REACTIVE PROPERTIES OF MESANGIAL CELLS OF THE RENAL GLOMERULUS DURING EXTREMAL LOADING OF THE KIDNEY

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UDC 616.611-008.615-091.8

KEY WORDS: mesangiocytes; mesangio-capillary prolapses; glomerular capillaries; reactive properties; endothelial barrages.

Although more than 300 years have elapsed since Malpighi discovered the renal glomerulus, some problems relating to its cellular structure have not yet been adequately studied. Three types of cells are distinguished in the glomerulus: 1) epithelial cells of the inner part of the glomerular capsule — podocytes; 2) endotheliocytes lining the glomerular capillaries internally; 3) mesangial cells (MC). Cells of the third type, which are among the most reactive components of the glomerulus, have received less study as regards their origin, structure, and functional role [4, 5, 11].

This paper gives the results of an electron-microscopic study of certain reactive properties of MC with an extremal functional load on the kidney.

EXPERIMENTAL METHOD

Three series of experiments were carried out on kidneys of 18 adult noninbred albino rats of both sexes: series I) production of acute ischemia by clamping the renal pedicle for 30 and 60 min, followed by restoration of the blood flow; II) stimulation of vasorenal hypertension by constricting the abdominal aorta above the site of origin of the renal arteries; series III) compensatory hypertrophy of the residual kidney. Ultrathin sections through the renal cortex were fixed in buffered OsO_4 solution, dehydrated, and embedded in a mixture of Epon with Araldite, for examination in the UÉMV-100B electron microscope. Kidneys of six rats served as the control.

EXPERIMENTAL RESULTS

MC are located among the loops of the glomerular capillaries, mainly of the centrolobular part of the glomerulus (Fig. 1). Their round, ovoid nuclei are surrounded by an osmiophilic membrane with irregular outlines. Electrondense chromatin granules are distributed diffusely in the karyoplasm. The rough endoplasmic reticulum contains many ribosomes and polysomes. In the cytoplasm of MC there are a few pinocytotic vesicles and mitochondria; individual lysosomes and microfilaments can be seen. The lamellar complex lies near the nucleus.

In their cytostructural features MC can be compared with cells of the juxtavascular islet and they belong to the reserve components of the juxtaglomerular complex [2, 7]. There is evidence [1, 4] that during functional overloading of its epithelioid cells, granules containing a renin-like substance may be found in MC. Some workers regard MC as derivatives of smooth myocytes [13, 15] of the afferent arteriole.

MC have cytoplasmic processes which penetrate into the space bounded by the approximated basal membranes of the glomerular capillaries. The processes are surrounded by a membrane-like matrix and they are in contact with narrow strips of the endothelial lining of the capillaries, which have no basal membrane. Along the length of these strips zones of proliferation of endothelium, performing the function of unique supporting senses or barrages (Fig. 2) can be distinguished. In our opinion they are adaptive miniature spring

Department of Human Anatomy, Ivano-Frankovsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Kupriyanov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 97, No. 1, pp. 95-98, January, 1984. Original article submitted February 15, 1983.

