EXPERIMENTAL MEGAURETER IN DOGS: DEVITALIZATION OF A SEGMENT OF URETER AS A MODEL AND CHARACTERISTICS OF ITS COURSE

I. S. Mudraya, V. I. Kirpatovskii, T. I. Makarova, and Yu. V. Kudryavtsev

UDC 616.617-007.61-092.9

KEY WORDS: experimental megaureter, contractile function.

Megaureter denotes enlargement of the ureter in both width and length, and also tortuosity, and is a syndrome encountered in several urologic diseases associated with a disturbed outflow of urine along the superior urinary tract. Two main groups of factors leading to the development of megaureter can be distinguished: mechanical obstruction to the outflow of urine and disease of the ureteric wall itself. The role of the mechanical factor in the development of megaureter has been determined sufficiently clearly and its details have been revealed by experiments on animals [3, 4]. Lesions of the ureteric wall, in the form of disturbances of the neuromuscular apparatus in megaureter have been discovered by microscopic investigations in man [1, 6]. Only sporadic experimental studies have been undertaken to determine the role of the functional state of the ureteric wall for function of the upper urinary tract [5]. The role of this factor in the pathogenesis of megaureter calls for further elucidation and experimental confirmation.

The aim of the present investigation was to discover if megaureter can be produced as a result of injury to a segment of the ureter, and to identify the characteristics of the contractile function of its wall.

EXPERIMENTAL METHOD

Experiments were carried out on 22 male and female dogs weighing 15-20 kg. Devitalization of the ureter was carried out under thiopental anesthesia, in its middle (17 dogs) or lower (five dogs) third: a length of ureter 3-6 cm long was excised and immersed for 5 min in distilled water, then reimplanted in the antegrade direction on a perforated intubation catheter, which was removed 1 week later. The method of "devitalization" and ureterocystostomy was carried out in the Laboratory of Experimental Models, Research Institute of Urology, under the direction of A. V. Morozov. After the operation the dogs were investigated by excretory urography, nephroscintigraphy with ^{131}I-hippuran, and also by study of ureteric function during the operation by methods of electroureterography (EUG), rheography (RG) of the ureter, and electromanometry at rest and during function tests [3]. The dogs remained under observation for 1 year after the creation of the experimental model. The contractile function of the ureteric fragments was investigated in a constant-temperature (37°C) chamber through which oxygenated Locke's solution was circulated by means of a mechanotron (6MKh2B). Histological investigations were carried out by the usual methods of paraffin wax embedding followed by staining with hematoxylin and eosin, with Van Gieson's picrofuchsine, and with orcein.

EXPERIMENTAL RESULTS

The typical roentgenologic picture of megaureter with the formation of ureteric strictures in the region of devitalization was observed in 15 experiments (Fig. 1a). In 12 cases the disturbances of the urodynamics progressed rapidly, and after 1 to 4 months a complete block of the outflow of urine from the kidney developed. Incidentally, all five dogs on which devitalization

Research Institute of Urology, Ministry of Health of the RSFSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Lopatkln.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 111, No. 4, pp. 427-430, April, 1991. Original article submitted September 20, 1990.

