



Bladder Leukoplakia: Prevalence, Risk Factors and Etiology

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Abstract: This article describes the concepts, prevalence, risk factors and etiology of bladder leukoplakia. It has been established that leukoplakia of the urinary bladder is a typical expression of metaplasia of the transitional epithelium into squamous epithelium with keratinization, caused and maintained by chronic inflammatory and neurotrophic processes in the urinary bladder. This disease occurs exclusively in female patients aged 16-80 years, whose average age is 32.6-39.5 years. The causes of bladder leukoplakia are impaired embryonic development of the bladder mucosa, the presence of a specific infection (tuberculosis, syphilis), vitamin A B hypovitaminosis, inflammation, hormonal imbalance, and destruction of the normal glycosaminoglycan layer of the urothelium under the influence of urogenital infection.

Key Word: bladder, leukoplakia, frequency, risk factors, etiology, morphology.

1. Definition and prevalence of bladder leukoplakia.

The first description of leukoplakia (cholesteatoma) belongs to K. Rokitsky in 1861. Pelican, who indicated the ability of leukoplakia to cancer transformation. Scientists have described bladder leukoplakia as the appearance of mucous silvery-white or pearlescent flat plaques of various sizes and shapes. [10] A.P. Frumkin also points out the possibility of malignancy of leukoplakia: "Leukoplakia of the urinary bladder is a typical expression of metaplasia of the transitional epithelium into squamous epithelium with keratinization, caused and maintained by chronic inflammatory and neurotrophic processes in the bladder. In some cases, the keratinizing epithelium covers significant spaces, leaving only relatively small gaps in the mucous membrane of normal color with dilated vessels, or occupies only separate areas of the mucous membrane of the bladder. The edges of the leukoplakic film in most cases are raised and separated, creating a false impression of the possibility of grasping such a film with forceps and removing it from the bladder mucosa. The keratinized epithelium can also be incrustated with phosphate salts, while losing its characteristic silvery color.

Foreign literature uses the term "squamous metaplasia". Domestic clinicians use the narrower term "leukoplakia" of the mucous membrane of the urinary bladder [10] Under the term "leukoplakia", clinicians combine all forms of squamous cell metaplasia of the epithelium [14]. Leukoplakia of the bladder is areas of flat whitish spots - plaques on the mucous membrane of the bladder, often with endoscopy of which resembles a picture of "melting snow". [eleven]. In the modern world, leukoplakia

is a pathological process, which is characterized by a violation of the basic functions of stratified squamous epithelium: the absence of glycogenesis and the occurrence of keratinization, which are normally absent [8]. Thus: leukoplakia of the urinary bladder is a pathological condition of the mucous membrane of the urinary bladder, which is an area of squamous metaplasia of the urothelium with keratinization of the integumentary layer. This is an altered bladder mucosa, which is a squamous metaplasia of the epithelium with varying degrees of keratinization in the form of foci of whitish plaque, clearly delimited from the unchanged mucosa [10,22].

It should be noted that under the term "leukoplakia" in some scientific and medical sources they say pre-cancerous diseases of the bladder [8]. According to the literature, during cystoscopy in 63.6–100% of patients with persistent dysuria and chronic pelvic pain, leukoplakia is found in the same urinary bladder-bladder triangle [2].

According to the authors studying this problem, during urethrocystoscopy, in 65-100% of patients with persistent dysuria and pain localized in the pelvis, an altered mucous membrane of the urinary bladder is found, which is a squamous metaplasia of the epithelium of the urinary bladder, 21 Researchers of several scientific discoveries [2,6] have found that this disease occurs exclusively in female patients aged 16-80 years, whose average age is 32.6-39.5 years. When evaluating the results of cystoscopy, hyperemia, edema, and metaplasia of the epithelium were identified. Leukoplakia in the form of squamous metaplasia of the epithelium with varying degrees of keratinization was found in the form of foci of white, loose plaque on the mucous membrane. According to the studies carried out by Notov G.K, the incidence of leukoplakia decreased with age -71% in the younger, 50% in the middle and 11% in the older age group. When assessing the incidence of exacerbations of chronic cystitis, it was found that frequent exacerbations (3 or more per year) were more typical for young and middle-aged women. So, in the younger age group, exacerbation of chronic cystitis was detected in 69% of cases, on average in 59% of cases, and in the older age - only in 25%. The results obtained showed that the frequency of exacerbations of cystitis, as well as the incidence of metaplasia in women of different age groups, decreased with increasing age; therefore, it can be concluded that metaplasia is characteristic of a younger age, and its appearance can be associated with more frequent exacerbations of cystitis.

2. Risk factors and etiology of bladder leukoplakia.

Al-Shukri S.Kh. and co-authors [2] indicate that in the development of diseases such as chronic cystitis and overactive bladder, age-associated factors play an important role, such as a decrease in estrogen levels in the postmenopausal period, impaired microcirculation in the bladder wall. The authors also trace the relationship between the severity of the symptoms of overactive bladder, pain syndrome and the presence of leukoplasty and urinary bladder in women. The results they obtained showed that the frequency of exacerbations of cystitis, as well as the incidence of metaplasia in women of different age groups, decreased with increasing age; therefore, it was concluded that metaplasia is characteristic of a younger age, and its appearance can be associated with more frequent exacerbations of cystitis. [eighteen]

According to some authors, the main starting point in the development of bladder leukoplakia is the long-term persistence of infectious agents in the urinary tract, resulting in damage to the urothelium and the development of metaplasia. [9]. The very etiology of this disease, squamous cell metaplasia, accounts for 56-68% of all chronic cystitis. [17] According to Terlizzi, the well-known infection of the lower urinary tract, which occurs in 98% of cases of E. coli, causes obvious changes in the tissues of the urinary bladder: colonization of the periurethral vaginal areas; ascending penetration into the lumen of the urinary bladder of E. coli cells into the ureas of plankton; surface adhesion and interaction with the bladder epithelium protection system.

