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EXPERIENCE OF SURGICAL TREATMENT OF LEUKOPLAKIA OF THE URINARY BLADDER IN WOMEN WITH CHRONIC CYSTITIS

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28 women with leukoplakia of the bladder, clinically manifested by dysuria and pain in the bladder were observed. All patients have a history of chronic urinary tract infection. At the time of inclusion in the study there were no signs of exacerbation of cystitis. All patients underwent laser ablation of the altered bladder mucosa. Control examinations were performed 1, 3, and 6 months after surgery. Positive dynamics of clinical indicators was noted after surgery in all patients. Tolerance to laser ablation was satisfactory, there were no postoperative complications. A complete recovery of urothelium in the operation area was achieved after 6 months according to control cystoscopy. The results of the study showed high efficiency and safety of laser ablation of the altered bladder mucosa in patients with leukoplakia.

Keywords: bladder leukoplakia; laser ablation; chronic cystitis.

ОПЫТ ОПЕРАТИВНОГО ЛЕЧЕНИЯ ЛЕЙКОПЛАКИИ МОЧЕВОГО ПУЗЫРЯ У ЖЕНЩИН С ХРОНИЧЕСКИМ ЦИСТИТОМ

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Под наблюдением находились 28 женщин с лейкоплакией мочевого пузыря, клинически проявлявшейся дизурией и болями в мочевом пузыре. У всех пациенток в анамнезе хроническая инфекция мочевых путей. На момент включения в исследования признаков обострения цистита не было. Всем больным выполнена лазерная абляция измененной слизистой мочевого пузыря. Контрольные обследования проводили через 1, 3 и 6 мес. после операции. У всех оперированных женщин отмечена положительная динамика клинических показателей. Переносимость лазерной абляции была удовлетворительная, послеоперационных осложнений не было. По данным контрольных цистоскопических исследований полное восстановление уротелия в зоне операции достигалось через 6 мес. после ее выполнения. Результаты исследования показали высокую эффективность и безопасность выполнения лазерной абляции измененной слизистой мочевого пузыря у больных лейкоплакией.

Ключевые слова: лейкоплакия мочевого пузыря; лазерная абляция; хронический цистит.

INTRODUCTION

The term "leukoplakia of the bladder" (LB) is applied to a pathological process in the bladder mucosa that is based on focal degeneration of the transitional epithelium into a flat (squamous metaplasia) epithelium with keratinization [1–3]. During cystoscopy LB appears as areas of whitish plaque, clearly separated from the unchanged mucosa. There are three consecutive stages in its development: squamous cell modulation, squamous cell metaplasia, and squamous cell metaplasia with keratinization [3, 4]. Its exact prevalence in the general population is unknown; however it is quite high in women with dysuria reaching up to 7%–8% [5]. LB is considered as one of the main causes of persistent chronic pelvic pain in women [6, 7]. On cystoscopy 114 of 177 women with

chronic pelvic pain syndrome were diagnosed with LB (64.4%) [8].

Chronic urinary tract infection and the presence of factors that result in inflammatory process (bladder stones, fistulas, etc.) are mainly considered responsible for causing LB [9]. The bladder mucosa normally has protective mechanisms owing to the presence of a thin layer consisting of the mucopolysaccharide substances, mucin, and glycosaminoglycans. This layer creates a barrier between the bladder wall and the urine preventing the adhesion of bacteria and other components of urine to the mucosa [10]. With leukoplakia its destruction occurs with an increase in the permeability of the epithelium. Concurrently, the difficulty of adaptive adjustment of the urothelium during bladder filling at the site of the disease, leads to the diffusion of urine components into the interstitium. This process is accompanied by irritation of the submucosal layer receptors and the development of disease symptoms. Thus, leukoplakia is characterized by the same pathogenic mechanisms as interstitial cystitis.

