Research article

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IMMUNOHISTOCHEMICAL ASSESSMENT OF BLADDER CANCER ON THE BACKGROUND OF THE CHRONIC INFLAMMATION

The study was performed as a part of research work "Studying the influence of inflammatory process on origin and development of cancer in the organs of genito-urinary system" (state registration number 0103U002379).

ABSTRACT. Background. The effect of chronic inflammation caused by uropathogenic strains of bacteria on bladder cancer is a little-studied subject. **Objective** of the research was to investigate the interrelationship between the expression of CD95, p53, Ki-67, Bcl-2, BAX, E-cadherin, β-catenin COX-2, eNOS, iNOS markers and the presence of concomitant urinary tract infection. **Methods.** Tumor specimens taken from 44 patients with superficial bladder cancer were divided in two groups according to the absence (I) or presence (II) of urinary tract infection. The level of markers expression was detected with the help of immunohistochemical methods. Specimens of bladder wall from 8 patients with benign prostate hyperplasia were used as a control. **Results.** Statistically significant increase of p53, Ki67 expression and decrease of CD95, BAX, E-cadherin and β-catenin expression in tumor tissue comparing with the control was found ($p < 0,05$). It is established that in the group I specimens expression of iNOS (1,0±0,87) in tumor tissue was less pronounced than in group II (1,95±0,57) ($p<0,05$). Presence of strong positive correlation between p53 and Ki67, bcl-2 and BAX expression in group I; bcl-2 and Ki67, BAX and β-catenin expression in group II were revealed ($p<0,001$). **Conclusions.** Decrease of apoptotic activity and adhesive properties, increase of proliferation of urothelium are typical characteristics of bladder cancer. Increase of the expression of iNOS on the background of the inflammatory process may be evidence in favor of the negative effects of inflammation on the course of cancer. The difference in interrelationships between the levels of apoptotic and proliferation markers expression in group I and II evidence changes of their interaction and can be the reason of unusual tumor development on the background of inflammatory process.

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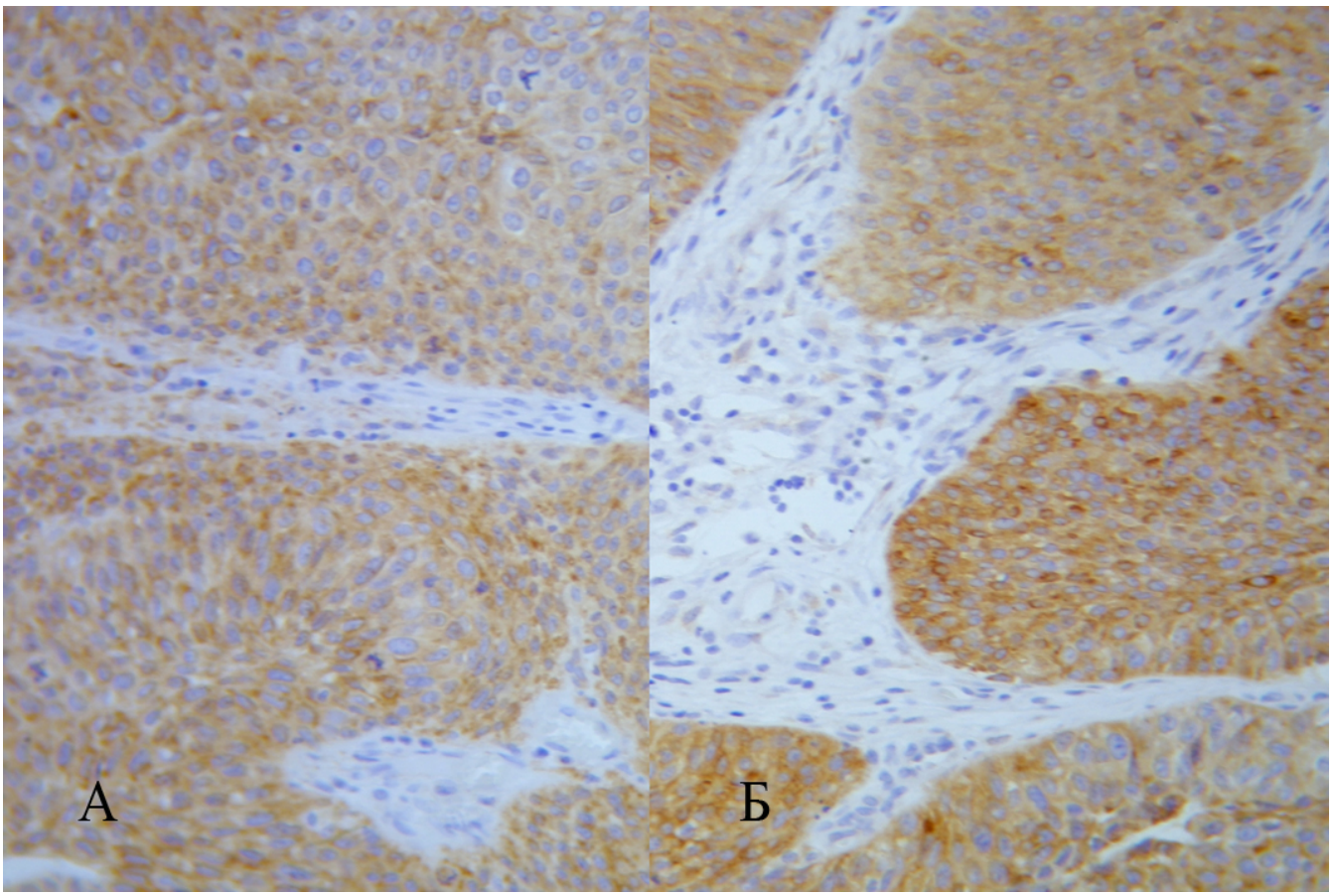

