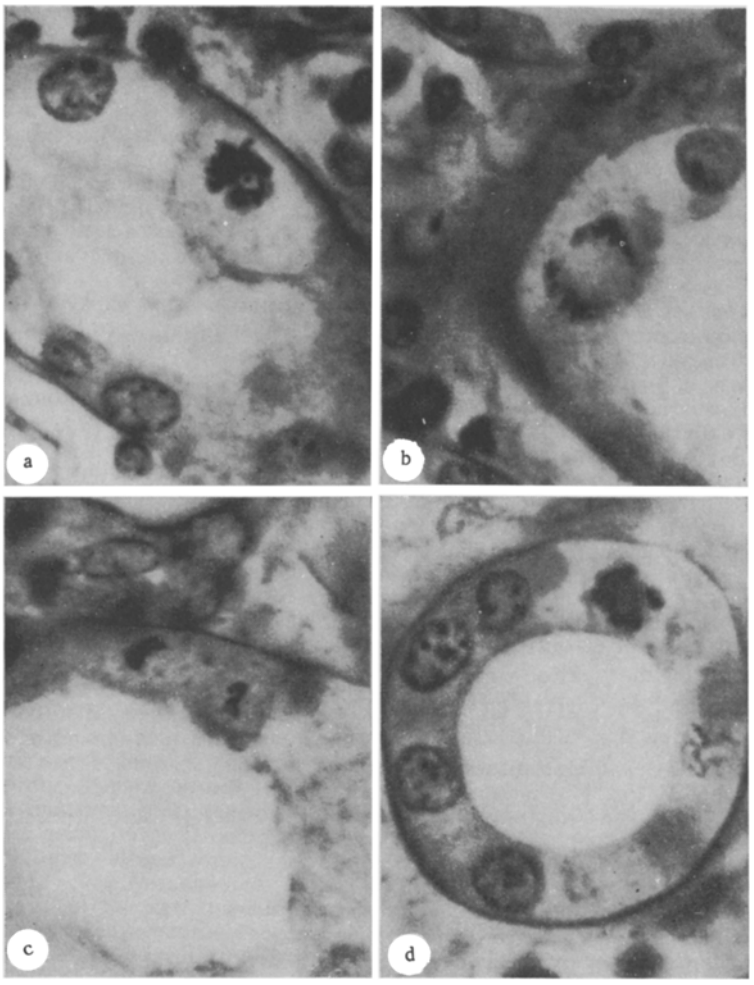

Fig. 1. Mitoses in tubules of allografted human kidneys (10 days after transplantation): a) metaphase; b) anaphase; c) telophase; d) pathological metaphase (C-metaphase). Hematoxylin-eosin, 600 ×.

a normal structure of the epithelium of the loops of Henle and the distal convoluted tubules). Venous congestion of the juxtamedullary portions of the cortex also was observed. Infiltration by lymphocytes was slight in degree and consisted of small foci.

Many mitoses were found in the proximal and distal portions of the nephrons (Fig. 1). A study of 10 preparations showed that there were 105, 98, 83, 102, 92, 95, 109, 103, 84, and 90 mitoses, respectively, per square centimeter of the section (total 961 mitoses, mean 96.1 mitoses/cm^2). The relative number of phases was: prophases 352, metaphases 551, anaphases 18, telophases 40. Prophases and metaphases accounted for 94% of all mitoses, anaphases and telophases for 6%. Among the metaphases there were colchicine-like forms with shortened, thickened chromosomes (64 of 551) and metaphases with deletions of single chromosomes (33 of 551). Pathological forms thus accounted for 17.6% of the metaphases.

Patient V. (Autopsy No. 397/72) died from acute cardiac failure 4 days after the operation of allografting of a cadaveric kidney. Microscopic investigation showed that the histological structure of the transplanted kidney was well preserved. The proximal convoluted tubules in many areas still retained a brush border on the apical surface of the epithelial cells; only a few cells showed vacuolation of the cytoplasm. The structure of the loops of Henle and the distal convoluted tubules was intact and normal. Infiltration of the connective-tissue stroma of the graft by lymphocytes was slight in degree.

Counting the dividing cells in seven specimens showed 48, 42, 39, 44, 46, 41, and 40 mitoses, respectively, per square centimeter (total 300 mitoses, mean 41.4 mitoses/cm^2 of the specimen). By far the predominant forms were prophases (82) and metaphases (214); metaphases with deletion of single chromosomes also were found (11 of 214). The proportion of pathological metaphases was thus 5.14%.

In both cases described, single cells containing one micronucleus besides a nucleus of the ordinary shape and size were found in the proximal and distal convoluted tubules of the allografts.

Rather fewer mitoses were found in four other allografted kidneys after a stay of 20, 10, 19, and 24 days in the recipient. In these cases the number of mitoses in the epithelium of the renal tubules ranged from 10 to 23 per square centimeter of the specimen. Investigation of the allografts in the late stages after the operation showed single mitoses in only one case (a graft remaining 4 months in the recipient).

The causes of appearance of mitoses in the epithelium of the renal tubules of the graft are not absolutely clear. These observations should be compared with information in the literature on the appearance of dividing cells in the epithelium of the renal tubules of patients dying from acute renal failure [5-7, 16]. Kan'shina [6] states that mitoses appear 4-8 days after the onset of anuria, when damage to the tubular epithelium is comparatively slight. The present observations must also be compared with the division of the tubular epithelial cells of rodent kidneys which has been described [1, 4, 9, 10, 13, 14]. There is interesting evidence to show that the number of mitoses in rat kidneys rises after temporary ischemia [14]. The number of mitoses in the epithelium of the loops of Henle increases 36 h after interruption of the circulation for 1 h, and it increases later in the distal convoluted tubules. The number of pathological mitoses rises, and ultimately atypical nuclei appear.

It is reasonable to suppose that mobilization of the epithelium of the human renal tubules and the onset of mitotic division by cells of the allografted kidney may be attributed to the effects of ischemia, an unavoidable factor in kidney transplantation experiments. The possibility cannot be ruled out that the accumulation of mitoses in metaphase and the appearance of pathological forms of metaphase may be to some extent also a result of immunodepressive therapy given in the postoperative period. A more definite answer to these questions will be obtained by comparing the results described above with the results of appropriate experiments on animals.

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