There are also opinions that the development of bladder leukoplakia is influenced by such factors as estrogenic insufficiency, neurogenic causes, viral diseases, allergic factors.

Chronic cystitis is often accompanied by the development of squamous cell metaplasia of the epithelium of the bladder mucosa, sometimes with keratinization (leukoplakia), which is detected in more than 60% of cases from all forms of chronic cystitis. The process of metaplastic transformation of the epithelium can also spread to the urethra. It is noted that bladder leukoplakia is associated with the most resistant to therapy forms of chronic cystitis, and the mechanisms of its development remain incompletely understood.

It is assumed that infection is a causal factor in urothelium damage and the formation of metaplasia, while further alteration occurs regardless of infection, leading to persistent dysuria [11]. These data correlate with modern concepts of disturbances in the regulation of cell proliferation and differentiation under conditions of chronic inflammation or irritation with a change in the direction of determination of the cambial stem cell and subsequent differentiation [8].

Leukoplakia is the most common histological form of chronic inflammatory process of the bladder and is detected in 50–82% of patients admitted to the clinic for chronic recurrent cystitis [22].

There is evidence of an increase in menopausal women in the incidence of urinary disorders, depending on the duration of postmenopause. This is due to a decrease in the level of estrogen and, against this background, to the involution of the transitional epithelium of the bladder and urethra, while the properties of the mucous membrane, including resistance to infectious agents, are disrupted. Consequently, in women of the post-menopausal period, elderly age, an additional hormonal factor appears, predisposing to urinary dysfunction and the development of chronic cystitis [1]. A feature of the course of cystitis in this age group is the development of inflammation, symptoms of the lower urinary tract without colonization of the urinary system by pathogenic microflora, which, however, can join, aggravating the patient's condition [19].

Historically, defects in the embryonic development of the bladder mucosa, the role of a specific infection (tuberculosis, syphilis), vitamin A hypovitaminosis have been considered as the reasons for the development of squamous cell metaplasia. Recently, the most probable theories of the origin of bladder leukoplakia are inflammatory, hormonal imbalance (the effect of estrogens) is the result of thermal, chemical exposure; violation of microcirculation in the wall of the bladder as well as destruction of the normal glycosaminoglycan layer of the urothelium under the influence of urogenital infection (Ch. trachomatis, U. urealiticum, N. gonorrhoeae, M. genitalium, Tr. vaginalis, Herpes simplex I, II).

According to Tushar Pandey, keratinizing squamous cell metaplasia in men is rare in urological practice with a frequency of 1: 10,000. In regions where schistosomiasis is rare, it usually occurs due to chronic irritation of the inflamed bladder mucosa by bacteria. Risk factors include chronic catheterization, neurogenic bladder, vitamin A deficiency, urinary fistula, and bladder outlet obstruction. There have been reports of keratinizing squamous cell metaplasia progressing to squamous cell carcinoma or concomitant squamous cell carcinoma.

A.Yu. Kolmakov in 2016 described the effect of schistosomal eggs (*Schistosoma haematobium*) on the bladder mucosa. The most common cause is genitourinary schistosomiasis (MS) with one of the most famous and dangerous complications - schistosomal bladder cancer (SSBD). During cystoscopy, the areas of squamous metaplasia always had clearly defined boundaries, representing thickened, slightly raised whitish spots with characteristic changes in the mucous membrane, described in detail in 1991 by E.G. Aslamazov - "sandy spots" and specific granulomatous ulceration of the urothelium. Visually, the surface of the mucous membrane was inlaid with phosphates, and the surrounding areas were

intensely hyperemic. When visualizing such a picture, a biopsy of the mucous membrane was performed. The incidence of metaplasia was in direct proportion to the stage of the tumor process.

The term "verrucous" leukoplakia refers to histological, but when describing the cystoscopic picture, it reflects well the thickness of the affected area. The roughness in this case is rough, reminiscent of the surface of the tongue, the color is dull white. Often such leukoplakia occurs in patients with cervical cancer or mixed infections [7]. In chronic cystitis, the entire mucous membrane of the bladder is involved in the pathological process; the region of the bladder triangle and the bladder neck is more affected [20]. According to Tsareva A.V. [22] precise statistics on the prevalence and incidence of bladder leukoplakia do not exist.

According to different authors, pricystoscopy in 63.6-100% of patients with persistent dysuria, chronic pelvic pain, leukoplakia is found with the location in the bladder neck and the bladder triangle [5,15]. Leukoplakia is detected in 60–67% of patients in the clinic with a diagnosis of chronic cystitis. The disease mainly affects women of working age (20–50 years old), significantly reducing the quality of life of patients, contributes to the development of a neurosis-like state, and leads to loss of working capacity. [3.8].

Conclusions:

Leukoplakia of the urinary bladder is a typical expression of metaplasia of the transitional epithelium in squamous epithelium with keratinization, caused and maintained by chronic inflammatory and neurotrophic processes in the bladder. This disease occurs exclusively in female patients aged 16-80 years, whose average age is 32.6-39.5 years.

The causes of bladder leukoplakia are impaired embryonic development of the bladder mucosa, the presence of a specific infection (tuberculosis, syphilis), vitamin A deficiency, inflammation, hormonal imbalance, and destruction of the normal glycosaminoglycan layer of the urothelium under the influence of urogenital infection.

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