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Professional Paper

URINE CYTOLOGY AND AXILLARY TESTING FOR INTERPRETATION AND FOLLOW-UP OF URINARY TUMORS

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SUMMARY – Microscopic appearance of cells in urine cytological samples is the formal diagnostic approach adjunct to cystoscopy for the detection and follow-up of urinary tumors. However, cystoscopy is a surgical method and cytology may miss low-grade papillary tumors. Several assays and markers have been developed to assist in this. When combined with conventional cytology, uro-oncological diagnostic performance is improved. We review the value of these non-invasive modalities in comparison with urine cytomorphology in the work-up of urothelial malignancies.

Key words: *urinary neoplasms; cytology; tumor markers*

Introduction

Urine cytology

Bladder cancer is the second most common malignancy of the urogenital tract and comprises up to 2-3% of all neoplasia, ranking forth in men and ninth in women[1]. More recent studies have downgraded the frequency in the United States[2,3]. In 90% of cases, the tumors grow from the urothelium. The accepted means for the detection of bladder cancer is cystoscopy plus urine cytology. In recent years, several non-surgical methods have been developed for early diagnosis of tumor relapse. The molecular pathways involved in tumorigenesis have led to molecular diagnostic assays. However, cytology remains the method of choice in the interpretation of in situ and high-grade tumors[1].

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The performance of urine cytology is associated with tumor grade (high-low), specimen type (voided-catheterized-cystoscopy induced-washings), and number of samples.

Sensitivity and specificity of cytology for the detection of high-grade urothelial tumors (Fig. 1)

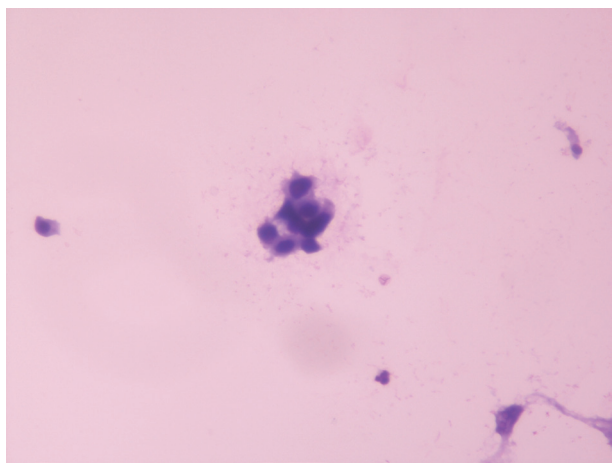

Fig. 1. High grade urothelial neoplasm. Aggregate of neoplastic cells. Papanicolaou stain x400.

and in carcinoma in situ (CIS) is high because these neoplasms shed many cells with obvious signs of malignancy in voided urine. In low-grade urothelial carcinoma, as well as in papillary urothelial neoplasm of low malignant potential (PUNLMP), cytology is neither sensitive nor specific[4].

Renal adenocarcinoma and adenocarcinoma of the prostate exfoliate cells into the urine and can be diagnosed by cytological examination. Staining with antibodies to EMA, CD15, and Vimentin can confirm the diagnosis for renal adenocarcinoma, and PSA immunostaining can establish the diagnosis for prostatic adenocarcinoma. Primary adenocarcinomas of the bladder are infrequent, comprising less than 2% of all bladder cancer cases.

Squamous cell carcinoma of the bladder is relatively uncommon and is strongly associated with Schistostoma haematobium, often endemic to Egypt. In this type the neoplasms are well-differentiated.

