An Experimental Histopathological Study on Some "Membranous" Lesions in Glomerular Loops

AN EXPERIMENTAL HISTOPATHOLOGICAL STUDY ON SOME "MEMBRANOUS" LESIONS IN GLOMERULAR LOOPS

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The term "membranous" has been originally applied to the thickened basement membrane of glomerular loops consistent with a nephrotic syndrome. Pathologic processes underlying the similar "membranous" thickenings of the glomerular basement membrane at the level of light microscopy such as glomerular lesions of membranous glomerulonephritis, wire-loop glomerular lesions of SLE, and various sclerosing processes of glomeruli have to be more precisely elucidated under the electron microscope. The common problem to these various pathologic processes lies in the thickening of the filter membrane of to some degree blood-supplied glomeruli associated with deranged permeability, which appears to be intimately related to the chronicity or prolongation of glomerulonephritis. In this report analyses of "membranous" glomerular lesions in Masugi nephritis of rats, and in experimental uremia and decreased renal blood flow in rabbits employing electron microscopy and fluorescent antibody technique are presented.

Masugi Nephritis of Rats: Masugi nephritis induced in rats by a single injection of anti-rat-kidney rabbit γ-globulin is characterized by development of a degenerative glomerulitis comparable in its histogenesis to that of wire-loop lesions in human SLE in the 1st phase, and by an exacerbation due to the occurrence of proliferative glomerulitis in the 2nd phase. The glomerular loops of rat kidneys in the 1st phase, already in a few hours after a single injection, showed thickening of the lamina densa up to 600 mμ and subendothelial deposition of finely granular electron-dense material measuring up to 800 mμ in thickness. The material demonstrated neither fibrillar structure nor periodicity. The capillary lumina showed some thrombosis and the endothelial cells exhibited enlargement of the cytoplasms accompanied
by swelling of mitochondria and vacuolization. Fusions of the foot processes of epithelium were also visible (Fig. 1). In the thickened areas of the loop walls deposition of anti-rat-kidney rabbit T-globulin and the property of complement fixation were clearly demonstrated by fluorescent antibody technique. The glomeruli in the 2nd phase, i.e., 4 to 7 days after injection or thereafter had diffusely thickened basement membrane including lamina densa with nodular projections toward epithelial side the maximal thickness of which measured 650 μ. The glomerular loops developed endothelial proliferation and some subendothelial deposition of electron-dense material. Formation of basement membrane-like materials along the proliferated cells was also noted in the specimen of more than 3 days after the initiation of 2nd phase. Enlargement of the epithelia associated with fusions of foot processes and deposition of hyaline droplets were recognized not infrequently. Fluorescent antibody technique revealed new fixation of rat T-globulin (probably anti-rabbit-T-globulin antibody) to the loop walls simultaneously with the onset of 2nd phase.

*Experimental Uremia in Rabbits:* In order to induce a uremic state in rabbits without preceding renal tissue alterations an extensive nephrectomy, i.e., initial 2/3 resection of unilateral kidneys followed by total nephrectomy of the opposite side at the intervals of 1 to 15 days was employed. In the extensively nephrectomized rabbits which developed an elevation of serum urea N level as far as 130 mg/dl residual glomeruli showed an increase in numbers of small vesicles in the cytoplasm of capillary endothelium, fusions of the foot processes of epithelial cells with deposition of electron-dense granular materials measuring up to 260 μ, and thickening of the basement membrane up to 130 μ having duplication of the lamina densa as far as the observation for 88 days after extensive nephrectomies (Fig. 2). The electron-dense materials noted here appear to be leaked plasma proteins including fibrinoid.

*Experimental Reduction of Renal Blood Flow in Rabbits:* For this purpose an incomplete ligation of left renal arteries of rabbits was carried out, and histological changes of the glomeruli in homolateral kidneys were studied by serial renal biopsies and following autopsies for 11 days after the treatments. The animals developed
neither hypertension nor a sign of uremia. Electron microscopic studies revealed in
the glomeruli of diseased kidneys a tendency to loss of endothelial pores, swelling
of endothelial cells, edematous thickening of the basement membrane measuring up
to $282 \mu m$ with duplication of the lamina densa, and fusions of the foot processes
and swelling of the mitochondria of epithelial cells (Fig. 3).

Reference


Fig. 1. A degenerative glomerulitis in Masugi nephritis. 7. 21 hours after injection of anti-rat-kidney rabbit $\gamma$-globulin. Autopsy. Rat R 68.
Fig. 2. Uremic glomerular lesion. 3 days after extensive nephrectomy. 2nd biopsy. Rabbit U 36.

Fig. 3. Edematous thickening of glomerular loop walls in decreased renal blood flow. 11 days after unilateral renal arterial constriction. Autopsy. Rabbit U 50.