Clinically, LB presents as bladder pain that increases upon filling, urination disorders (pollakiuria, nocturia, imperative urges to urinate), and often as dyspareunia [5, 11]. These symptoms may have different degrees of severity with the greatest intensity when the disease is localized in the neck of the bladder. LB is often the cause of persistent dysuria and pain above the womb and in the urethra after a treatment for cystitis, despite an unremarkable urine analysis and the absence of bacteriuria [8]. It is also associated with a significant decrease in the quality of life of patients [9].

Conservative treatment methods for patients with LB include antibacterial, anti-inflammatory, immunocorrective therapy, and intravesical instillation of hyaluronic acid preparations [3, 9]. However, these are generally ineffective and usually improve only the 1st stage of the disease comprising the squamous cell modulation [2]. The most effective treatment modality is surgery. Transurethral resection and coagulation of leukoplakia foci are widely employed [5, 13, 14]. In recent years, laser treatments have also gained momentum for LB due to their advantages of causing minimal surgical trauma, good hemostasis, absence of intraoperative complications, rapid cleaning of the bladder mucosa from the scab, and a short period of postoperative rehabilitation [15, 16].

The aim of the study was to evaluate the effectiveness of laser ablation of LBin women with chronic recurrent cystitis.

MATERIALS AND METHODS

Thirty-two women with LB, aged 19–56 years (mean age, 39.6 years) were under the care of the Urology Department of the hospital at the Medical Center of the President of the Republic of Kazakhstan (Nur-Sultan city). Dysuric symptoms (frequent and painful urination, nocturia, urgent urge to urinate) and discomfort and/or painful bladder were observed in 28 patients. These symptoms disturbed 3 (10.7%) patients for less than 3 years, 16 (57.2%) for 3–6 years, 6 (21.4%) for 6–9 years, and 3 (10.7%) for more than 10 years. The severity of symptoms was independent of the age of the patients; however, it increased with the disease duration. In 4 women, LB was accidentally detected during ureterorenoscopy performed for urolithiasis. It should be noted that these patients did not have any complaints of urination disorders and painful bladder. All 32 patients were found to have LB lesions located in the area of the Lieto triangle. At the same time, 4 (12.5%) patients had separate nodules of metaplasia in the urogenital triangle, 18 (56.2%) had LB portions involving 1/3rd of its area; while in 6 (18.8%) patients 2/3rd of the area was involved, and in 4 (12.5%) patients the entire surface of the urogenital triangle was involved.

Previously, all 28 patients with LB and the presence of clinical symptoms were repeatedly prescribed courses of a conservative therapy (non-specific anti-inflammatory drugs, antibacterial drugs, instillation of antiseptics in the bladder, physical therapy, etc.) with a short-term or no positive effect. As outpatients, patients underwent laboratory tests including bacteriological examination of urine, ultrasound examination of the kidneys and bladder with the determination of residual urine, uroflowmetry, and diagnostic cystoscopy.

At the time of hospitalization, all patients had no signs of active inflammatory process in the bladder; the titer of microorganisms did not exceed 103 CFU/ml. According to ultrasound data, the volume of residual urine in the patients did not exceed 50 ml. All 28 patients with LB underwent laser ablation of the altered bladder mucosa under intravenous anesthesia. After determining the endoscopic landmarks, using a Karl Storz cystoscope (17 Ch), biopsy of the altered mucosal areas was obtained. Then a flexible light fiber with an end emitter of a Dornie Multi Beam diode laser (Germany) was carried out through the working channel of the cystoscope and laser ablation of a section of the altered urothelium was made in a

Results of examination of patients before and after laser ablation of bladder leukoplakia (*n* = 28)
Результаты обследования больных до и после лазерной абляции лейкоплакии мочевого пузыря (*n* = 28)

Index	Before surgery	1 month after surgery	3 months after surgery	6 months after surgery
Average quantity of urination per day	11.2 ± 2.1	7.8 ± 1.8*	7.2 ± 1.2*	6.2 ± 1.8*
Average index Q_{max}, ml/s	12.9 ± 1.3	15.8 ± 2.6	18.1 ± 2.9*	18.2 ± 2.8*
Amount of residual urine, ml	44.8 ± 6.1	18.6 ± 3.1*	9.8 ± 1.8*	8.1 ± 2.6*

