ROLE OF SECRETION OF THE HYPOTHALAMIC SUPRAOPTIC AND PARAVENTRICULAR NUCLEI IN THE PATHOGENESIS OF EXPERIMENTAL UROLITHIASIS

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UDC 616-61/.62-003.7-092:616.831.41-008.6

KEY WORDS: neurosecretion; supraoptic nuclei; paraventricular nuclei; posterior lobe of the pituitary; urolithiasis.

Determination of the precise pathogenetic nature of urolithiasis is an urgent problem in urology. Despite many investigations in this direction, all that has so far been finally explained is that urolithiasis is a result of disturbance of metabolism and, in particular, of mineral metabolism.

We know that one of the central stages in the regulation of water and salt metabolism is the hypothalamic–hypophyseal neurosecretory system (HHNS). Consequently, this system must participate in the pathogenesis of urolithiasis, and its study must be of theoretical and practical importance for the prevention and treatment of this type of pathology.

On these grounds it was decided to study the morphological and physiological state of the HHNS in experimental urolithiasis.

EXPERIMENTAL METHOD

Experiments were carried out on 100 noninbred sexually mature male rats. The well-known model of oxamide calculus formation [5, 6] was used. Ninety rats were given oxamide (oxalic acid diamide) daily in a dose of 0.05 g/100 g body weight. The experimental animals were killed five at a time, 20 and 40 min, 1, 3, and 5 h, 1, 3, and 5 days, and 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10 weeks from the beginning of the experiment. The control group consisted of 10 rats not receiving oxamide. Serial sections through the anterior hypothalamus and pituitary were stained by the Gabe–Dyban method [3] and with Gomori's hematoxylin to reveal neurosecretion.

EXPERIMENTAL RESULTS

Depending on the state of the HHNS, three periods could be distinugished in the time course of experimental urolithiasis. Period I of the experiment (from 20 min to 7 days) was characterized by activation of the HHNS (Fig. 1: a-c). Functional activation of neurons was expressed as enlargement of the granules of neurosecretion, an increase in the mass of neurosecretion and in the size of the neurons and their nuclei and nucleoli (Fig. 1a), corresponding to the phase of stimulation of synthesis. Stimulation of synthesis was followed by stimulation of liberation of neurosecretion. At these times of our experiments, evidence in support of stimulation of liberation of neurosecretion was given by accumulation of neurosecretory material by the axon cone and its appearance along the course of the axon (Fig. 1b) in the hypothalamic-hypophyseal tract and the posterior lobe of the pituitary. The process of activation in neurons of the supraoptic nuclei (SON) was intensive in character as early as 20 min after the beginning of the experiment, and it took place so rapidly that by 5 h all neurons were in a state of active synthesis and liberation of neurosecretion. In the paraventricular nuclei (PVN) the changes developed more slowly. Functional activity of the neurons intensified with an increase in their size.

Stimulation of liberation in period I did not lead to exhaustion of neurosecretion due to other stimulating agents, as has been shown in many "dehydration" experiments [4, 7, 8]. Exhaustion of neurosecretion under conditions of dehydration is the result of the increased

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0007-4888/83/9504-0531$07.50

