HISTOGENESIS OF MESANGIAL CELLS OF THE RENAL GLOMERULI

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UDC 611.611-018.1

By the use of the indirect Coons' method using antisera against human uterine smooth muscle myosin, no evidence was obtained to support the smooth-muscle nature of the mesangial cells of the renal glomeruli in autopsy or experimental material.

Key words: myosin; mesangial cells; Coons' method.

In 1929 Zimmermann [18] described cells of a new type, besides the "Polkissen" and endothelial cells, in the renal glomeruli which he called mesangial cells. Because of uncertainty regarding the function and localization of these cells, different workers have suggested different terms to describe them: intercapillary cells, cells of the third type, capillary parietal cells, and glomerular smooth-muscle cells.

The mesangial cells are embedded in the matrix between the basement membrane and endothelial cells of the glomerular capillaries. Most workers identify the mesangial cells with smooth-muscle cells on general ultrastructural grounds [12, 16, 17], their staining properties [9], and other indirect evidence [6]. That these cells are common in nature is also indicated by the discovery of smooth-muscle actomyosin in the mesangial cells [5]. Since this was the only immunomorphological investigation so far undertaken and since it did not rule out the possibility of crossed reactions between the antisera used and other tissue structures, the problem of the smooth-muscle nature of the mesangial cells remains open.

A more exact criterion of the histogenetic kinship between the smooth muscles and mesangial cells would be the discovery of myosin in these cells as the principal contractile protein. The present investigation was carried out for this purpose.

EXPERIMENTAL METHOD

A monospecific serum against myosin of human uterine smooth muscles, obtained by immunizing a rabbit with the myosin–antimyosin precipitation arc, was used [1]. In sections of different organs treated by Coons' method, the antiserum revealed the muscle coat of the blood vessels and smooth muscles of the esophagus, intestine, and uterus of both man and animals. The myocardium, striated muscles, epithelium of the liver and kidneys and glandular structures, and other cells and fibrous structures did not react with the antiserum against smooth-muscle myosin. In a special investigation with this antiserum the smooth-muscle nature of the myoepithelial cells was confirmed [2].

In the investigation described below the material consisted of kidneys from adults and newborn infants dying from various causes unconnected with disease of the kidneys, normal kidneys of mice and rats, and kidneys of mice with experimental amyloidosis. The last group of kidneys was used as an example of active reorganization and proliferation of the mesangial cells, a characteristic feature also of other nosological forms of kidney pathology [7, 13, 15]. Sections 4 μ in thickness, cut in a cryostat, were fixed in 96% alcohol for 10 min and treated with antiserum against myosin by the indirect Coons' method, using donkey antibodies against rabbit immunoglobulin [3]. Serial control sections were incubated with nonimmune

Laboratory of Age Pathology, Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Kraevskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 79, No. 3, pp. 115-117, March, 1975. Original article submitted April 22, 1974.

serum and with antisera against amyloid fibrils and mouse plasma protein. Histological sections were stained with hematoxylin-eosin and thioflavine T.

EXPERIMENTAL RESULTS

Under the influence of antiserum against smooth-muscle myosin intense and specific fluorescence of the smooth muscles of blood vessels of different sizes in the renal medulla and cortex and also of smooth-muscle elements of the capsule and wall of the renal pelvis was observed in all cases in the experimental and autopsy material, but the glomeruli always remained dark (Figs. 1 and 2). In infections treated with nonimmune sera, the autofluorescence of the elastic fibers and weak background fluorescence of the remaining structures still persisted (Fig. 1b). Only in cases of amyloidosis were amyloid masses clearly revealed in the glomeruli under the influence of antisera against amyloid fibrils and plasma proteins.

Unlike in Becker's experiments [5], no evidence of the smooth-muscle nature of the mesangial cells could be obtained. The difference between the results can be explained by the nonidentity of the sera used. In the present investigation a monospecific serum against human uterine smooth-muscle myosin was used. Becker [5], on the other hand, worked with an antiserum which reacted with both smooth-muscle and endothelial cells. The fluorescence in the renal glomeruli which he mentions was therefore most probably due to the endothelial and not to the mesangial cells, more especially because the latter are difficult to distinguish by light microscopy.

