Role of Prostatic Epithelium Basement Membrane Incompetence in the Pathogenesis of Chronic Prostatitis

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Prostatic inflammation is associated with infections penetrating through the urethra. This inflammation is treated by long courses of wide-spectrum antibiotics. However, the most frequent cause of prostatitis is *Escherichia coli* and other enteric flora. Electron microscopy of biopsy specimens from the prostate detected gaps in the prostatic epithelium basement membrane, their size explaining the penetration of enteric flora into the prostate. These data suggest another view on the pathogenesis of prostatitis and approaches to improvement of therapy for this disease.

Key Words: *prostatitis; basement membrane; epithelium; Escherichia coli; urogenital infection*

Inflammation in the male reproductive tract can be a result of acute and chronic infections. Inflammations of this kind tell on spermatozoon function and spermatogenesis [8,10,12]. Negative effects of bacteria on the spermatozoon mobility were described [2].

It is obvious that acute infections, such as gonococcal or chlamydial, are sexually transmitted and get into the prostate through the urethra. The most incident bacterium identified in chronic prostatitis (if the microorganisms are detected) is *Escherichia coli*, the bacterium normally populating the intestine. Courses of therapy for gonococcal or chlamydial infection are short (no longer than 1 week), while chronic prostatitis is recommended to be treated by strong antibacterial therapy continued for up to several months [5]. There are good grounds to suggest that in chronic prostatitis the microorganisms penetrate into the prostate directly from the intestine. Gaps emerging in the prostatic epithelium basement membrane offer a principal chance for transport of the enteric microflora.

We studied structural microscopic defects in the basement membrane in prostatitis.

MATERIALS AND METHODS

Material for electron microscopy of the prostatic epithelium basement membrane was collected by diagnostic biopsy carried out in order to exclude prostatic tumors in 3 patients aged 64, 67, and 71 years, in whom chronic prostatitis was confirmed by ultrasonic studies. None of these patients received antibacterial therapy during at least 2 months before biopsy. No other diseases of the urogenital system were detected in these patients.

The material for electron microscopy was fixed in 2.5% glutaraldehyde in 0.1% cacodylate buffer (pH 7.2-7.4) and in 1% osmic acid, after which was embedded in epon-araldite mixture. Semithin and ultrathin sections were sliced on a Reichert UltraCut III ultramicrotome. Ultrathin sections were sliced from the preselected basement membrane sites stained with lead citrate and examined under a Hitachi700 electron microscope.

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RESULTS

Electron microscopy of the epithelial basal zone revealed sites in which the basement membrane has continuous structure, normal morphology, and consists of two layers: lamina lucida (LL) and lamina densa (LD). LL lies directly under the epithelial basal layer cells and is connected to them by tonofilaments, while LD contacts with the sublying connective tissue (Fig. 1). This structure of the zone separating the epithelium from deeper compartments is normal.

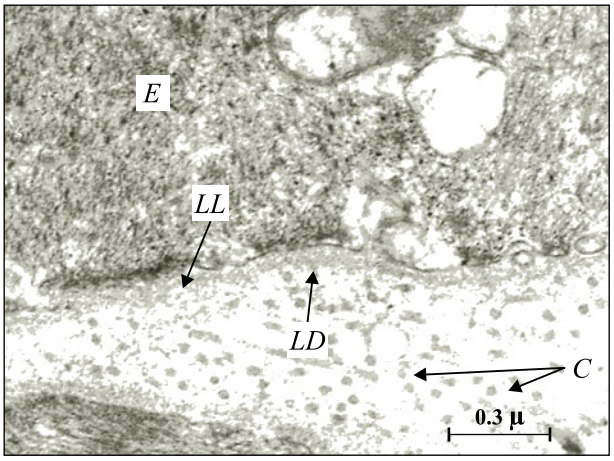

Fig. 1. Prostatic epithelium: basement membrane of normal morphology consists of LL and LD bound by fixing fibrils to epithelial cells (E) and connective tissue collagen fibrils (C).

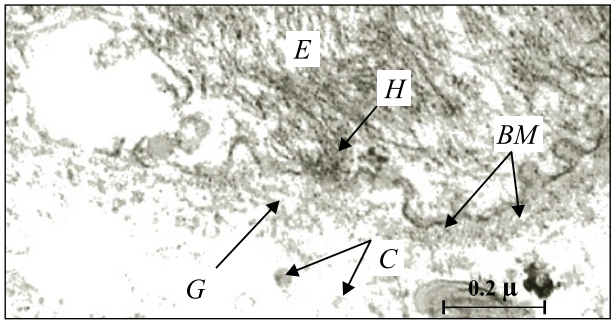

Fig. 2. Basement membrane (BM) adjacent to epithelial cell (E) plasma membrane. Zones with gaps (G) in the basement membrane are seen. C: connective tissue collagen fibrils; H: hemidesmosomes.