Note. * Significant whencompared with the results before treatment ($p < 0,05$)

continuous mode at a power of 10–20 W. The duration of the surgery depended on the area of the altered epithelium and averaged 8–10 minutes. After completion of the treatment, the bladder was drained with a Foley's urethral catheter. In the postoperative period, patients underwent a complex conservative therapy (non-specific anti-inflammatory drugs, antibacterial, and hemostatic drugs). All patients were prescribed phytotherapy with Canefron N, according to the standard methods for the prevention of exacerbations of lower urinary tract infections [17], continuously for the first 6 months, and then recommended to repeat treatment courses for 3 months twice a year. Control studies and cystoscopy were performed for patients 1, 3, and 6 months after the treatment. The effectiveness of the treatment was assessed on the basis of the subjective improvement of patients'health, absence of cystitis relapses, and cystoscopic picture-restoration of the epithelium of the bladder mucosa without signs of metaplasia.

RESULTS

All patients responded well to the surgical treatment. No postoperative complications were observed in any of the patients after laser ablation. The urethral catheter was removed on the 2nd day postoperatively, and urination was restored in all patients. By the time of discharge from the hospital (3rd day postoperatively), all women reported improvements in their subjective health – reduced pain in the bladder during urination and decrease in the frequency of urination. One month postoperatively, examination of the patients revealed significant improvements in the main observed indicators. All 28 patients had a significant decrease in the severity of dysuria. We observed a decrease in the number of urinations per day and an increase in the rate of urine flow according to uroflowmetry. All patients noted the disappearance or significant reduction of pain in the bladder. In control examinations at 3 and 6 months, positive changes were observed that were detected 1 month after the surgery (see table 1). Three months postoperatively, the women observed normalization in general health, along with the absence of urination disorders. At 6 months postoperatively, none of the treated patients had relapses of cystitis, and the patients noted an improvement in their quality of life.

Intraoperatively all patients underwent a biopsy of the altered sections of the bladder mucosa. On histopathology, all patients showed signs of chronic inflammatory process in the bladder wall with varying degrees of squamous cell metaplasia. Histologically, the bladder mucosa was described asbeing lined with a multilayered flat non-corneal epithelium with acanthotic strands of various sizes due to the proliferation of cells of the malpighian layer and the proliferation of basal cells. The basal membrane was well traced throughout. The underlying stroma had moderate edema, nodules of fibrosis, diffuse lymphoplasmocytic infiltration, and vessels with thickened walls. In cells of the multilayered flat epithelium, especially in the spiny layer, large vacuoles were observed in the perinuclear zone, indicating a vacuolar dystrophy (Fig. 1).

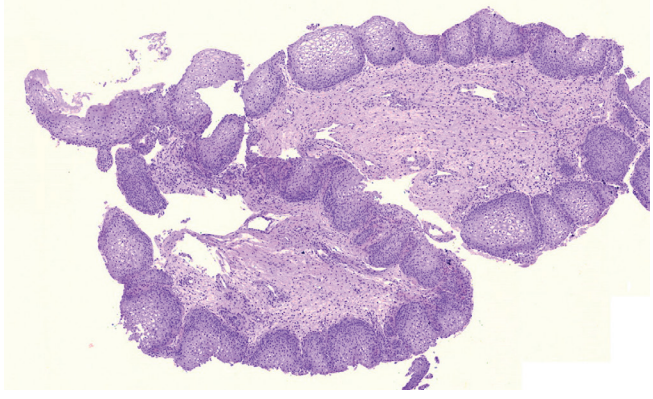

Fig. 1. The mucous membrane of the bladder. Chronic cystitis with squamous metaplasia of the epithelium. In the cells of the stratified squamous epithelium, especially in the spiky layer, the presence of large vacuoles (vacuole dystrophy) in the perinuclear zone are revealed (stain hematoxylin-eosin, ×100)
Рис. 1. Образец слизистой оболочки мочевого пузыря. Хронический цистит с плоскоклеточной метаплазией эпителия. В клетках многослойного плоского эпителия, особенно в шиповатом слое, наличие больших вакуолей в перинуклеарной зоне — вакуольная дистрофия (окраска гематоксилином и эозином, увеличение ×100)

