MORPHOLOGY OF THE JUXTAGLOMERULAR APPARATUS OF ALLOGRAFTED HUMAN KIDNEYS IN THE EARLY PERIODS AFTER TRANSPLANTATION

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In the early stage of existence of the allografted kidney in the recipient, hyperplasia of cells of the juxtaglomerular apparatus — epithelioid-modified cells of the afferent arteriole and of Goormaghtigh's cells (the lacis) — is observed. These changes are combined with elevation of the juxtaglomerular index, and in conjunction with the results of karyometric investigation, they are evidence of activation of the juxtaglomerular apparatus of the allografted human kidney during the first month after transplantation.

KEY WORDS: *Kidney; transplantation; juxtaglomerular apparatus.*

The juxtaglomerular apparatus (JGA) of the kidney is one of the most important components of the renin-angiotensin system. Its structure has been the subject of many investigations [1, 3, 5, 7-10]. However, no special studies of the histological and cytological characteristics of the JGA of human allografted kidneys could be found in the literature. The investigation described below was carried out to study this problem.

EXPERIMENTAL METHOD

Material obtained after removal of allografted kidneys (because of rupture or hemorrhage) and postmortem material, altogether from 14 allografted kidneys which had been present for 2 to 35 days in the recipient's body, was studied. Pieces of cortex were fixed in 10% neutral formalin and some material was fixed in Helly's mixture. The material was embedded in paraffin wax. Sections 3-7 μ thick were stained by the ordinary histological methods and also by Masson's method and the PAS and Feulgen reactions were carried out. Eight kidneys from persons dying from accident or acute heart failure were used as the control. Sections through the cortex of six (of 14) allografted kidneys present in the recipient's body for between 4 and 20 days and from five control kidneys were stained by Bowie's method [9, 10] to reveal the specific granularity of the JGA. The juxtaglomerular index (JGI) was determined by the method of P. and W. Hartroft [9].

EXPERIMENTAL RESULTS

On general inspection of allografted kidneys during autopsy or after their removal at operation extensive hemorrhages were usually found in the subcapsular zone and focal hemorrhages in various parts of the cortex. Histological investigation revealed multiple hemorrhages in superficial areas of the cortex of the allografts. In some cases a more or less well marked cellular immune response (perivascular and pericorpuscular zones of lymphocytic infiltration) was observed. Close to the hemorrhages zones of necrobiotic and degenerative changes were found in the parenchyma, especially the epithelium of the proximal tubules. These areas, in turn, were founded by wide zones in which the degenerative changes in the parenchyma were slight in degree. It was in these zones that the histological structure and cytological features of the JGA of the transplanted cells could be studied in the greatest

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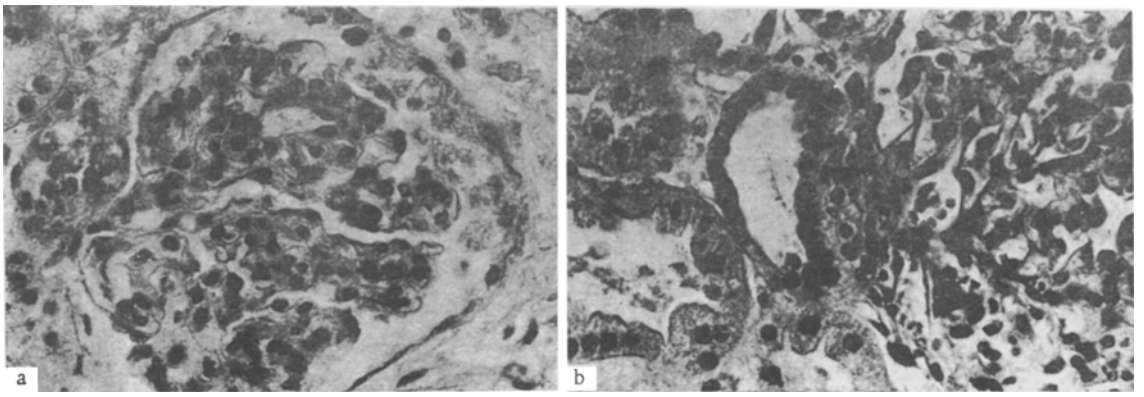

Fig. 1. Juxtaglomerular apparatus of allografted kidney of patient R. (20 days after transplantation): a) large epithelioid-modified JGA cells (afferent arteriole); b) hyperplasia of cells. Hematoxylin-eosin, 200×.