Fig.1. Urinary bladder carcinoma. COX-2-positive cells in tumor stroma and epithelium with concomitant inflammation (А) and in the epithelium without inflammation (Б). Immunohistochemical reaction, additional staining with Mayer's hematoxylin. ×200.

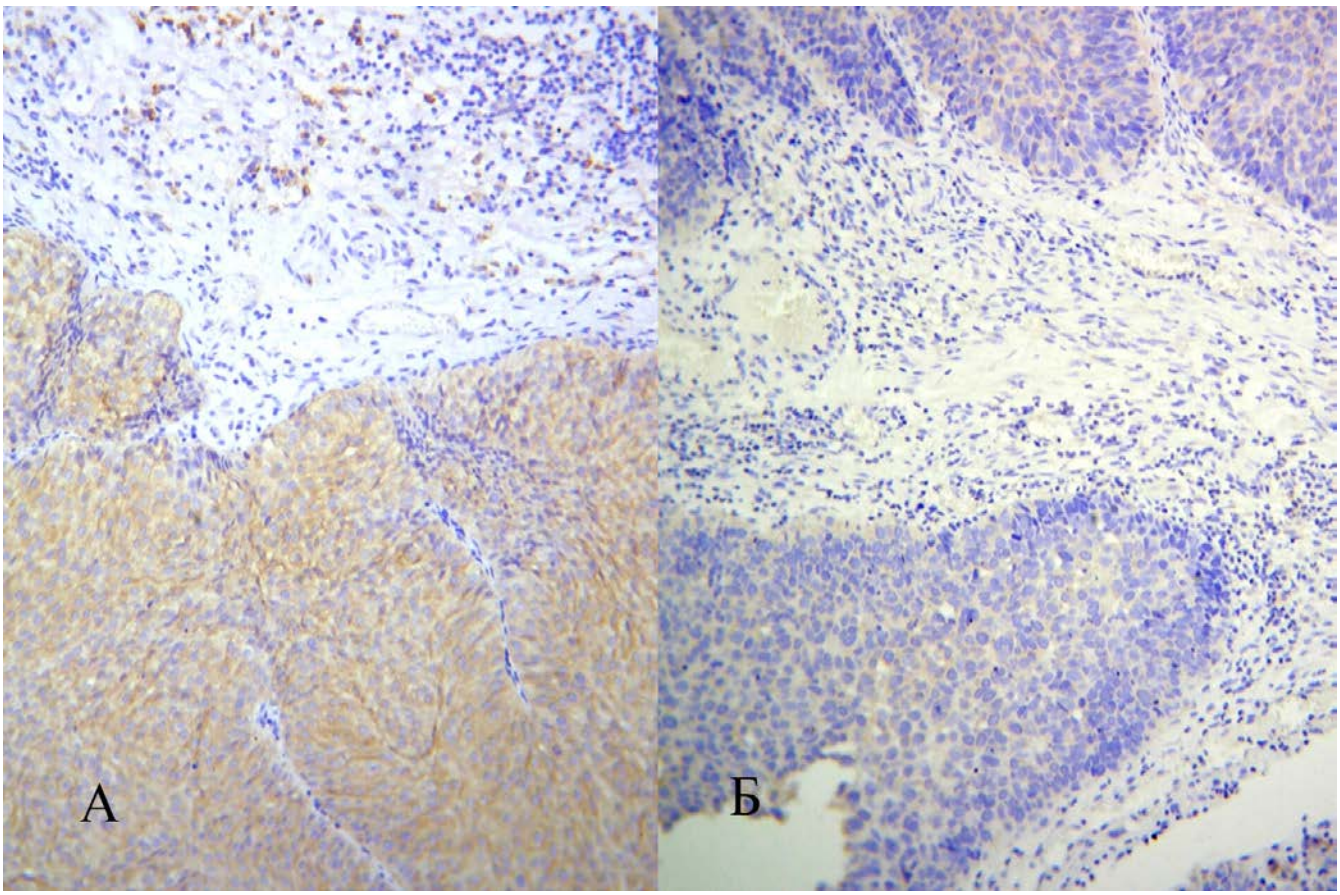

Fig. 2. Urinary bladder carcinoma. iNOS-positive cells in tumor stroma and epithelium with (А) and without (Б) concomitant inflammation. Immunohistochemical reaction, additional staining with Mayer's hematoxylin. ×100.