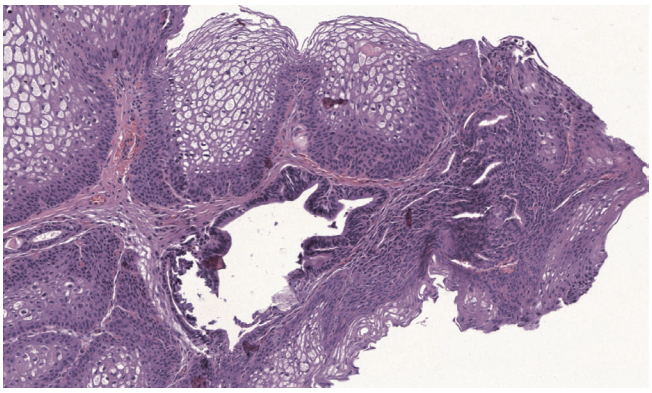

Fig. 2. The mucous membrane of the bladder. Chronic cystitis with squamous metaplasia of the epithelium and foci of glandular cystitis. In the cells of the stratified squamous epithelium, the presence of huge vacuoles with a shift of the nucleus to the periphery (balloon dystrophy) is revealed. In the underlying stroma are glandular structures of various sizes (glandular metaplasia) of the epithelium of the Brunn's glands) (stain hematoxylin-eosin, ×200)

Рис. 2. Образец слизистой оболочки мочевого пузыря. Хронический цистит с плоскоклеточной метаплазией эпителия и очагами железистого цистита. В клетках многослойного плоского эпителия наличие огромных вакуолей со смещением ядра на периферию — баллонная дистрофия. В подлежащей строме железистые структуры различного размера (железистая метаплазия эпителия брунновских желез) (окраска гематоксилином и эозином, увеличение ×200)

In a number of samples at various sites in the cells of the squamous epithelium, over the entire thickness of the layer, large vacuoles were present with an offset core to the periphery, indicating a balloon degeneration, and the stroma was determined to be comprising glandular structures of various sizes (Fig. 2).

During control cystoscopy, a month after the laser ablation, areas of coagulated mucosa, moderate edema, and moderate hyperemia were observed in the surgical zone. At 3 months postoperatively, moderate edema and moderate hyperemia persisted; however, a fresh whitish epithelium appeared with a still weakly expressed vascular pattern. At the control examination, 6 months postoperatively, the normal structure of urothelium in the bladder was restored.

DISCUSSION

The use of laser ablation of the altered bladder mucosa is an effective treatment for women with LB and chronic recurrent cystitis. The advantages of this technique are its minimally invasive nature, no complications, minimal time of anesthesia and surgery, and the surgical effect of a diode laser only on the surface layer of the metaplastic epithelium without damaging the urothelial growth layer. According to our observations, the diode laser provides a high-quality ablation of metaplasia, and the end-beam fiber provides maximum access throughout the surgical field, a spot work even in hard-to-reach areas behind the neck of the bladder, and also allows performing comfortable coagulation hemostasis after taking a biopsy from the bladder mucosa. This ultimately leads to a rapid and complete restoration of normal urothelium and, in turn, the earliest relief from dysuria and pain symptoms. We believe that the absence of clinical symptoms in 4 women with metaplasia of the bladder (who were observed without any surgical treatment), was due to the lack of urine permeability through the bladder mucosa. All 4 patients were of fertile age: 3 patients aged 31–40 years; while 1 was 41 years old. Histological examination of the biopsy revealed chronic cystitis with squamous epithelial metaplasia without keratinization. We believe that such changes in the bladder epithelium by the type of metaplasia without clinical symptoms do not warrantsurgical intervention; such patients should be monitored in an outpatient facility.