Non-keratinized squamous cell carcinomas can be cytologically misinterpreted as urothelial carcinomas. In these tumors, immunocytology is necessary using CK8/18 cytokeratins (Fig. 2). In uncommon

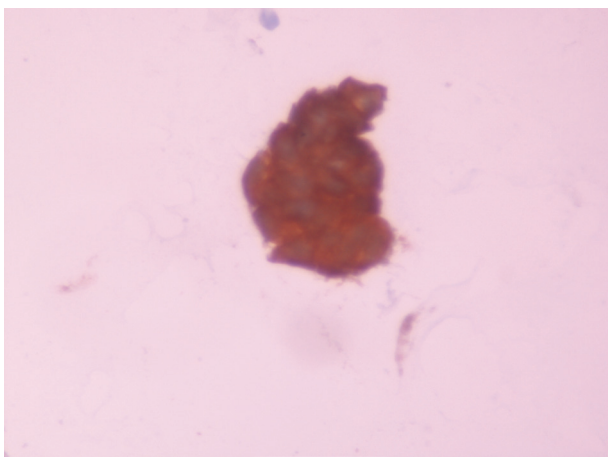

Fig. 2. High grade urothelial neoplasm. Papillary formation of neoplastic cells. CK8/18 immunostain x400.

lymphomas, the cytological diagnosis is established by combined morphologic-immunophenotypic features[5].

The accuracy of urine cytology is influenced by tumor grade, specimen collection method, and adequacy[6]. High-grade carcinoma exfoliates evident abnormal cells into urine samples, resulting in high diagnostic accuracy with cytohistological correlation up to 98%, as reported by Bastacky et al.[7]. In contrast, for low-grade urothelial neoplastic lesions (papillary neoplasm of low malignant potential and low-grade papillary urothelial carcinoma), sensitivity and specificity scores are low at 8.5% and 50.0%, respectively, as observed by Raab et al.[8]. Specimen collection also affects the predictive value of urine cytology. A number of studies indicate that the greater the number of cell samples the more the sensitivity, principally in the interpretation of high-grade lesions[9-12].

Two types of illnesses can be distinguished based on clinical outcome: a more fatal and a less fatal one[13]. The extent of tumor penetration and tumor grade influence the illness fatality and molecular data suggest conflicting primary genetic changes[14]. At first presentation, approximately 75% cases are superficial, while 25% cases involve the muscularis propria of the urinary bladder as reported by Ro et al.[15]. A high recurrence rate has been reported for superficial tumors (50-70%) within 5 years and a considerably low growth rate (about 10%), resulting in consequently long survival rates[16-18].

Tumors infiltrating the muscularis propria have a far worse outcome, with an overall five-year recurrence-free survival rate of only 69%, and just 39% in patients harboring regional lymph node metastasis, as observed by Steven et al.[19].

In 1945, Papanicolaou and Marschall[20] introduced urine cytology as a diagnostic tool in the work-up of urinary tract oncology. They initiated a development that rendered urine cytology a valid diagnostic method of urological and uro-oncological diagnosis and follow-up.

Subsequently, Kohler and Milstein[21] described the first monoclonal antibody, an innovation in the field of immunology.

Morphological evaluation of exfoliated cells in urine is a supplement to endoscopic and ultrasonographic evaluation of the urinary tract in the diagnostic approach for urothelial carcinoma, with exceptional specificity and sensitivity for high-grade tumors[22].

Urine cytology has been evaluated and validated in various clinical settings and has been taken into consideration by the World Health Organization classification of 2004[23]. The limitations of conventional morphology-based urine cytology have been outlined[24-26], and experienced cytologists have developed clear rules for its use[27].

Morphometric advancements can supplement diagnostic information, as reported by Vom Dorp et al.[28].

Urine immunocytology

Urine immunocytology assigns antibodies against cell surface antigens expressed by urothelial carcinoma cells[29].

Cytokeratin immunostains are utilized for the diagnosis of the transitional cell neoplasms (kidney, urinary bladder and urethra) in cytology, as reported by several authors[30]. This panel includes cytokeratin AE1/AE3, cytokeratin 20 (CK20), a marker of umbrella cells[31], and cytokeratin fragments[32]. CK20 positive atypical urothelial cells are suggestive of low-grade transitional cell carcinomas of the lower and upper urinary tract[33-35]. As recently reported, transitional cell carcinomas express placental S100 protein, GATA binding protein 3 (GATA3), cytokeratins 7 and 20(CK7 and CK20), uroplakin III, and p63. Expression of both CK20 and proliferation associated marker ki-67 suggests a poor prognosis[36,37]. A study on human keratins has been published by Moll et al. in 2008[38].