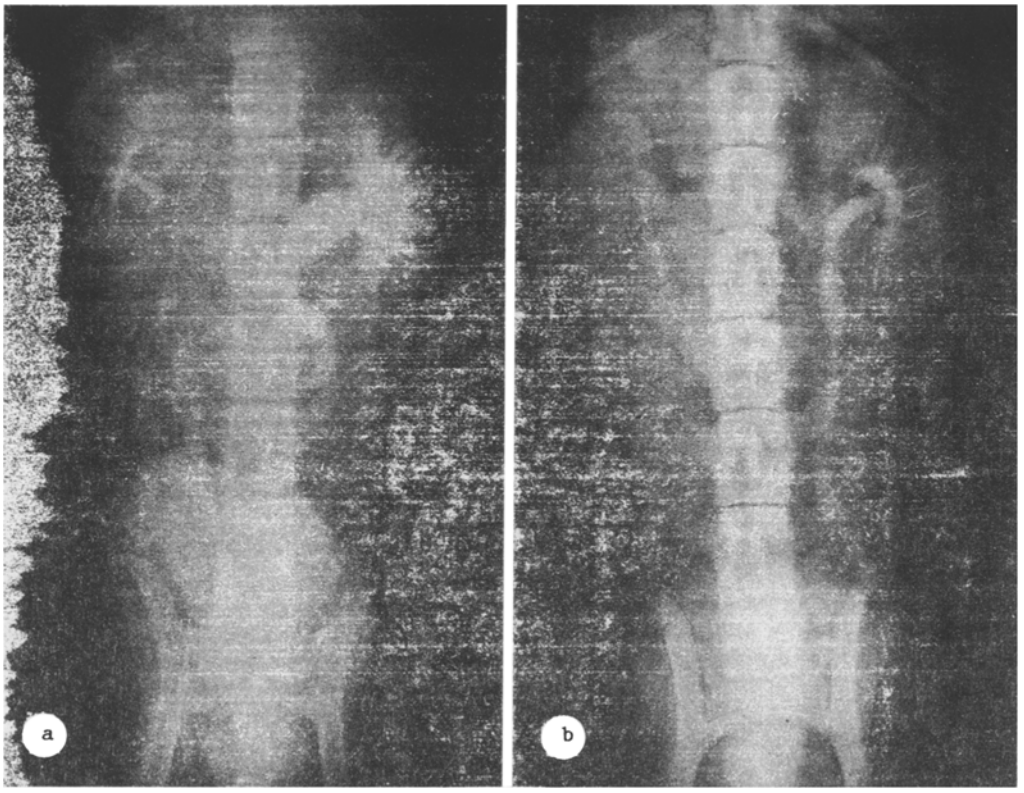

Fig. 1. Examples of excretory urograms of dogs with experimental megaureter as a result of devitalization of a segment of the lower (a) and middle (b) third of the ureter.

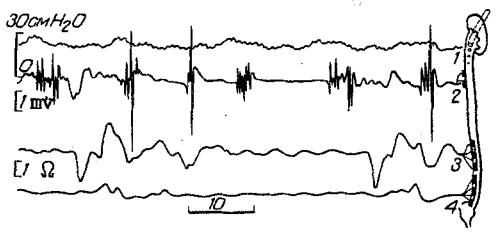

Fig. 2. Example of recording intrapelvic pressure (1), electroureterogram (2), and rheogram (3, 4) of experimentally modeled megaureter in a dog.

was carried out on the lower third of the ureter and ureterocystostomy performed by the antireflux method with the devitalized segment were included in this group of observations.

The remaining seven dogs developed megaureter without any significant constriction of the ureteric lumen, that could have been a mechanical obstruction to the outflow of urine (Fig. 1b). Nevertheless, radioisotope studies revealed slowing of evacuation and diminution of secretion on the side of the model; in some dogs, impairment of evacuation against the background of chronic urostasis led to inhibition of secretion in the later stages.

When assessing changes in contractile function of the wall of the megaureter we found a marked decrease in its relative force of contractions (the force of isometric contractions of the fragments normalized for the area of cross section). Maximal isometric tension of the devitalized fragments (0.15 ± 0.04 mN/mm^2) and of fragments located above (0.86 ± 0.33 mN/mm^2) and below the region of devitalization (0.37 ± 0.13 mN/mm^2) was significantly less than in unchanged canine ureters (2.60 ± 0.44 mN/mm^2). Under these circumstances the actual character of the contractions changed. Unorganized spontaneous contractile activity was observed against the background of inconstant resting tone, which was not regularized by electrical stimulation, and fragments of the megaureter responded to identical electric pulses with contractions of different strengths (Fig. 2). Changes in

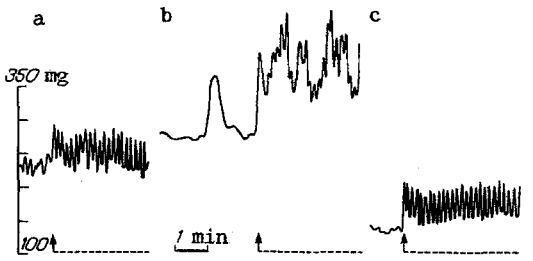

Fig. 3. Example of recording isometric contractions of isolated fragments of canine megaureter: a) upper third, b) devitalized part, c) lower third. Arrows with broken lines indicate period of electrical stimulation with above-threshold square pulses with a frequency of 6/min.

TABLE 1. Parameters of Function Tests of Upper Urinary Tract in Dogs with Unchanged Ureters (I) and with Experimental Megaureter (II) at Rest (a) and after Loading Test Parenteral Injection of 2 mg/kg of Lasix (b) and Perfusion at the Rate of 4.2 ± 0.8 ml/min (c)

Experimental conditions and number of observations	Intraureteric pressure (basal, peristaltic), cm water	Electroureterogram, amplitude, frequency		Rheogram of ureter, amplitude, frequency	
		mV	of complexes per minute	Ω	of complexes per minute
I:					
a 45	8±1/29±4	8,7±1,7	10±1	1,7±0,5	10±1
b 24	37±5/42±8	5,4±2,6	22±2	2,8±0,8	21±2
c 27	45±5/52±10	8,0±1,9	15±1	1,7±0,8	15±1
II:					
a 27	11±1*/31±5	3,7±0,8*	9±2	2,5±0,6*	9±1
b 9	20±5/44±9	4,7±1,5	9±2	1,7±0,6	11±2
c 14	34±5/66±14	3,2±1,1	12±2	1,9±0,3	10±1

Legend. Asterisk indicates values differing significantly ($p < 0.05$) from parameters of unchanged ureters.

contractile function of fragments of the megaureteric wall described above were more marked in the devitalized region, but were often observed in other parts also.