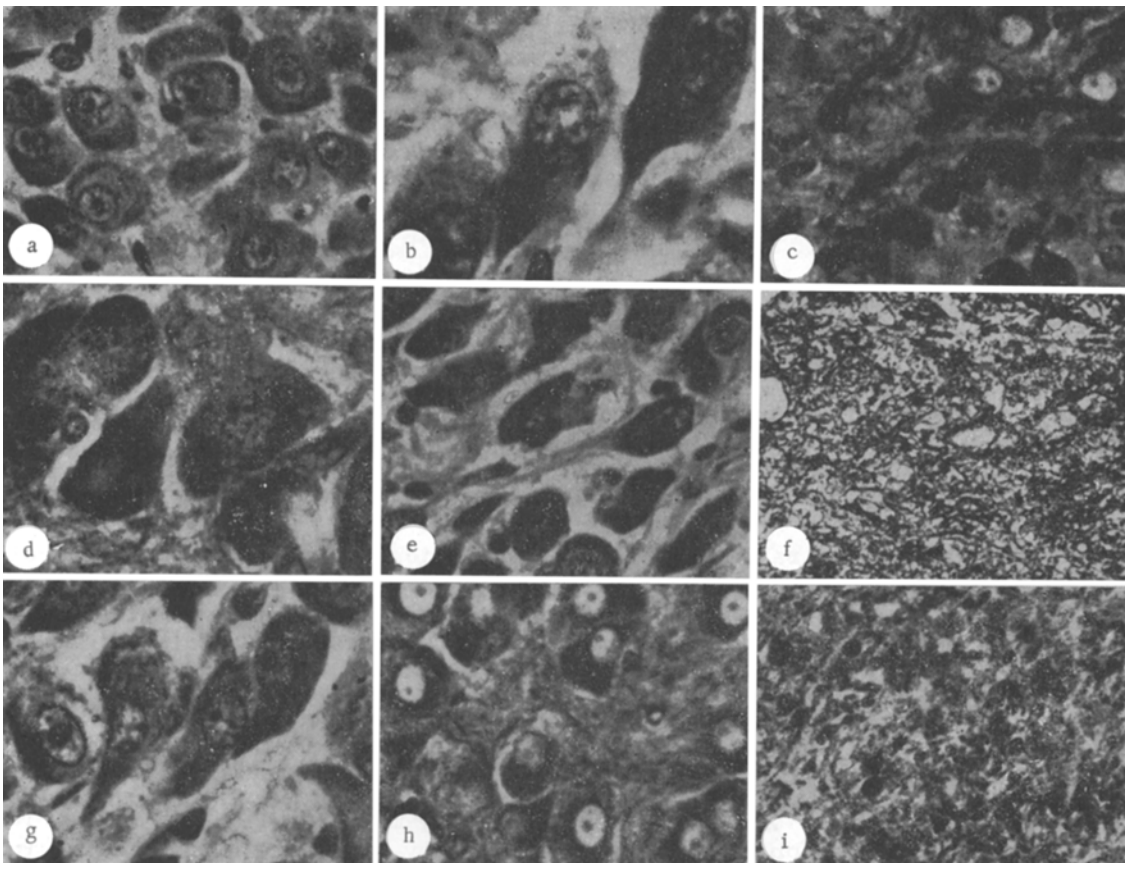

Fig. 1. Stages of changes in neurosecretion of HHNS in the course of experimental urolithiasis. a-c) Stage of increased functional activity: a) increase in mass of neurosecretion and enlargement of its granules in cytoplasm of SON neurons 20 min after injection of oxamide. Stained with chrome hematoxylin, 650 ×; b) SON neurons in state of filling and liberation of neurosecretion 3 h after injection of oxamide. Stained with chrome hematoxylin, 1600 ×; c) large quantity of neurosecretion among PVN neurons and along their axons after administration of oxamide for 5 days. Stained with aldehyde-fuchsine, 650 ×. d-f) Stage of depression and inhibition of functional activity of the HHNS: d) nuclei and nucleoli in SON neurons masked by coarse neurosecretory material after administration of oxamide for 2 weeks. Stained with aldehyde-fuchsine, 970 ×; e) SON neurons in a state of homogenization of neurosecretion after 3 weeks of administration of oxamide. Stained with chrome hematoxylin, 650 ×; f) reduction of neurosecretion in posterior lobe of pituitary after 5 weeks of oxamide administration. Stained with aldehyde-fuchsine, 260 ×. g-i) Restoration of functional activity of HHNS: g) granules of neurosecretion are clearly visible in cytoplasm of SON neurons, neurons themselves are filled and liberating neurosecretion after administartion of oxamide for 6 weeks. Stained with chrome hematoxylin, 970 ×; h) SON neurons with clearly distinguishable nucleus and nucleolus, granules of neurosecretion in cytoplasm after 10 weeks of oxamide administration. Stained with aldehyde-fuchsine, 650 ×; i) considerable increase in neurosecretion in posterior lobe of pituitary after administration of oxamide for 10 weeks. Stained with aldehyde-fuchsine, 260 ×.

demand of the body for antidiuretic hormone (ADH). Under the conditions of the present experiments, because of the body's reduced demand for this hormone, intensive utilization of the released neurosecretion did not take place and its quantity was not reduced in all parts of the HHNS until functional activity of the hypothalamic neurons was depressed.

Analysis of the results of the investigations from the 1st to the 5th weeks (period II) of the experiment showed lowering of the functional activity of SON and PVN neurons and inhibition of liberation of neurosecretion (Fig. 1: d-f). In the period mentioned, increased

homogenization of neurosecretion took place and the neurons underwent pycnosis (Fig. 1: d, e). Along the course of the hypothalamic–hypophyseal tract and in the posterior lobe of the pituitary (Fig. 1f) the content of neurosecretion was extremely reduced.

Depression of functional activity of the hypothalamic neurons was accompanied by the formation of renal calculi, followed by macroscopically evident transformation of the kidneys and marked structural changes in the kidney tissue [2].

Depression of the functional activity of hypothalamic neurons is the result of the reduced demand of the body for ADH, and it must be regarded as an adaptive reaction of the body aimed at regulating disturbed metabolic processes. However, the HHNS was unable to regulate the disturbed metabolism and pathological changes in the kidneys intensified [2].

The morphological and functional state of the HHNS from the 6th week until the end of the experiments (period III) indicated recovery of synthesis and liberation of neurosecretory material (Fig. 1: g-i). In the 6th week of the experiment granules of neurosecretion were present in the cytoplasm of most neurons (Fig. 1i). In the period of recovery of synthesis and liberation of neurosecretion the pathological process in the kidneys continued to progress [2].

The results indicate that ADH, together with local factors, plays a role in aggravation of the pathological changes in the kidneys [2] at late stages of the experiment.

It can accordingly be concluded from these results that changes in ADH secretion by neurons of the supraoptic and paraventricular nuclei participate in the pathogenesis of urolithiasis, and this is a matter to be taken into account during the management of this condition.

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