Renal adenocarcinoma and adenocarcinoma of the urinary bladder stain positive for EMA, CD15 and Vimentin markers, as reported by Wilkerson et al.[39]. GATA-3 and p40 are used to separate metastatic urothelial carcinoma from squamous cell carcinoma, as reported by Brandler et al.[40]. Lymphomas of the urinary bladder are usually of B-cell and MALT types and express CD20, and CD19, CD20 and FMC7, respectively[41].

Plasmacytoid carcinoma (PUC) is a rare aggressive variant of urinary bladder cancer with poor outcomes. Malignant cells have a plasmacytoid morphology with abundant cytoplasm and eccentric nuclei. In immunocytochemistry, the neoplastic cells are reactive for cytokeratin subtypes AE1/AE3, CK7, CK8/18, and plasma cell antigen CD138[42].

Fibroblasts growth factor (FGF) and its receptor (FGFR) are markers for surveillance[43]. FGFR3 alterations are associated with low-grade tumors and favorable prognosis[44,45]. Tumor suppression gene p53 genetic alteration and increased ki-67 proliferative activity correlate with high-grade tumors and poorer prognosis[46].

The Paris System working group was composed of pathologists and urologists, and met in 2013 at the venue of the International Congress of Cytology, proposing the Paris system to standardize urine cytology[47]. In interpretation of urine samples that often contain few and misrepresented cells, immunocytology is an accepted method[48,49].

FISH

Genetic alterations are involved in triggering and progression of bladder tumors. Loss of a part or the whole of chromosome 9 is the most frequent genetic alterations associated with bladder tumors. The other chromosomes involved are chromosomes 17, 7.11 and 1. Fluorescence in situ hybridization uses fluorescent labeled DNA probes to chromosomal centromeres, and is performed to monitor patients for onset or relapsed urothelial neoplasms. In a study by Halling et al. in 2000, sensitivity of FISH for the detection of urothelial carcinoma was found to be better to that of cytology, while the specificity of FISH and cytology for urothelial carcinoma were not found to besignificantly different (50).

IMMYNOCYT TEST

The immunocyt test combines urinary cytology and fluorescence immunocytochemistry by monoclonal antibody 19A211 labeled with Texas red, which detects a high molecular weight form of CEA, and antibodies M344 and LDQ10 labeled with fluorescein that detects cytoplasmic mucin antigens expressed in low-grade bladder carcinoma cells. Pfister et al. reported a significant increase in sensitivity when including immunocyt in urinary cytology examinations[51].

However, this method has a low specificity compared with urine cytology[52].

TELOMERASE

Telomerase is an enzyme acting on chromosomal instability by synthesizing telomeres. Bladder cancer can produce telomerase and thus regenerate telomeres and prevent apoptosis (cell death). It is detected using the telomeric repeat amplification protocol method (TRAP) or by polymerase chain reaction (PCR). A meta-analysis of 42 tumor markers and assays for the diagnosis of bladder cancer has shown that telomerase has the highest sensitivity (75%)[53]. In this study, it was also shown that the specificity of urine cytology was higher (94%) and the difference was statistically significant in comparison to the specificity of other assays except the specificity of telomerase, which was not found to be significantly different[53].

HYALURONIC ACID AND HYALURONIDASE

Urine hyaluronic acid (HA) is a glycosaminoglycane and hyaluronidase (HAase) is an endoglycosidase which degrades hyaluronic acid into fragments, which are associated with bladder cancer angiogenesis and metastasis [54].

NUCLEAR MATRIX PROTEIN 22 (NMP 22)

NMP-22 is released from the nuclei of tumor cells during apoptosis. When released in urine, it is detected by an enzyme-linked immunoassay kit using monoclonal antibodies. Grossman et al. investigated the diagnostic performance of NMP22 testing in a cohort of 1331 patients with predilection for bladder cancer. The sensitivity was found to be 55.7% and the specificity 85%, while the sensitivity and specificity for urine cytology were 15.8% and 99.2%, respectively[55]. 99% of relapses were found by combining NMP22 assay and cystoscopy, while cystoscopy alone recognized only 91.3% and sensitivity was not significantly increased by voided cytology[56].

