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

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The histological structure of 13 allografted cadaveric kidneys was studied after remaining in the body of the recipients for between 121 days and 3 years 10 months. The structure of the juxtaglomerular apparatus (JGA) in grafted kidneys with a well preserved structure was essentially indistinguishable from that of JGA of the control kidneys. This conclusion is supported by the results of karyometric investigation and of counting the juxtaglomerular index. During the development of considerable destructive and degenerative changes in the allografted kidney, partial or complete involution of JGA may take place.

KEY WORDS: *human kidney; allografting; juxtaglomerular apparatus.*

In previous publications [1-4] structural changes were described in the juxtaglomerular apparatus (JGA) of allografted human kidneys in the early stages after transplantation. The changes consisted of hyperplasia of epithelioid-modified cells (EMC) of the efferent arteriole and of Goormaghtigh's cells, forming the lacis of the JGA. The phenomenon of hyperplasia of JGA is accompanied by an increase in the juxtaglomerular index. The results, combined with those of karyometric investigation, indicated activation of JGA of the allografted human kidney during the first month after transplantation.

The object of this paper is to describe changes in the structure of JGA of allografted cadaveric human kidneys in the late stages after transplantation.

EXPERIMENTAL METHODS

The histological structure of 13 allografted kidneys was studied after remaining in the recipient's body for between 121 days and 3 years 10 months (12 kidneys were removed at autopsy and one on account of functional failure). These 13 cases were divided into groups A and B. Group A included 10 cases, in six of which (subgroup 1 of group A) the recipient died after 130-605 days from septicopyemia arising against the background of prolonged immunodepressive therapy; in the other four cases (subgroup 2 of group A) failure of the grafted kidney took place on account of a chronic rejection reaction (the case in which the nonfunctioning kidney was removed belonged to this subgroup). Group B included three cases in which, judging from

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the history, function of the allografted kidneys was satisfactory. Two recipients died from severe complications resulting from prolonged immunodepression (hematogenous generalization of tuberculosis, pneumonia with abscess formation), and one patient died from serum hepatitis.

Material was fixed in 10% neutral formalin or in some cases with Helly's mixture. Sections 3-7 μ thick were stained by the ordinary histological method and also by Masson's method, the PAS reaction, and Feulgen's method. The karyometric investigation was carried out by Khesin's method [5] on seven allografted kidneys: four from group A, three from group B. In eight cases the juxtaglomerular index was determined by the method of P. and W. Hartroft [6]. Sections stained by Bowie's method [6, 7] were used for this purpose. Sections from the kidneys of persons dying from head injury, acute heart failure, or benign brain tumor served as the control.

EXPERIMENTAL RESULTS

Pyemic foci were found in the allografted kidneys of subgroup 1 of group A. The grafted kidneys were variegated in appearance and flabby in consistency because of irregular congestion and edema. On section, foci of suppurative liquefaction could be seen in their cortex. In these areas total destruction of the malpighian bodies and their JGA were observed. Close to the suppurative foci the renal gomeruli and JGA were undergoing destruction. In regions more remote from the pyemic foci a few glomeruli could be seen near which cells of the JGA were detectable. The EMC of the afferent arterioles in these cases were not appreciably different in appearance and size from the corresponding cells in the control. However, the third component of JGA — epithelium of the macula densa — appeared considerably altered. Its cells were flattened and contained hyperchromic nuclei. The fact that these cells belonged to the epithelium of the macula densa could be deduced only from their localization.

The most conspicuous feature in the allografted kidneys of subgroup 2 of group A was the appearance of interstitial sclerosis against the background of plasma-cell infiltration. Marked atrophy of the tubular epithelium was observed in different parts of the nephrons, together with coarse sclerosis of the renal glomeruli. All three components of JGA had virtually completely disappeared because of replacement of Goormaghtigh's cells by connective tissue, sclerosis of the wall of the afferent arterioles, and atrophy of the epithelium of the distal tubules, especially in the region of the macula densa.