During the 1-year follow-up period, none of the patients had an exacerbation of the infectious process in the bladder that was also facilitated by prescribing therapeutic and preventive courses of phytotherapy.

CONCLUSION

Laser ablation of altered mucosa is an effective and safe method for the surgical treatment of patients with LB and chronic urinary tract infection.

REFERENCES

1. Лоран О.Б., Синякова Л.А., Косова И.В., Охриц В.Е. Лейкоплакия мочевого пузыря — новый взгляд на проблему // Эффективная фармакотерапия. – 2008. – № 4. – С. 50–52 [Loran OB, Sinyakova LA, Kosova IV, Okhrits VE. Leykoplakiya mochevogo puzyrya – novyy vzglyad na problemu. *Effektivnaya farmakoterapiya.* 2008;(4):50-52 (In Russ.)]
2. Жарких А.В. Применение лазерной абляции при лечении женщин с хроническим рецидивирующим циститом и лейкоплакией мочевого пузыря: Автореф. дис. … канд. мед. наук – СПб., 2015. [Zharkikh AV. Primenenie lazernoy ablyatsii pri lechenii zhenshchin s khronicheskim retsidiviruyushchim tsistitom i leykoplakiey mochevogo puzyrya. [dissertation] Saint Petersburg; 2015. (In Russ.)]
3. Неймарк А.И., Ильинская Е.В., Лебедева Р.Н., Таранина Т.С. Диагностика и лечение лейкоплакии мочевого пузыря у женщин // Урология. – 2009. – № 2. – С. 18–22. [Neymark AI, Il'inskaya EV, Lebedeva RN, Taranina TS. Leucoplakia vesicae

in females: diagnosis and treatment. *Urologiia*. 2009;(2):18-22 (In Russ.)]