The NMP22 assay was compared to photodynamic diagnosis (PPD) of bladder cancer. Urine samples taken from 100 patients suspected of harboring cancer were tested for NMP22 and by cytology, and afterwards by PPD. Sensitivity and specificity were 65% and 40% respectively, and 44% and 78% by cytology respectively. In bladder wash out samples, sensitivity and specificity of cytology was 75% and 62%. In contrast, PPD sensitivity and specificity were 93% and 43%. NMP22 scoring was of limited value due to low sensitivity, possibly because of false positive results in benign conditions. The conclusion was that NMP22 testing in combination with PPD cannot be suggested for the detection or follow-up of bladder tumors in daily clinical practice[57].

BTA-TRAK and BTA-stat

BTA-TRAK and BTA-stat assays measure the human complement factor H related protein in urine, which belongs to the wide family of Bladder Tumor Antigens (BTAs). They are basement membrane degradation complexes released after tumor cell invasion[58].

NOVEL IMAGING MODALITIES

Several imaging modalities have been used in the identification of suspected cancer and primary/recurrent non-muscle-invasive bladder cancer (NMIBC), in addition to the classic White Light Imaging (WLI). Recently, a new digital image enhancing endoscopic system (IES) has been introduced to serve this purpose[58,60].

Conclusion

We believe that none of the non-invasive tests alone can lead urologists to more secure diagnosis and monitoring of patients with bladder cancer, and neither can reducing cystoscopic investigation frequency. The combination of cystoscopy, urine cytomorphology, urine immunocytology, and molecular urine markers testing, enhances the diagnostic performance of standard procedures, to the benefit of patients and clinicians in daily practice.

References

1. Tanagho EA, McAnich JW. SmithYs General Urology, 15th ed. 2000, Lange Medical Books/McGraw-Hill.
2. Miremami J, Kyprianou N. The Promise OF Novel Markers in Bladder Cancer. Int J Mol Sci. 2014;15,23897-908.
3. Smith ZL,Guzzo ThJ. Urinary markers for bladder cancer. F1000Prime REPORTS. 2013;5:21:1-6.
4. Raab SS, Lenel JC, Cohen MB. Low grade transitional cell carcinoma of the bladder. Cytologic diagnosis by key features as identified by logistic regression analysis. Cancer. 1994 Sep 1;74(5):1621-6.
5. Murphy WM. Current status of urinary cytology in the evaluation of bladder neoplasms. Hum Pathol. 1990;21:886-96.
6. Brimo F, Vollmer RT, Case B, Aprikiraan A, Kassouf W, Auger M. Accuracy of Urine Cytology and the Significance of an Atypical Category. Am J of Clin Pathol. 2009;785-93.
7. Bastacky S, Ibrahim S, Wilczynski SP, et al. The accuracy of urinary cytology in daily practice. Cancer. 1999;87:118-28.
8. Raab SS, Grzybicki DM, Vrbin CM, et al. Urine cytology discrepancies: frequency, causes, and outcomes. Am J Clin Pathol. 2007;127:946-53.
9. Hermansen DK, Badalament RA, Bretton PR, et al. Voided urine flow cytometry in screening high-risk patients for the presence of bladder cancer. J Occup Med. 1990;32:894-7.
10. Beyer-Boon ME, de Voogt HJ, van der Velde EA, et al. The efficacy of urinary cytology in the detection of urothelial tumours: sensitivity and specificity of urinary cytology. Urol Res. 1978;6:3-12.
11. Planz B, Jochims E, Deix T, et al. The role of urinary cytology for detection of bladder cancer. Eur J Surg Oncol. 2005;31:304-8.
12. Badalament RA, Kimmel M, Gay H, et al. The sensitivity of flow cytometry compared with conventional cytology in the detection of superficial bladder carcinoma. Cancer. 1987;59:2078-85.
13. Mitra AP. Urine Cytologic Analysis: Special Techniques for Bladder Cancer Detection. Connection. 2010:169-77.