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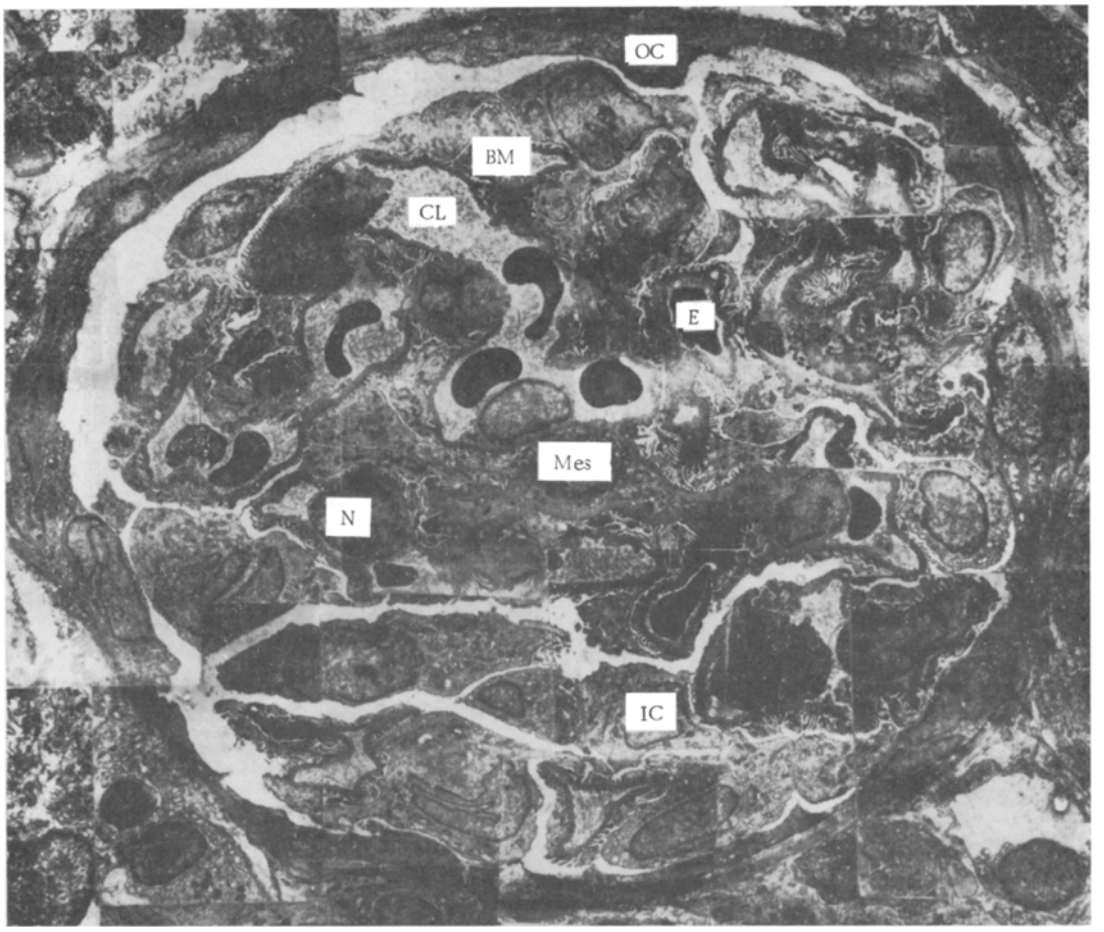

Fig. 1. Panoramic electron micrograph of rat renal glomerulus. OC) Cells of outer part of capsule, IC) cells of inner part of capsule (podocytes), CL) capillary lumen, N) nucleus of endotheliocyte, E) erythrocyte, BM) basal membrane, Mes) mesangial cell. 3000 ×.

shock absorbers which, depending on the state of the hemodynamics in the glomerular capillaries, swell or become flat, and adapt the diameter of their lumen to the hydrostatic pressure of the circulating blood.

A change in intensity of the blood flow in the capillaries or in the pressure gradient and tension of their walls during temporary circulatory ischemia followed by restoration of the circulation, and a disturbance of homeostasis in the glomeruli in glomerulopathies cause considerable ultrastructural changes in the glomerular capillaries and nephrons and bring MC and, in particular, their processes into a reactive state. This is manifested as the ultrastructural equivalent of an increase in the synthetic function of these cells and a tendency for the processes to migrate, or even to "settle" in the lumen of the capillaries [3, 4, 15].

