MICROSPECTROPHOTOMETRIC STUDY OF THE SIALOMUCIN CONTENT OF THE GLOMERULAR FILTER IN THE NEPHROTIC SYNDROME

G. G. Avtandilov and B. N. Tsibel'

UDC 616.61-002-07:616.633.963.1-074

The sialomucin content was studied in the glomerular filter of the human kidney in certain pathological states. Sialomucins were detected in paraffin sections by staining by Hale's method and were investigated in the scanning microspectrophotometer. A significant decrease was found in the content of sialomucins in lipoid nephrosis, secondary amyloidosis, and membranous-proliferative glomerulonephritis, accompanied by a nephrotic syndrome. In subacute glomerulonephritis with a nephrotic syndrome no decrease was found in the sialomucin content. It is suggested that the selective proteinuria is connected with a decrease in the sialomucin content in the glomerular filter.

KEY WORDS: *microspectrophotometry; glomerular filter; sialomucins; nephrotic syndrome.*

The structure of the glomerular filter and its changes in the nephrotic syndrome have not been adequately explained. Views regarding the function of the basal membrane as a high-molecular-weight "sieve" and on the connection between the filtration size and proteinuria and the degree of polymerization of the substance of the lamina densa do not take into account the role of the sialomucins of the glomerular filter, which are contained in the cytoplasm of the podocytes, endothelium, and lamina rara interna.

It has been suggested that the sialomucin (glycocalyx) of the podocytes plays the role of a fine filter and holds back substances with a molecular weight of between 70,000 and 200,000, whereas the lamina densa is a coarse filter, holding back substances with molecular weights of over 200,000-240,000 [10]. Other workers [2, 9, 11] consider that the sialomucins are not a true filtering barrier, but as a layer of active polyanions, they hold back protein molecules both at the level of the endothelium and the lamina rara interna and on the outer surface of the filter [12], and they may perhaps extract them from the primary urine. In experimental aminonucleoside nephrosis a decrease in the sialic acid concentration in the glomerular filter [7] and focal defects of the epithelial cover of the membranes [12] were found and preceded the proteinuria. A decrease in the intensity of staining of the basement membranes of the glomeruli by Hale's method has been found in the nephrotic syndrome in man and has been associated with a decrease in the sialomucin content [6]. However, the results of the reaction were assessed visually by these workers.

To continue the study of the structure of the basement membrane of the capillaries in proteinuria a microspectrophotometric investigation was made of the sialomucin content in the glomerular filter of the human kidney in certain pathological states.

EXPERIMENTAL METHODS

The sialomucin content in the basement membranes of the glomerular capillaries of the human kidney in lipoid nephrosis (five cases), subacute glomerulonephritis (two), secondary amyloidosis (two), congenital nephrosis (one), and membranous-proliferative glomerulonephritis (one), accompanied by a nephrotic syndrome, and also in lobular glomerulonephritis (two cases) and amyloidosis of the kidney (one case) without a nephrotic syndrome. Material was fixed in 10-12% neutral formalin and embedded in paraffin wax *en bloc* with the control fragment (kidneys from healthy persons of the same age, dying accidently, served as the control).

Department of Pathological Anatomy, Central Postgraduate Medical Institute, Moscow. Department of Pathological Anatomy, Arkhangel'sk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Smol'yannikov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 5, pp. 613-615, May, 1978. Original article submitted July 28, 1977.

 0007-4888/78/8505-0674$07.50

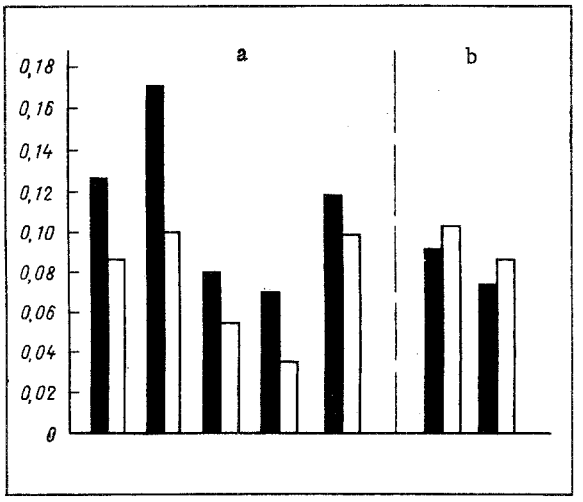

Fig. 1. Sialomucin content in sections of kidneys from normal subject and patients with lipoid nephrosis (a) and subacute glomerulonephritis (b). Black columns represent control, white columns experiment. Ordinate, optical density, proportional to sialomucin content (Hale-positive substances).