14. Mitra AP, Datar RH, Cote RJ. Molecular pathways in invasive bladder cancer: New insights into mechanisms, progression, and target identification. J Clin Oncol. 2006 Dec 10;24(35):5552-64.
15. Ro JY, Staerkel GA, Ayala AG. Cytologic and histologic features of superficial bladder cancer. Urol Clin North Am. 1992 Aug;19(3):435-53.
16. Althausen AF, Prout GR Jr., Daly JJ. Non-invasive papillary carcinoma of the bladder associated with carcinoma in situ. J Urol. 1976 Nov;116(5):575-80.
17. Lutzeyer W, Rubben H, Dahm H. Prognostic parameters in superficial bladder cancer: An analysis of 315 cases. J Urol. 1982 Feb;127(2):250-2.
18. Holmang S, Hedelin H, Anderstrom C, Johansson SL. The relationship among multiple recurrences, progression and prognosis of patients with stages Ta and T1 transitional cell cancer of the bladder followed for at least 20 years. J Urol. 1995 Jun;153(6):1823-7.
19. Steven K, Poulsen AL. Radical cystectomy and extended pelvic lymphadenectomy: Survival of patients with lymph node metastasis above the bifurcation of the common iliac vessels treated with surgery only. J Urol. 2007 Oct;178(4):1218-24.
20. Papanicolaou GN, Marshall VF. Urine sediment smears as a diagnostic procedure in cancers of the urinary tract. Science. 1945;101:519-20.
21. Köhler G, Milstein C. Continuous cultures of fused cells secreting antibody of predefined specificity. Nature. 1975;256(5517):495-7.
22. Niedworok C, Rembrink, Hakenberg OW, Börgermann C, Rossi R, Schneider T, Becker M, Szarvas T, von Ostau C, Swoboda A, Rübben H, vom Dorp F. Stellenwert der Urinzytologie in der Diagnostik von High-grade-Urotheltumoren. Der Urologe. 2009;48(9):1018-24.
23. Tschirdewahn S, Boergermann C, Becker M, Szarvas T, Rübben H, Fvom Dorp F. Urinzytologische Diagnostik vor dem Hintergrund der neuen histopathologischen Klassifikation. Urologe. 2009;48:615-8.
24. Fernández MI, Parikh S, Grossman HB, Katz R, Matin SF, Dinney CP, Kamat AM. The role of FISH and cytology in upper urinary tract surveillance after radical cystectomy for bladder cancer. Urol Oncol. 2012 Nov-Dec;30(6):821-4.
25. Messer J, Shariat SF, Brien JC, Herman MP, Ng CK, Scherr DS, Scoll B, Uzzo RG, Wille M, Eggener SE, Steinberg G, Terrell JD, Lucas SM, Lotan Y, Boorjian SA, Raman JD. Urinary cytology has a poor performance for predicting invasive or high-grade upper-tract urothelial carcinoma. BJU Int. 2011 Sep;108(5):701-5.
26. Wijkström H, Du Reitz B, Tolf A. Urinary cytology, cytometry, and new approaches in the assessment and monitoring of urothelial cancer. Droller MJ (Ed.), Urothelial tumors—American Cancer Society atlas of clinical oncology, BC Decker Inc., Hamilton, Canada (2004).
27. P. Rathert. Urinzytologie beim Harnblasenkarzinom: Kritische Wertung Urologe A, 2003;42:908-11.
28. Vom Dorp F, Pal P, Tschirdewahn S, Rossi R, Börgermann C, Schenck M, Becker M, Szarvas T, Hakenberg OW, Rübben H. Correlation of pathological and cytological-cytometric grading of transitional cell carcinoma of the urinary tract. Urol Int. 2011;86(1):36-40.
