SOME HISTOLOGICAL ASPECTS OF HOMOTRANSPLANTED KIDNEY IN MAN

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The histopathological aspects of the renal lesions occurring after homotransplantation are well known. The aetiology of the lesions is however often the subject of discussions. Renal lesions occurring after a homotransplantation could be due either to the previous disease affecting the new kidney, an immunological reaction of the host versus the graft, or to the toxic action of the various drugs used in the treatment of the patient. The purpose of this paper is to present some unusual histological lesions found in a patient with no previous history of glomerular nephritis.

Fig. 1. Nephrectomy specimen. Dilatation and marked tortuosity of the ascending limb of Henle's loop. Thickening of the basel membrane of the descending limb with marked interstitial infiltration. (P.A.S. 150 ×.) (Reduced 25% for reproduction.)

The patient was a 28-year-old male who developed a renal insufficiency due to a juvenile nephronophthisis. As far as we know no previous cases of this disease had been reported in adults. The diagnosis was based on the typical family history, the existence of polydypsia since early childhood, without signs of glomerular involvement and the final progression to renal insufficiency. This diagnosis was confirmed by the histological study of the kidney obtained at the moment of the transplantation. Figure 1 shows a typical aspect of the lesions observed in the papillary region. In February 1964 a homotransplantation was performed
Fig. 2. General survey of the renal function and of the immunosuppressive treatment after homotransplantation.

Fig. 3. Biopsy 12 months after transplantation. Note focal dilatation of capillary loops with swollen endothelium, interstitial oedema and lymphocytic infiltration. (P.A.S. 750 ×) (Reduced 25%).
with the kidney of the sister who had no evidence of renal disease. After an initial diuresis of two litres the patient developed an oliguria of 600 to 1000 ml which persisted for 10 days.

Fig. 4. Biopsy 12 months after transplantation. Cystic dilatation of capillary loops. Marked endothelial proliferation of 2 small cortical arteries. (P.A.S. 500 ×) (Reduced 25%)

Fig. 5. Removed kidney 17 months after transplantation. Two different stages of the evolution of glomerular lesions. The glomerulus at the right presents a marked dilatation of the capillary loops. Considerable proliferation and shrinkage of the glomerulus on the left. (P.A.S. 300 ×) (Reduced 25%)
A first renal biopsy was performed at that moment. This biopsy showed tubular lesions with a flat epithelium. There was also interstitial oedema and localized lympho-plasmocytic infiltration around the small vessels of the kidney cortex. The glomeruli were normal. This was interpreted as a minor form of tubular necrosis. Without special therapy a diuretic phase followed during which urine volumes of 3000 ml and more were observed. Thirty-two days after transplantation the patient developed signs of rejection. He was treated with high doses of Prednisone (Figure 2) and Imuran. During two episodes of leucopenia the dosage of Imuran was reduced. A second renal biopsy showed only the existence of a massive interstitial oedema without cellular infiltration. This early rejection was well controlled and the creatinine clearance rose to 60 ml per minute. The blood pressure was normal after reduction of the dosage of steroids. A control biopsy after 4 months showed the same picture and the absence of glomerular lesions. From the 6th to the 12th month after transplantation a progressive lowering of the creatinine clearance was noted, the diastolic blood pressure remained above 100 mm Hg and a slight proteinuria appeared. An increase in the doses of Imuran and Prednisone remained without effect on the clinical symptoms. A biopsy performed after 12 months showed vascular and glomerular lesions. There was a proliferation of the intima of the small arterioles, with a moderate lymphoplasmoocyte infiltrate around the vessels. In some glomeruli an unusual lesion was observed, consisting of dilatations of isolated capillary loops, associated with focal intra- and extracapillary proliferations. The dose of Prednisone was increased to 30 mg/day, but the creatinine clearance decreased progressively and 17 months after transplantation values of 16 ml per minute were obtained. Because of an important increase in blood pressure the kidney was removed.

The macroscopic examination revealed a smooth pale kidney, weighing 198 g. Histologic examination disclosed glomerular vascular, interstitial and tubular lesions.

The glomerular lesions were polymorphic. Some glomeruli presented an unusual lesion of focal dilatations of the capillary loops. In some of these lesions the endothelium is swollen.

Fig. 6. Same picture of capillary dilatation with proliferation of the endothelium. (P.A.S. 400 x). (17 months after transplantation). (Reduced 25%)
and in some instances there is endothelial proliferation. The basement membrane surrounding these dilated loops is distended as if the mesangial cells which normally support the capillary loops had disappeared, resulting in fusion of adjacent capillary loops. At a later stage the capsular epithelial cells proliferate. Bowman’s space is then occupied by crescents of epithelial cells containing numerous hyaline droplets. The capillary loops are progressively repelled by this extracapillary proliferation and reduced to a skeleton of basement membrane-like material.

Figs. 7 and 8. Other aspects of these unusual marked focal dilatation of the capillary loops. (P.A.S. 750 ×) (17 months after transplantation). (Reduced 25%).
All the arteries of the kidney presented an obliterative proliferation of the intima, without hyalinisation of the media. The lamina elastica interna is reduplicated. In some arterial segments the lamina elastica interna may even disappear.

*Figs. 9 and 10.* In a further stage of evolution, extracapillary proliferation with shrinkage of the dilated loops. (P.A.S. 500 x) (17 months after transplantation).

(Reduced 25%)
Disseminated lesions of tubular atrophy and regeneration similar to those described in the rat after local irradiation (Maldague, 1962) are found in this kidney.

There is interstitial oedema with focal lympho-plasmocytic infiltrates, without sclerosis.

Figs. 11 and 12. Classical aspects of the intimal proliferation of the endothelium of arteries and associated lesions of the lamina elastica interna. (Verhoef's stain for elastin, 300 ×). (17 months after transplantation). (Reduced 25%).
Discussion

The vascular lesions found in this kidney after 17 months of homo-transplantation are similar to those described by Porter (1964). There are good reasons to believe that these lesions can be due to an immunologic reaction. The interpretation of the glomerular lesions is however more difficult. In our opinion the earliest lesion responsible for the capillary dilatations could be a lesion of the mesangial cells. Endothelial proliferation and the formation of extracapillary crescents of epithelial cells occur later. This interpretation is supported by the fact that experimental lysis of the mesangial cells results in fusion of the capillary loops and formation of intraglomerular cysts (Kawaji and Oyama, 1960). The origin of this mesangial lesion is more difficult to determine. Similar lesions have however been reported in rabbits after administration of large doses of cortisone acetate (Bouissou, Familiadès, Rakotondrainibe and Castagnol, 1964). This suggests that the lesions observed in this case might at least in part, be due to the long term administration of high doses of Prednisone. It is however evident that more experimental data are urgently needed in order to distinguish the lesions due to rejection phenomena from the toxic effects of the immuno-suppressive therapy.

REFERENCES


DISCUSSION

The Chairman: Merci beaucoup, M. Michielsen, pour ces très belles images. Je crois qu’il a été fort utile de suivre, grâce à vous, une observation étudiée en détail tout au long de son évolution. Ainsi ceux qui dans l’assistance, n’ont pas vu un de ces cas auront une idée plus concrète des problèmes réels qui se posent au médecin.

Nous allons rester dans ces problèmes de clinique et d’anatomie pathologique, en demandant à MM. Traeger et Fries de présenter leurs premiers cas d’hétérotransplantation.