Sections 5 μ thick were stained by Hale's method at pH 1.8 and examined in the integrating scanning microspectrophotometer [1]. The optical density of the basement membranes of the glomerular capillaries was measured under a magnification of 450 times and at a wavelength of 610 nm (area of probe 0.25 μ^2). From 30 to 60 measurements were made in each case. The same preparations were reinvestigated with a digital scanning microspectrophotometer [3]. The results were subjected to statistical analysis. The results of investigations of the same sections by the two different microspectrophotometers proved to be identical.

EXPERIMENTAL RESULTS

In all cases of lipoid nephrosis (including an "acute" with a duration of about 2 months) a significant decrease was found in the intensity of staining of the basement membranes by Hale's method (Fig. 1). A decrease in the intensity of staining of the basement membranes also was found in membranous-proliferative glomerulonephritis and in amyloidosis accompanied by a nephrotic syndrome. The results may indicate a decrease in the sialomucin content in the outer cover of the membranes, for a positive Hale's reaction in the basement membranes is due to the presence of sialomucins [6, 9, 11]. In congenital nephrosis the decrease in the intensity of staining of the membranes compared with normal was not significant. In subacute glomerulonephritis an increase was observed in the intensity of staining of the membranes by Hale's method, whereas in lobular glomerulonephritis not accompanied by a nephrotic syndrome a decrease in the intensity of staining was found in one case and a small increase in the other.

The decrease in the sialomucin content, revealed by microspectrophotometry, may be responsible for the selective proteinuria and may be evidence of a role of sialomucins in the filtration of the primary urine. Considering their localization, sialomucins may be synthesized by podocytes, and in that connection primary degenerative changes in the podocytes in lipoid nephrosis appear probable. Injury to the podocytes in lipoid nephrosis is associated with a factor produced by a clone of T lymphocytes [14]. A cytotoxic effect of lymphocytes isolated from patients with lipoid nephrosis has also been described in the literature [8]. In amyloidosis injury to the podocytes is probably secondary in character, and the decrease in the sialomucin content in their processes, just as in the lamina rara interna, may be connected with the deposition of amyloid in the basement membranes [4]. Despite the nephrotic syndrome, in subacute glomerulonephritis some increase was observed in the density of the sialomucins in the glomerular filter, possibly on account of collapse of the glomeruli, accompanied by thickening of the basement membranes. The proteinuria in subacute glomerulonephritis is connected, not with a decrease in the sialomucin content, but with defects in the basement membranes [5, 15].

The results thus confirm the role of the sialomucins of the glomerular filter in the filtration process.

LITERATURE CITED

1. G. G. Avtandilov, Yu. I. Blagoveshchenskii, A. S. Dalmatov, et al., Arkh. Pathol., No. 10, 70 (1970).

2. P. I. Lysenko, Arkh. Patol., No. 4, 56 (1977).
3. B. L. Pereverzev, V. M. Andreev, S. I. Konovalov, et al., Tsitologiya, No. 8, 1050 (1974).
4. V. V. Serov and I. A. Shamov, Amyloidosis [in Russian], Moscow (1977).
5. B. N. Tsibel', Arkh. Patol., No. 9, 39 (1966).
6. E. B. Blau and J. E. Haas, Lab. Invest., 28, 477 (1973).
7. E. B. Blau and A. F. Michael, Proc. Soc. Exp. Biol. (New York), 141, 164 (1972).
8. K. Eyres, N. P. Mallick, and G. Taylor, Lancet, 1, 1158 (1976).
9. M. G. Farquhar, Kidney Int., 8, 197 (1975).
10. P. C. Graham and M. J. Karnovsky, J. Exp. Med., 124, 1123 (1966).
11. D. B. Jones, Lab. Invest., 21, 119 (1969).
12. G. Rennke and M. A. Venkatachalam, Kidney Int., 11, 144 (1977).
13. G. B. Ryan and M. J. Karnovsky, Kidney Int., 8, 219 (1975).
14. R. J. Shalhoub, Lancet, 11, 556 (1974).
15. J. Steyskal, C. L. Pirani, M. Okada, et al., Lab. Invest., 28, 149 (1973).

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

V. N. Blyumkin and S. L. Orduyan

UDC 616.61-089.843.004.8:
616-091.1-07:616.611-031.64-091-07

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

Laboratory of Pathomorphology, Institute of Transplantation of Organs and Tissues, Ministry of Health of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 85, No. 5, pp. 615-618, May, 1978. Original article submitted July 26, 1977.

 0007-4888/78/8505-0676$07.50