References:

1. Burger M, Catto JW, Dalbagni G, Grossman HB, Herr H, Karakiewicz P, et al. Epidemiology and risk factors of urothelial bladder cancer. European urology. 2013;63(2):234-41. doi: 10.1016/j.eururo.2012.07.033. PMID: 22877502.

2. Abdulamir AS, Hafidh RR, Kadhim HS, Abubakar F. Tumor markers of bladder cancer: the schistosomal bladder tumors versus non-schistosomal bladder tumors. J Exp Clin Cancer Res. 2009;28:27. doi: 10.1186/1756-9966-28-27. PMID: 19243595; PMCID: PMC2650688.

3. Ruddon RW. Cancer biology. 4th ed. Oxford; New York: Oxford University Press; 2007. XIV, 530 p.

4. Laulier C, Lopez BS. The secret life of Bcl-2: apoptosis-independent inhibition of DNA repair by Bcl-2 family members. Mutat Res. 2012;751(2):247-57. doi: 10.1016/j.mrrev.2012.05.002. PMID: 22677530.

5. Bullwinkel J, Baron-Luhr B, Ludemann A, Wohlenberg C, Gerdes J, Scholzen T. Ki-67 protein is associated with ribosomal RNA transcription in quiescent and proliferating cells. J Cell Physiol. 2006;206(3):624-35. doi: 10.1002/jcp.20494. PMID: 16206250.

6. Romanenko A, Morimura K, Kinoshita A, Wanibuchi H, Vozianov A, Fukushima S. Aberrant expression of E-cadherin and beta-catenin in association with transforming growth factor-beta1 in urinary bladder lesions in humans after the Chernobyl accident. Cancer science. 2006;97(1):45-50. doi: CAS [pii]10.1111/j.1349-7006.2005.00131.x. PMID: 16367920.

7. Koksal IT, Ates M, Danisman A, Sezer C, Ciftcioglu A, Karpuzoglu G. Reduced E-cadherin and alpha-catenin expressions have no prognostic role in bladder carcinoma. Pathol Oncol Res. 2006;12(1):13-9. doi: PAOR.2006.12.1.0013. PMID: 16554911.

8. Marks F, Furstenberger G, Muller-Decker K. Tumor promotion as a target of cancer prevention. Recent Results Cancer Res. 2007;174:37-47. PMID: 17302183.

9. Heller A. Apoptosis-inducing high (.)NO concentrations are not sustained either in nascent or in developed cancers. ChemMedChem. 2008;3(10):1493-9. doi: 10.1002/cmdc.200800257. PMID: 18759245.

10. Yamana K, Bilim V, Hara N, Kasahara T, Itoi T, Maruyama R, et al. Prognostic impact of FAS/CD95/APO-1 in urothelial cancers: decreased expression of Fas is associated with disease progression. Br J Cancer. 2005;93(5):544-51. doi: 10.1038/sj.bjc.6602732. PMID: 16091761; PMCID: PMC2361597.

11. Gonzalez-Campora R, Davalos-Casanova G, Beato-Moreno A, Garcia-Escudero A, Pareja Megia MJ, Montironi R, et al. BCL-2, TP53 and BAX protein expression in superficial urothelial bladder carcinoma. Cancer Lett. 2007;250(2):292-9. doi: S0304-3835(06)00566-0 [pii]; 10.1016/j.canlet.2006.10.011. PMID: 17126995.

12. Bryan RT, Atherfold PA, Yeo Y, Jones LJ, Harrison RF, Wallace DM, et al. Cadherin switching dictates the biology of transitional cell carcinoma of the bladder: ex vivo and in vitro studies. J Pathol. 2008;215(2):184-94. doi: 10.1002/path.2346. PMID: 18393367.

13. Shie JH, Kuo HC. Higher levels of cell apoptosis and abnormal E-cadherin expression in the urothelium are associated with inflammation in patients with interstitial cystitis/painful bladder syndrome. BJU Int. 2011;108(2 Pt 2):E136-41. doi: 10.1111/j.1464-410X.2010.09911.x. PMID: 21166752.

14. Alvarez V, Lodillinsky C, Umerez S, Sandes E, Eijan AM. Inhibition of bacillus Calmette-Guerin-induced nitric oxide in bladder tumor cells may improve BCG treatment. Int J Mol Med. 2005;16(4):565-71. PMID: 16142388.

15. Cho KH, Hyun JH, Chang YS, Na YG, Shin JH, Song KH. Expression of nitric oxide synthase and aquaporin-3 in cyclophosphamide treated rat bladder. Int Neurourol J.14(3):149-56. doi: 10.5213/inj.2010.14.3.149. PMID: 21179332; PMCID: PMC2998401.

16. Salim EI, Morimura K, Menesi A, El-Lity M, Fukushima S, Wanibuchi H. Elevated oxidative stress and DNA damage and repair levels in urinary bladder carcinomas associated with schistosomiasis. International journal of cancer. 2008;123(3):601-8. doi: 10.1002/ijc.23547. PMID: 18478569.