Effects of Ultralow Doses of Antibodies to Prostate-Specific Antigen on Morphological and Functional State of Rat Prostate

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Morphological and morphometric assays showed that administration of antibodies to the prostate-specific antigen in ultralow doses for 1.5 months delayed the development of atrophic and sclerotic processes in rats with chronic aseptic prostatitis. The concentration of zinc ions playing an important role in binding of androgens increased in the prostate of rats receiving the preparation. Studies of copulatory behavior showed that male rats with chronic prostatitis receiving antibodies to the prostate-specific antigen displayed increased sexual activity compared to control and intact animals.

Key Words: *chronic aseptic inflammation; prostate; antibodies to prostate-specific antigen; rats*

Noninfectious prostatitis is the most common pathology of the prostate [6]. This disorder is often resistant to medicinal treatment and characterized by persistent morphologic changes in the glandular tissue and stroma of the prostate (even when the symptoms and laboratory markers of inflammation disappear) [7,12]. The search for new methods for therapy of patients with this disease is an urgent problem [4,6].

The prostate-specific antigen (PSA) is localized in the cytoplasm of acinar cells and epithelium of prostatic ducts [15]. The increase in PSA content serves as a marker of tumor process [5]. Recent studies showed that the content of PSA increases in patients with various diseases of the urogenital system, including inflammation of the prostate [4,13].

Here we studied the effects of ultralow doses of antibodies to PSA (AB-PSA) obtained using homeopathic potentiation technology (mixture of homeopathic dilutions C12+C30+C200) on morphological and functional characteristics of the prostate in rats with chronic aseptic inflammation.

MATERIALS AND METHODS

Experiments were performed on 56 male outbred rats aging 2.5 months and weighing 250 g (Laboratory of Biological Modeling, Institute of Pharmacology). The animals were kept according to the requirements of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986). Before and during the experiments the rats were maintained in a vivarium under standard conditions and had free access to food and water. Chronic prostatitis was modeled by stitching the prostate with a silk thread under ether anesthesia [3]. One month after surgery AB-PSA were administered intragastrically in a dose of 1.5 ml for 45 days. Control animals received an equivalent volume of the solvent (distilled water) according to the same schedule. Ten rats of each group and 10 intact animals were killed by cervical dislocation 2.5 months after surgery. After autopsy the ventral lobe of the prostate was prepared. The samples from 5 animals of each group were subjected to histological assay. The ventral lobe of the prostate was fixed in Carnoy's fluid and embedded in paraffin. Deparaffinized sections (5 μ) were stained with hematoxylin and eosin and by the Van Gieson technique specific for the connective tissue [9]. The ratio between structural elements of the prostate was determined on Van Gieson-stained preparations [10]. The gland was scanned in two perpendicular directions (from the capsule to capsule) using an Avtandilov morphometric grid. The number of grid points corresponding to structural elements of the prostate (epithelium, lumen of the ducts, and interstitium) was estimated in each 3rd field of view. In the interstitium, vessels and connective tissue (collagen fibers, matrix, and cells) were counted. As differentiated from the prostate in humans, the interstitium of rat prostate contain no muscle cells [14]. Therefore, we did not count muscle fibers. The percentage between these structures was calculated. Taking into

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0007-4888/03/supp-0091$25.00

TABLE 1. Effects of AB-PSA on the Ratio (% of Total Content) of Structural Elements in the Prostate in Rats with Chronic Prostatitis ($\bar{X}\pm m$, n=5)

Structural elements	Intact	Chronic prostatitis	
		control	experiment
Ductal epithelium	23.12±1.55	16.64±0.96*	19.23±0.48*+
Ductal lumen	61.98±2.30	54.3±2.3*	52.60±0.95*
Connective tissue	13.36±0.63	29.64±0.98*	26.98±1.36*+
Vessels	1.56±0.45	1.48±0.19	1.14±0.14

Note. Here and in Table 2: *p<0.05 compared to intact rats; +compared to the control.

TABLE 2. Effects of AB-PSA on Sexual Behavior of Rats with Chronic Prostatitis ($\bar{X}\pm m$)

Parameter	Intact (n=10)	Chronic prostatitis	
		control (n=8)	experiment (n=8)
Latency of mounting, sec	231.88±8.88	189.00±11.90	114.88±15.99*
Number of mountings	7.50±2.39	5.88±1.60	11.75±2.10+
Number of copulations	1.70±0.72	1.25±0.41	2.35±0.31

account the important role of zinc ions in binding of androgens in the prostate [11], the remaining samples were placed in ethanol. The concentration of Zn^{2+} was measured by emission spectral analysis.

Since chronic prostatitis is accompanied by the reduction of sexual activity [1,8,12], we studied copulatory behavior in rats of these groups. To determine sexual activity males were kept together with females in estrus, which was induced by 4-fold treatment with 0.05% folliculin in a daily dose of 0.02 mg. The phase of the estrous cycle was determined by cytological analysis of vaginal smears. The effects of AB-PSA on copulatory behavior were determined in the open-field test [2]. We recorded the latency of the first mounting (time between the appearance of females and first mounting), total count of mountings, and number of copulations.

The results were analyzed by nonparametric Mann-Whitney test.

RESULTS

Atrophic and sclerotic changes in the prostate developed 2.5 min after stitching with a silk thread. The relative area of the epithelium in prostatic ducts decreased, while the relative area of the connective tissue increased compared to the control (Table 1). Moreover, the relative area of the lumen of prostatic ducts decreased after surgery, which indirectly indicates that secretory activity of the gland was suppressed.

In rats subjected to surgery and receiving AB-PSA for 45 days the area of the secretory epithelium in prostatic ducts increased, while the relative area of the connective tissue decreased compared to the control (Table 1).

The concentration of Zn^{2+} ions in the ventral lobe of the prostate in control animals was 0.96±0.06 mg/100 g. In rats receiving AB-PSA the content of these ions increased to 2.09±0.023 mg/100 g (p<0.05 compared to the control).

The latency of mounting in males with chronic prostatitis receiving distilled water was comparable with that in intact rats (Table 2). In animals with chronic prostatitis treated with AB-PSA this parameter did not differ from the control, but was below the baseline level (p<0.05, Table 2). The total number of mountings was similar in intact and control males. In rats receiving AB-PSA this parameter 2-fold surpassed the control. The number of copulations differed insignificantly.

Thus, morphological and morphometric assays showed that administration of AB-PSA in ultralow doses for 1.5 months delayed the development of atrophic and sclerotic processes in rats with chronic aseptic prostatitis. The concentration of zinc ions playing the important role in binding of androgens increased in the prostate of rats receiving AB-PSA. Male rats receiving AB-PSA displayed increased sexual activity compared to control and intact animals.

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