29. Malte Böhm, Martin Schostak, Oliver W. Hakenberg. Urinary immunocytology—Promise or nonseller? A review with an opinion. Urologic Oncology: Seminars and Original Investigations Volume 32, Issue 4, May 2014, Pages 383–390.
30. Parker J, Spiess PE. Current and emerging bladder cancer urinary biomarkers. Sci World J. 2011;11:1103-12.
31. Melissourgos ND, Kastrinakis NG, Skolarikos A, Pappa M, Vassilakis G, Gorgoulis VG, et al. Cytokeratin-20 immunocytology in voided urine exhibits greater sensitivity and reliability than standard cytology in the diagnosis of transitional cell carcinoma of the bladder. Urology. 2005;66:536-41.
32. Hakenberg OW, Fuessel S, Richter K, Froehner M, Oehlschlaeger S, Rathert P, et al. Qualitative and quantitative assessment of urinary cytokeratin 8 and 18 fragments compared with voided urine cytology in diagnosis of bladder carcinoma. Urology, 2004;64:1121-6.
33. Lin S, Hirschowitz SL, Williams C, Shintako P, Said J, Rao JY. Cytokeratin 20 as an immunocytochemical marker for detection of urothelial carcinoma in atypical cytology: preliminary retrospective study on archived urine slides. Cancer Detect Prev. 2001;25:202-9.
34. Bhatia A, Dey P, Kumar Y, Gautam U, Kakkar N, Srinivasan R, et al. Expression of cytokeratin 20 in urine cytology smears: a potential marker for the detection of urothelial carcinoma. Cytopathology. 2007;18:84-6.
35. Mai KT, Teo I, Robertson SJ, Marginean EC, Islam S, Yazdi HM. Immunostaining as a diagnostic aid in cytopathologic study of upper urinary tract urothelial carcinoma. Acta Cytol. 2009;53:611-8.
36. Ye YK, Bi XC, He HC, et al. CK20 and Ki-67 as significant prognostic factors in human bladder carcinoma. Clin Exp Med. 2010;10:153-8.
37. Bertz S, Otto W, Denzinger S, et al. Combination of CK20 and Ki-67 immunostaining analysis predicts recurrence, progression, and cancer-specific survival in pT1 urothelial bladder cancer. Eur Urol. 2014;65:218-26.
38. Moll R, Divo M, Langbein L. The human keratins: biology and pathology. Histochem Cell Biol. 2008;129:705-33.
39. Wilkerson ML, Lin F, Liu H, Cheng L. The application of immunohistochemical biomarkers in urologic surgical pathology. Arch Pathol Lab Med. 2014;138:1643-65
40. Brandler TC, Aziz M, Rosen L ,Bhuiya TA, Yaskiv O. Usefulness of GATA-3and p40 immunostains in the diagnosis of metastatic urothelial carcinoma in cytology specimens. Cancer Cytopathology. 2014;122(6):468-73.
41. Venyo AK. Lymphoma of the urinary bladder. Advances in Urology Volume 2014(2014):327917.
42. Molek KR, Seili-Bekafigo I, Sternberger C, Jonjic N, Dordevic G. Plasmacytoid Urothelial Carcinoma-Diagnostic Challenge in Cytology. Diagn Cytopathol. 2013;41(4):369-73.
43. Zuiverloon TC, van der Aa MN, van der Kwast TH, et al. Fibroblast growth factor receptor 3 mutation analysis on voided urine for surveillance of patients with low-grade non-muscle-invasive bladder cancer. Clin Cancer Res. 2010;16:3011-8.