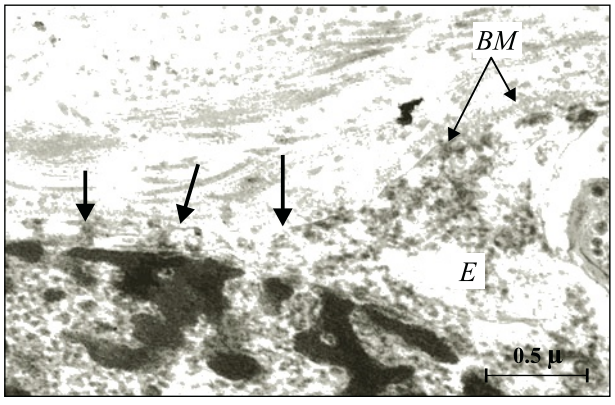

Fig. 3. No basement membrane (BM) in some zones (bold arrows). E: epithelial basal cell.

A different picture was found in the material from patients with chronic prostatitis. Areas of LD loosening were found in some basement membrane zones, the fibrils constituting LD were scanty, the filaments fixed to the hemidesmosome were retained (Fig. 2). The fibrillar structure of LD was worthy of note. The size of loose areas reached 1.0 μ and was comparable to the diameter *E. coli* most often found in prostatic secretion in chronic prostatitis.

In some zones, the basement membrane was not loose, but was completely absent and hence, allowed direct contact between the basal layer of the epithelium and the connective tissue. The size of these zones (gaps) reached several tens of microns.

Figure 3 shows a fragment of the basal cell of the epidermis contacting with the basement membrane. The absence of basement membrane and direct contact of the basal part of the epithelial cells with connective tissue are seen on the left.

The epithelial basement membrane is a dynamic structure modifying its morphology *in vitro* and *in vivo* [6,11]. Our results suggest physical potentiality of enteric flora penetration into the prostate through the basement membrane of the prostatic epithelial cells damaged in inflammation, because the gaps in the basement membrane were significantly larger than the majority of microorganisms inhabiting the human intestine.

For example, the diameter of *E. coli*, most often detected in chronic prostatitis, does not exceed 1 μ, while some gaps in the basement membrane are several times larger. *E. coli* is a large (according to microbiological notions) bacterium, and hence, other smaller bacteria populating the intestine can easily penetrate through the damaged basement membrane.

Half of specimens of the semen from 1256 men whose marriage was infertile contained a great variety of microorganisms, including aerobic cocci. *Enterococcus faecalis* were detected in 53% patients, micrococci in 20%, and α-hemolytic streptococci in 16%. High incidence of urogenital *E. faecalis* infection was also associated with a lower quality of the semen [7].

The seminal specimens from men examined for fertility problems contained even a greater variety of microorganisms, including anaerobic microflora [3].

It was assumed that the bacteria responsible for infection of the semen could get into it through the urethra or in sexual intercourse [9]. *E. coli*, modifying the spermatozoon mobility, were most often found in men with urogenital infections or infected semen [1]. One more possible route for penetration of the micro-

organisms into the prostate is from the intestine. This route of infection explains the efficiency of long antibiotic therapy of chronic prostatitis and high probability of subsequent relapses after therapy is discontinued. It is obvious that complete cleansing of the intestine by short courses of antibiotics is rather difficult, and hence, long courses of antibiotic therapy are needed. Restoration of normal or somewhat modified enteric flora after antibiotic discontinuation is inevitable, and hence, a relapse of prostatitis is quite probable.

The possibility of autoimmune nature of chronic prostatitis is therefore clear. The immunocompetent cells, which can be transported through damaged basement membrane of the prostatic epithelium because of migration of microorganisms from the intestine, presumably recognize the molecular design of the inner side of the basement membrane as a foreign one, thus promoting the development of an autoimmune process.

All this means that only a combination of antibacterial therapy, aimed at elimination of the infection that penetrated into the prostate, with repair of the prostatic epithelium basement membrane integrity, preventing penetration of new microorganisms from the intestine, can effectively eradicate chronic prostatitis.

Morphological changes in the basement membrane, impairing its integrity, which have been detected in our study, can be universal, developing in inflammatory processes in other organs and tissues. The possibility of *Shigella* penetration into the stomach through the basement membrane has been demonstrated on guinea pigs [4].

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