Investigation of the contractile function of obstructed and nonobstructed megaureter in the course of the operation revealed similar changes: the EUG and RG of the ureter, characterizing the function of excitation and contraction of the wall had multiple indentations, which varied in amplitude and direction. Complexes of EUG and RG often were not in harmony with periods of rise of the intraureteric pressure, and they also differed in shape and amplitude. The disorganization of function was aggravated by the irregularity of sequence of the EUG and RG complexes even in the resting state, and by nonsynchronized contractions of neighboring segments (Fig. 3).

Quantitative analysis revealed a very small increase of intraureteric pressure at rest, a decrease in amplitude of the EUG, and an increase in the amplitude of RG of the complexes (Table 1). Changes also were found in reactivity of the megaureter during loading tests; compared with the unchanged ureters, the rise of basal pressure was less marked in the megaureter, there was virtually no increase in the frequency of electrical activity in its wall, and no increase was observed in the amplitude of the RG complexes. The increase in range of the peristaltic oscillations of pressure (the difference between peristaltic and basal pressure) also must be emphasized in the megaureter after loading tests: 24-32 cm water compared with 5-7 cm water in the unchanged ureters.

The results of the function tests show that local injury to a segment of the ureter leads to disorganization of the contractile function of the entire organ, and this itself may be a factor causing disturbance of the outflow of urine. The disturbed evacuatory function is compensated by hyperfunction of the megaureter. Insuificiency of the contractile function of the megaureteric wall also is accompanied by disturbance of individual stages of its regulation and, in particular, the chronotropic stage. Weakening of the responses to loading tests is evidence of reduction of the functional reserves of the organ.

The histological studies confirmed changes in structure of the megaureteric wall: various degrees of myofibrosis, perimuscular sclerosis, sclerosis of the laminar propria of the urothelium, were found in the region of "devitalization"; single smooth-muscle cells or groups of them were in a state either of atrophy or of hypertrophy to a varied degree. Signs of perimuscular sclerosis were seen in segments of the ureters above the devitalization. Evidence of hydronephrosis and nephrosclerosis, culminating in secondary contracted kidney, were observed.

Thus the study demonstrated the possibility of creating a model of megaureter in dogs by injuring a segment of the ureter. The formation of nonobstructive megaureter in 41% of experiments with devitaliation of a segment of the upper third of the ureter demonstrates the important role of a functional stricture — without anatomical narrowing — in the pathogenesis of this threatening syndrome. Formation of obstructive megaureter in 100% of cases in experiments with devitalization of the ureterocystostomy can probably be explained by the anatomic and functional characteristics of this part of the urinary tract, and it is in agreement with the fact that strictures are observed more frequently in the lower part in patients with megaureter.

LITERATURE CITED

1. N. A. Lopatkin and A. V. Lyul'ko, Anomalies of the Urogenital System [in Russian], Kiev (1987), pp. 188-198.
2. I. S. Mudraya and A. V. Morozov, Urol. Nephrol., No. 3, 20 (1989).
3. J. L. Lockhart, G. N. Sfakianakis, W. Al-Sheikh, et al., J. Urol. (Baltimore), **128**, No 3, 633 (1982).
4. P. C. Ryan and J. M. Fitzpatrick, J. Urol. (Baltimore), **137**, No. 5, 1034 (1987).
5. K. Shigemi, J. Iwate Med. Assoc., **37**, No. 2, 299 (1985).
6. S. Tokunaka, T. Gotoh, T. Koyanagi, and N. Miyata, J. Urol. (Baltimore), **131**, No. 2, 383 (1988).

CHANGES IN THE PERITONEUM OF THE SMALL INTESTINE AND DIAPHRAGM IN EXPERIMENIAL PORTAL HYPERTENSION

V. A. Khoroshaev, V. M. Vorozheikin, and I. M. Baibekov

UDC 611.381:616.26/341:616.149-008.341.1

KEY WORDS: peritoneum of diaphragm and small intestine; mesothelium; portal hypertension.

Normally balanced secretion and absorption of fluid takes place constantly in the peritoneal cavity, so that the quantity of fluid remains stable [2, 4]. The intensity and direction of circulation of fluid are maintained by the activity of the different parts of the peritoneum, whose structural organization has been adequately studied [1, 3, 6-8]. Portal hypertension (PH), a complication of several diseases of the digestive and cardiovascular systems, is accompanied as a rule by an increase in the quantity of free fluid in the peritoneal cavity, or ascites [5], which develops as a result of predominance of transudation over resorption. Our knowledge of the pathogenesis of ascites at the present time does not give a clear idea of the role of changes in the regions of the peritoneum responsible for transudation and resorption, or of its formation.

The aim of this investigation was to study morphological changes in various parts of the peritoneum and, in particular, that covering the small intestine, through which transudation takes place, and the diaphragmatic peritoneum, responsible for resorption of fluid from the peritoneal cavity.

Laboratory of Pathological Anatomy, Tashkent Branch, All-Union Research Center for Surgery, Academy of Medical Sciences of the USSR.

(Presented by Academician of the Academy of Medical Sciences of the USSR D. S. Sarkisov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 111, No. 4, pp. 430-432, April, 1991. Original article submitted June 22, 1990.

0007-4888/91/0004-0554$12.50