On the basis of the results of these experiments, three types of mesangial processes can be distinguished depending on their degree of migration. Processes of type 1 only make contact with the capillary endothelium at the boundary with the barrages described above. Processes of type 2 appear swollen, they loosen the structure of the barrages, and begin to prolapse into the capillary lumen. Processes of type 3 are appreciably enlarged in volume, perforate the endothelial barriers, and penetrate into the capillary lumen as fungiform diverticula of different sizes. They consist of electron-transparent material and have no organelles. Under normal conditions processes of types 1 and 2 are usually found and those of type 3 are much less common. During simulation of vasorenal hypertension in rats (experiments of series II) an increase in the number and volume of type 2 processes was observed in the early stages of the experiments, in agreement with the results of corresponding experiments on dogs [11].

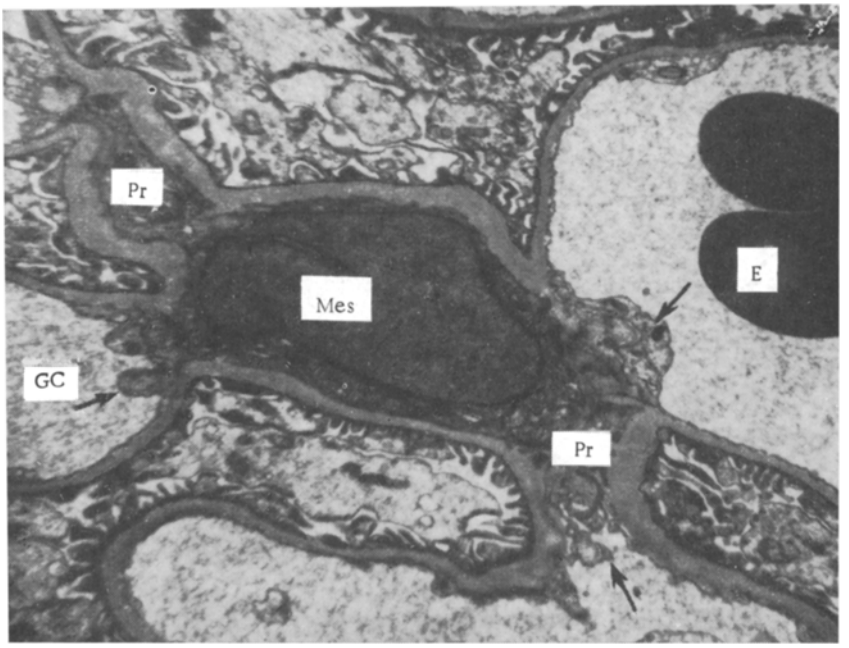

Fig. 2. Relationship of MC (Mes) and its processes (Pr) to surrounding glomerular capillaries (GC). Arrow indicates endothelial barrages, E) erythrocytes. 8000 ×.