4. Неймарк А.И., Ильинская Е.В., Таранина Т.С. Клинико-лабораторные особенности у женщин с лейкоплакией мочевого пузыря // Сибирский медицинский журнал (Иркутск). – 2007. – Т. 70. – № 3. – С. 51–54. [Neymark AI, Il'inskaya EV, Taranina TS. Clinic-laborotorial features of cystitis in women with leucoplakia of urinary bladder. *Sibirskii meditsinskii zhurnal*. 2007;70(3): 51-54 (In Russ.)]
5. Wang H, Chong T, Tang XY, Zheng WB. Transurethral resection in women with symptomatic keratinizing squamous metaplasia of urinary bladder: A retrospective study of 92 cases. *Low Urin Tract Symptoms*. 2020;12(2):137-142. https://doi.org/10.1111/luts.12294.
6. Лоран О.Б., Синякова Л.А., Косова И.В., Охриц В.Е. Лейкоплакия мочевого пузыря как причина стойкой дизурии // Медицинский совет. – 2009. – № 1. – С. 9–12. [Loran OB, Sinyakova LA, Kosova IV, Okhrits VE. Leykoplakiya mochevogo puzyrya kak prichina stoykoy dizurii. *Meditsinskiy sovet*. 2009;(1):9-12 (In Russ.)]
7. Kasianandan A, Kannan K. Leukoplakia of the bladder: a case report and literature review. *Int Urogynecol J*. 2012;23(1):131-133. https://doi.org/10.1007/s00192-011-1491-3.
8. Аль-Шукри С.Х., Кузьмин И.В., Слесаревская М.Н., и др. Расстройства мочеиспускания у больных с синдромом хронической тазовой боли и лейкоплакией мочевого пузыря // Урологические ведомости. – 2016. – Т. 6. – № 2. – С. 5–10. [Al'-Shukri SKh, Kuz'min IV, Slesarevskaya MN, et al. Disorders of urination in patients with chronic pelvic pain syndrome and bladder leukoplakia. *Urologicheskie vedomosti*. 2016;6(2):5-10. (In Russ.)] https://doi.org/10.17816/uroved625-10.
9. Benelli A, Varca V, Vaccaro C, et al. Keratinizing squamous metaplasia of the bladder: Our experience and current approaches. *Urologia*. 2020;87(2):97-100. https://doi.org/10.1177/0391560318810197.
10. Wei DC, Politano VA, Selzer MG, Lokeshwar VB. The association of elevated urinary total to sulfated glycosaminoglycan ratio and high molecular mass hyaluronic acid with interstitial cystitis. *J Urol*. 2000;163(5):1577-1583. https://doi.org/10.1016/S0022-5347(05)67682-3.
11. Khan MS, Thornhill JA, Gaffney E, et al. Keratinising Squamous Metaplasia of the Bladder: Natural History and Rationalization of Management Based on Review of 54 Years' Experience. *Eur Urol*. 2002;42(5):469-474. https://doi.org/10.1016/s0302-2838(02)00358-5.
12. Слесаревская М.Н., Кузьмин И.В., Игнашов Ю.А. Особенности симптоматики и психоэмоционального статуса у женщин с синдромом хронической тазовой боли // Урологические ведомости. – 2015. – Т. 5. – № 3. – С. 16–19. [Slesarevskaya MN, Kuz'min IV, Ignashov YA. Characteristics of symptoms and psychosomatic status in women with chronic pelvic pain syndrome. *Urologicheskie vedomosti*. 2015;5(3):16–19. (In Russ.)]. https://doi.org/10.17816/uroved5316-19.
13. Царева А.В. Способ хирургического лечения лейкоплакии мочевого пузыря // Сибирский медицинский журнал (г. Томск). – 2009. – Т. 24. – № 3. – С. 38–41. [Tsareva AV. Surgical treatment of urinary bladder leukoplakia. *Siberian medical journal*. 2009;24(3):38-41. (In Russ.)]
14. Нотов К.Г., Сазонова И.Д., Домахин И.А., и др. Результаты хирургического лечения лейкоплакии мочевого пузыря у женщин с хроническим циститом // Бюллетень Сибирского отделения Российской академии медицинских наук. – 2013. – Т. 33. – № 3. – С. 37–39. [Notov KG, Sazonova ID, Domakhin IA, et al. The results of surgical treatment of leukoplakia of the bladder in women with chronic cystitis. *Bull Sib Otd Ross Akad Med Nauk*. 2013;33(3):37-39. (In Russ.)]
15. Слесаревская М.Н., Соколов А.В., Жарких А.В. Преимущества лазерной коагуляции лейкоплакии мочевого пузыря // Урологические ведомости. – 2012. – Т. 2. – № 1. – С. 16–22. [Slesarevskaya MN, Sokolov AV, Zharkikh AV. Preimushchestva lazernoy koagulyatsii leykoplakii mochevogo puzyrya. *Urologicheskie vedomosti*. 2012;2(1):16–22. (In Russ.)]. https://doi.org/10.17816/uroved2116-22.
16. Хамзин А.А., Фролов Р.А. К вопросу об эффективности лазерной абляции измененной слизистой оболочки мочевого пузыря / Сборник тезисов V Российского конгресса по эндоурологии и новым технологиям; Ростов-на-Дону, 8–10 сентября 2016 г. – Ростов н/Д, 2016. – С. 71–72. [Khamzin AA, Frolov RA. K voprosu ob effektivnosti lazernoy ablyatsii izmenennoy slizistoy obolochki mochevogo puzyrya. In: Proceedings of the V Russian Congress on endourology and new technologies; Rostov-na-Donu, 8–10 Sep 2016. Rostov n/D; 2016. p. 71-72. (In Russ.)]
17. Амдий Р.Э., Аль-Шукри С.Х., Кузьмин И.В., и др. Опыт применения канефрона при лечении острого неос-

ложненного цистита у женщин // Урологические ведомости. – 2016. – Т. 6. – № 2. – С. 16–22. [Amdiy RE, Al'-Shukri SKh, Kuz'min IV, et al. Use of Kanefron in treatment of acute uncomplicated cystitis in women. *Urologicheskie vedomosti*. 2016;6(2):16-22 (In Russ.)]. https://doi.org/10.17816/uroved6216-22.

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