Fluorescence of the mesangial cells under the influence of sera containing autoantibodies against smooth muscles (the sera were taken from patients with chronic hepatitis) was observed by Gabbiani et al. [8] and Nagle et al. [11]. Besides smooth muscles, this serum stained cells of varied origin: megakaryocytes, platelets, lymphocytes, and epithelial cells of the liver and intestine. This polyvalent action of the serum can probably be explained by its containing autoantibodies not against myosin but, as these workers consider, against actin, identical with thrombosthenin. Consequently, the presence of this protein cannot be confirmation of the smooth-muscle nature of the mesangium. Nevertheless, the same workers [8] point out that absorption of this serum with human uterine actomyosin does not always remove the specific fluorescence.

Investigations have shown that the serum of patients with chronic hepatitis contains antibodies of at least two types: against the sarcolemma and against the myofibrils of smooth muscles [10].

According to the latest evidence [14] all six antisera against the individual contractile proteins of the human uterus (actomyocin, actin, myosin, heavy and light meromyosin, tropomyosin) are not strictly specific with respect to smooth muscles, for these antisera revealed smooth muscles and epithelium of the liver, intestine, and bile ducts equally. Meanwhile antiactin serum and, to a lesser degree, antiserum against heavy meromyosin stained the renal glomeruli diffusely.

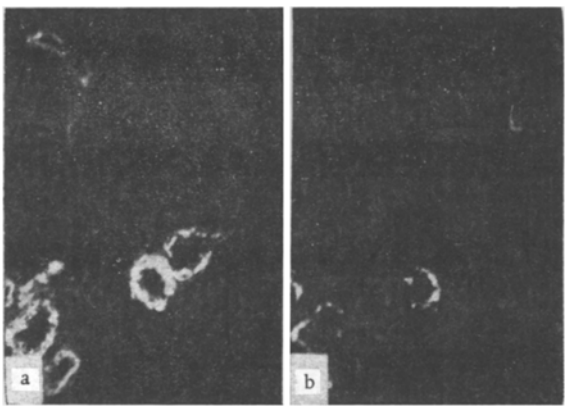

Fig. 1. Human kidney: a) specific fluorescence of muscular coat of several blood vessels, glomeruli remain dark (section treated with antiserum against human uterine smooth-muscle myosin, 50×); b) control. Autofluorescence of elastic membranes of blood vessels (section incubated with nonimmune serum, 60×).

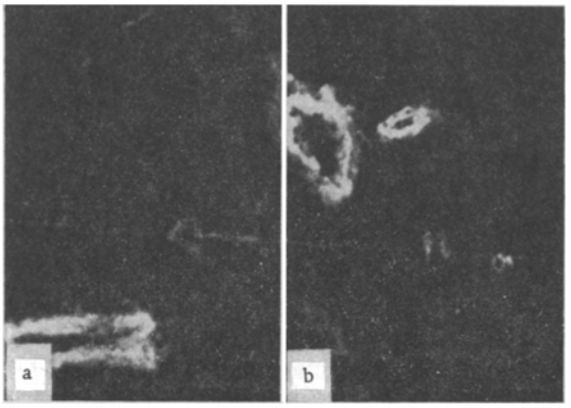

Fig. 2. Detection of muscle coat of blood vessels and weak background fluorescence of glomeruli and tubules in rat (a) and mouse (b) kidney. Sections treated with antiserum against human uterine smooth-muscle myosin by indirect Coons' method, 60×.

To sum up the data of the investigations cited [5, 8, 10, 11, 14], it must be accepted that different cells contain a common antigen, possibly the antigen responsible for fluorescence of the mesangium in the renal glomeruli. The results of the present investigation did not confirm the smooth-muscle nature of the mesangial cells, probably because of the monospecificity of the antiserum against smooth-muscle myosin, which does not contain foreign antibodies. On the other hand, the histogenic connection between the mesangial and smooth-muscle cells cannot be categorically rejected purely on the basis of immunomorphological investigations, for results have been obtained to show that intermediate forms, in which trace quantities of myosin are difficult to demonstrate [4], exist between smooth muscles and fibroblasts.

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