A characteristic feature of allografted kidneys of group B was alternation of zones with marked degenerative and sclerotic changes and extensive areas occupied by relatively unchanged parenchyma. Numerous malpighian bodies were distributed in these zones, with clearly distinguishable structural components of the JGA near them. The number and size of the EMC of the afferent arterioles were a little greater than in the control, and in the lacis zone solitary Goormaghtigh's cells with two or three nuclei were present. The epithelial cells of the macula densa had the typical structure and were almost indistinguishable from the corresponding cells in the control kidneys.

The results of the karyometric investigation (Tables 1 and 2) show that in the later periods of existence of the allografted kidneys in the recipient's body there was a definite parallel between the structure of JGA and changes in the microscopic structure of the tubules

TABLE 1. Mean Logarithms of Volumes of Nuclei (in μ^3) of Cells of JGA of Allografted Human Kidneys in Later Periods of Stay in Recipient's Body (subgroup 1 of group A; M±m)

Patient's initial	EMC	t^*	Goormaghtigh's cells	t^*	Epithelium of macula densa	t^*
R	1,736±0,01315	1,8	1,746±0,01533	4	1,994±0,01890	6
V	1,800±0,01892	2	1,736±0,01646	4,4	2,015±0,01391	3,7
Kh.	1,799±0,01447	1,6	1,617±0,01322	7	1,960±0,01207	8
Shch.	1,723±0,01240	2,4	1,630±0,01649	6	2,008±0,01514	4
Control (weighted mean)	1,764±0,004491		1,811±0,04645		2,070±0,004153	

*Here and in Table 2 values of t were calculated relative to weighted mean (control).

TABLE 2. Mean Logarithms of Volumes of Nuclei (in μ^3) of Cells of JGA of Allografted Human Kidneys in Late Periods of Stay in Recipient's Body (group B; M±m)

Patient's initial	EMC	t^*	Goormaghtigh's cells	t^*	Epithelium of macula densa	t^*
K	1,834±0,01668	4	1,800±0,01755	1	2,059±0,01461	1
T	1,836±0,01487	4,5	1,771±0,01802	2,2	2,057±0,01423	1
P	1,909±0,01447	9	1,817±0,01342	1	2,060±0,01217	1
Control (weighted mean)	1,764±0,004491		1,811±0,04645		2,070±0,004153	

of grafted kidney. If the parenchyma of the graft was well preserved (group B) the size of the nuclei of the Goormaghtigh's cells and the epithelium of the macula densa did not differ significantly from the size of the nuclei of these cells in the control ($t < 3$). Meanwhile the size of the nuclei of EMC of the afferent arterioles was greater than in the control ($t > 3$) (Table 2). When gross disturbances of the structure of the grafted kidney were present (subgroup 1 of group A) the changes in volume of the nuclei of EMC of the efferent arterioles were not significant ($t < 3$) but the decrease in size of the nuclei of the Goormaghtigh's cells and epithelium of the macula densa was significant ($t < 3$).

The juxtaglomerular index of the allografted kidneys of groups A and B was the same as in the control kidneys. In three of eight cases this index was 3-6. The estimate according to the Hartrofts' scale did not exceed 1+ or 2+, indicating low secretory activity of the JGA cells containing specific granules stained by Bowie's method. In the other cases no JGA cells with specific granules in their cytoplasm could be found.

The structure of JGA of the allografted human kidneys investigated after a long period in the recipient's body (from 121 days to 3 years 10 months) thus differend depending on the state of the grafted kidney. In cases when no considerable destructive or degenerative changes had developed in the kidney and its function remained good, the structure of JGA was essentially indistinguishable from the structure of JGA of the control kidneys. This phenomenon of "normalization" of the structure of JGA merits attention because, as the writers showed previously [1-4], during the first month after transplantation hyperplasia of JGA takes place in the allografted human kidney, evidence of its activation. Similar results were obtained by other workers in experiments on animals [8]. If the function of the grafted kidney remains preserved for a long time, the JGA becomes adapted to the new conditions and is reorganized in accordance with the hemodynamic requirements of the graft. Should sclerosis develop in the graft (as the result of a chronic rejection reaction) or should destructive processes ensue, death of JGA takes place. In that case the allografted kidney completely loses its JGA – a vital regulator of the internal blood flow through the kidney and an essential component under normal physiological conditions.

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