44. van Rhijn BW, Zuiverloon TC, Vis AN, et al. Molecular grade (FGFR3/MIB-1) and EORTC risk scores are predictive in primary non-muscle-invasive bladder cancer. Eur Urol. 2010;58:433-41.
45. Serizawa RR, Ralfkiaer U, Steven K, et al. Integrated genetic and epigenetic analysis of bladder cancer reveals an additive diagnostic value of FGFR3 mutations and hypermethylation events. Int J Cancer. 2011;129:78-87.
46. Sun W, Zhang PL, Herrera GA. p53 protein and Ki-67 overexpression in urothelial dysplasia of bladder. Appl Immunohistochem Mol Morphol. 2002 Dec;10(4):327-31.
47. Ghosh A. Review Article. The Paris System. A new insight into reporting urine cytology. Journal of Pathology of Nepal. 2016;6:953-8.
48. Metzgeroth G, Kuhn C, Schultheis B, Hehlmann R, Hastka J. Diagnostic accuracy of cytology and immunocytology in carcinomatous effusions. Cytopathology. 2008;19:205-11.
49. Shidham VB. Appendix II: immunocytochemistry of effusions—processing and commonly used immunomarkers. Shidham VB, Atkinson BF (Eds.), Cytopathologic diagnosis of serous fluids, Saunders WB, Philadelphia (2007), pp. 237–258.
50. Halling K, King W, Sokolowa I, et al. A comparison of cytology and fluorescence in siyu hybridization for the detection of urothelial carcinoma. J Urol. 2000;164:1768-75.
51. Pfister C, Chautard D, Devonec M, et al. Immunocyt test improves the diagnostic accuracy of urine cytology: Results of a French multicenter study. J Urol. 2003;169:921-4.
52. Reynolds JP, Voss JS, Kipp BR, Karnes RJ, et al Comparison of urine cytology and fluorescence in situ hybridization in upper urothelial tract samples. Cancer Cytopathology 2014;122(6):459-67.
53. Sanchini M, Gunelli R, Nanni O, et al. Relevance of urine telomerase in the diagnosis of bladder cancer. JAMA. 2005;294:2052-6.
54. Lokeshwar V, Cerwinka W, Lokeshwar B. HYAL1 Hyaluronidase: A molecular determinant of bladder tumor growth and invasion. Cancer Res. 2005;65:2243-50.
55. Grossman H, Messing E, Soloway M, et al. Detection of bladder cancer using a point of care proteomic assay. JAMA. 2005;293:810-6.
56. Grossman HB, Soloway M, Messing E, Katz G, Stein B, Kassabian V, Shen Y. Surveillance for recurrent bladder cancer using a point-of-care proteomic assay. JAMA. 2006 Jan 18;295(3):299-305.
57. Tritschler S, Scharf S, Karl A, et al. Validation of the diagnostic value of NMP22 BladderChek Test as a marker for bladder cancer by photodynamic diagnosis. Eur Urol. 2007;51:403-7.
58. Van Rhijn BW, Van der Poel HG, Van der Kwast TH. Urine markers for bladder cancer surveillance: A systematic review. Eur Urol. 2005;47:736-48.
59. Kamphuis GM, de Bruin DM, Brandt MJ, Knoll T, Conort P, Lapini A, et al. Comparing image perception of bladder tumors in four different Storz professional image enhancement system modalities using the íSPIES app. J Endourol. 2016;30:602-8.
60. Malmstrom PU, S, Boström PJ, Malavaud B, et al. Non-muscle-invasive bladder cancer: a vision for the future. Scandinavian Journal of Urology. 2017;51(2):87-94.

Sažetak

CITOLOŠKA ANALIZA URINA I POPRATNI PREGLED ZA INTERPRETACIJU I PRAĆENJE URINARNIH TUMORA

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Pregled stanica urinarinih citoloških uzoraka mikroskopom je formalni dijagnostički pristup koji se, uz citologiju, koristi za otkrivanje i praćenje urinarnih tumora. No citoskopija je kirurška metoda, a citologiji mogu promaknuti papilarni tumori niskog stupnja. Razvijeno je nekoliko analiza i biljega koji u tome pomažu. Kada se koriste uz konvencionalnu citologiju, poboljšava se uspješnost uro-onkološke dijagnostike. Pružamo pregled korisnosti ovih ne-invazivnih modaliteta u usporedi s urinarnom citomorfologijom u analizi malignih tumora mokraćnog mjehura.

Ključne riječi: *urinarne neoplazme; citologija; tumorski biljezi*