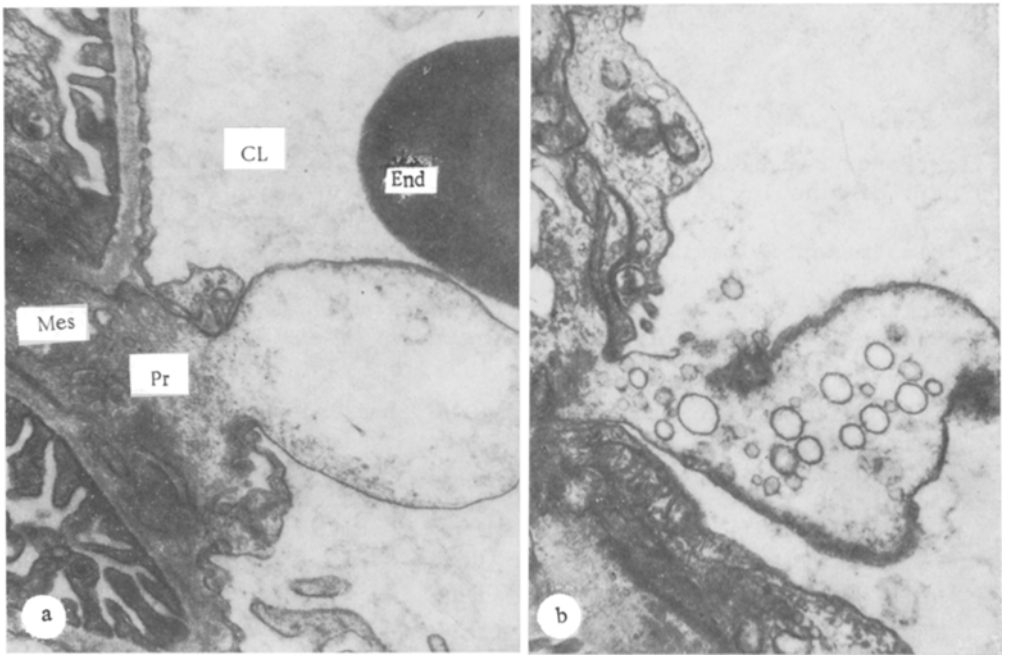

Fig. 3. Reaction of MC processes to extremal factors acting on residual kidney. a) After ischemia for 30 min with circulation restored for 3 days; b) 30 days after ischemia for 60 min. CL) Capillary lumen, Mes) mesangiocyte, Pr) processes of mesangial cells; End) endotheliocytes. Magnification: a) 20,000, b) 45,000 ×.

Club-shaped diverticula of type 3 projecting into the capillary lumen differ in size. They are connected by their narrow necks with the perinuclear cytoplasm of MC. Marked hypertrophy of the type 3 processes was observed in the experiments of series I, 3 days after restoration of the circulation (Fig. 3a), and also during compensatory hypertrophy of the residual kidney.

In the pale hyaloplasm of some of these reactively changed mesangiocapillary prolapses vacuoles could be detected whose contents were eliminated into the capillary lumen through areas of destroyed plasmalemma of the process (Fig. 3b). In the cytoplasm of MC, at the bases of the processes hypertrophied mitochondria and signs of intensification of the biosynthetic function of other cell organelles can be observed.

In clinical practice the hyperplastic potential of the mesangium in response to glomerular injury is manifested particularly during circulation of heterologous or autologous immune complexes in the blood. They are eliminated from the circulation by MC and deposited in the form of solid residues consisting of immunoglobulins G and M, and also of a fraction of complement C3. Proliferation of the mesangium causes its interposition, when processes of MC insinuate between the basal membrane and endothelium of the capillaries. This structural-spatial interposition lies at the basis of the morphogenesis of the membranous-proliferative or mesangiocapillary form of glomerulonephritis [5, 8].

A definite analogy can be traced between the clinical-anatomical data and our experimental results. It is reflected in the stereotyped mesangioproliferative reaction in response to disturbance of the integrity of the glomerular filter in different forms of glomerulopathies.

The functional importance of the diverticulum-like prolapses of MC has been the subject of many hypotheses. They have been ascribed phagocytic properties [14], the excretion of certain macromolecules by exocytoses [12], the ability to evacuate waste products which accumulate in the glomerulus [4, 9, 11], the function of baro- and chemoreceptors [1, 6, 13], contractile properties affecting ultrafiltration of the plasma through components of the glomerular filter [6, 10], and participation along with the bodies of MC in the production of the membrane-like PAS-positive material of which the mesangial matrix consists [9, 14], and so on.

The results of these observations support the view that the processes of MC perform a drainage function, cleansing the intensively functioning glomerular filter and, in particular, its basal membrane, which is in direct contact with the mesangium. The need for drainage of waste products increases sharply when the kidney is exposed to pathological influences with an acute disturbance of the hemodynamics in the glomerular capillaries, which induces reactive hypertrophic changes described above in MC and their processes. Further experimental research with injection of various markers into the blood stream will help to solve this problem finally. The possibility cannot be ruled out that processes of MC are polyfunctional in nature.

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