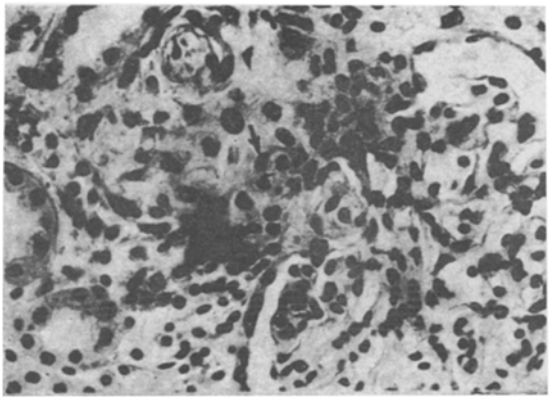

Fig. 2

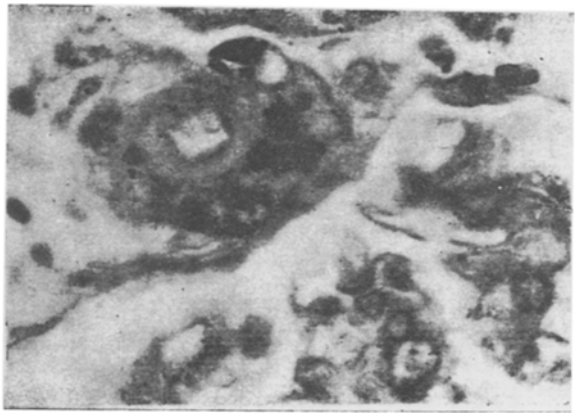

Fig. 3

Fig. 2. Three-pole mitosis of Goormaghtigh's cell of JGA. Allografted kidney of patient K. (4 days after transplantation). Hematoxylin-eosin, 200×.

Fig. 3. Granules in cytoplasm of epithelioid-modified JGA cells (afferent arteriole). Stained by Bowie's method, 600×.

detail. In the intact zones of cortex described below the proximal and distal tubules had the typical structure (the brush border in the proximal tubules was completely intact). The malpighian corpuscles had their normal configuration. The space of Bowman's capsule could be clearly distinguished in them, the capillary loops were clearly outlined, unchanged erythrocytes were seen in the lumen of the capillaries, and nuclei of the endothelium, podocytes, and mesangial cells could be made out. Under these circumstances the structure of the JGA was intact (Fig. 1). Afferent arterioles approaching these malpighian corpuscles had cuff-like thickenings. Their walls consisted of a flat endothelial lining and two or three layers of large smooth-muscle cells of the JGA with epithelioid modification. They measured 20-30 μ in diameter and their nuclei were spherical in shape and appeared larger than the nuclei of the same cells in the JGA of the control kidneys. A karyometric study of the JGA of the allografted and control kidneys by Khesin's method [4] revealed a highly significant increase in the volumes of the nuclei of the epithelioid-modified cells of the grafted kidneys compared with the control. In all cases studied, $t>3$ [12].

Considerable changes in the Goormaghtigh's cells (GC) composing the lacis, a group of JGA cells bounded at their sides by afferent and efferent arterioles of the malpighian corpuscle and at their base by the epithelium of the macula densa of the distal portion of the nephron, also were observed in the allografted kidneys studied. The number of GC was greater than in the control. Most GC contained large, pale nuclei, larger than those of GC in the JGA of the control kidneys. The increase in size of the nuclei of GC in the allografted kidneys was highly significant, as the karyometric investigation showed [2].

TABLE 1. Values of JGI for Control Kidneys

Cause of death	JGI
Head injury	3
" "	0
" "	0
Acute heart failure	4
Ditto	0

TABLE 2. Values of JGI for Allografted Kidneys

Time after transplantation (in days)	Causes of removal of graft or of patient's death	JGI
20	Rupture of graft	101
7	Ditto	90
4	Acute heart failure	45
6	Ditto	41
7	Toxemia	14
4	Cerebral edema	13

At the same time, it must be emphasized that the increase in nuclear volumes of the epithelioid-modified cells and GC of the transplanted kidneys was combined with proliferation. For instance, nuclei of GC dividing by the formation of a constriction ring were frequently seen [the allografted kidneys of patients R. and K. (rupture of the graft) and patient V. (death from acute heart failure 4 days after transplantation)]. Single mitotically dividing GC also were found and, in one case (allografted kidney of patient K., removed because of rupture 4 days after transplantation) a three-pole mitosis in a GC was observed (Fig. 2).

The results of the study of the JGI of the allografted kidneys are given in Tables 1 and 2.

In the allografted kidneys JGI reached high values, much higher than JGI for the control kidneys. The patterns obtained by staining by Bowie's method in many cases corresponded to 3+ and 4+ on the Hartrofts' scale (Fig. 3), evidence of increased renin production by the epithelioid-modified JGA cells of the allografted kidneys.

The results indicate that hyperplasia of the epithelioid-modified cells of the afferent arteriole and of GC (the lacis), similar to the postischemic hyperplasia of the JGA cells produced experimentally in the isologous kidney in animals, described in the literature [6, 8], takes place in the JGA of allografted human kidneys in the early period after transplantation. The hypothesis regarding activation of JGA of the allografted kidney is supported by the results of the study of the JGI. The facts indicate the need for a further study of structural and functional changes in this most important regulator of the intramural renal blood flow after transplantation.

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