



The role of urinary cytology for detection of bladder cancer

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Accepted for publication 9 December 2004

KEYWORDS

Urinary cytology;
Bladder cancer

Abstract Purpose. The aim of the present study was to test the value of urinary cytology in the diagnosis of bladder cancer.

Materials and methods. One thousand three hundred and eighty voided urine and bladder wash specimens of 495 patients were evaluated by urinary cytology. All patients then underwent transurethral resection of suspicious bladder areas if cystoscopy and/or preceding biopsy were positive. Statistical differences were analysed using the two-sided Fisher's exact test and Cochran's test ($p < 0.05$).

Results. In 495 patients including 142 patients with bladder cancer urinary cytology revealed a sensitivity of 38.0% and a specificity of 98.3% with a positive and negative predictive value of 90.6 and 78.6, respectively. Sensitivity increased significantly with malignancy grade ($p < 0.05$). In high grade tumours sensitivity improved from initial 52.2% up to 78.3% after the third sample. In sensitivity and specificity of voided urine and barbotage washing samples no significant difference was detected.

Conclusions. Urinary cytology has its place as an additive diagnostic tool to cystoscopy. None of the currently available urinary markers can replace cystoscopy but are helpful for specific diagnostic problems.

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Introduction

Cystoscopy and biopsy is the golden standard for detection of urothelial carcinoma of the urinary bladder but it is invasive and causes significant patient discomfort. Urinary cytology is a non-invasive method for detection of urothelial

carcinoma of the urinary bladder. Urinary cytology has high sensitivity in high grade bladder tumours but is less sensitive in grade 1 tumours with a sensitivity of 0-50% and a still high specificity of 99%.¹⁻⁴

The ideal marker should be rapid, inexpensive and non-invasive with high sensitivity and specificity. In the present study we evaluated conventional urinary cytology in 626 patients to establish whether a higher number of samples affects the sensitivity of cytology. We compared voided urine

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and barbotage bladder washings in terms of sensitivity and specificity. Methods based on the immunocytological detection of antibodies Immuno-cyt, Lewis X and p486 3/12, NMP test, BTA test, telomerase test, FDP test, haemoglobin dip stick, flow and DNA image cytometry and fluorescence in situ hybridisation are discussed. In face of these new markers and tests and the results of our study we ask whether urinary cytology still mandatory.

Material and methods

Patient population

Six hundred and twenty-six patients were evaluated by urinary cytology. Mean age was 62 ± 14 years.⁴⁻⁹ We excluded those with renal cell carcinoma, prostate cancer, metastatic disease, carcinomas others than of urothelial origin and patients after radical cystectomy. Four hundred and ninety-five patients fulfilled the inclusion criteria and 1380 urinary specimens with 346 voided urine and 149 bladder wash of first sample were evaluated. Additional bladder wash specimens were obtained of 42 patients with histologically confirmed bladder cancer. In a subgroup of patients a second and third sample was obtained. Bladder wash and/or voided urine specimens were obtained from patients who had symptoms suggestive of bladder tumours or were being followed after treatment of transitional cell carcinoma of the bladder.⁵ The study included patients with urolithiasis and chronic inflammation. A tumour of the upper urinary tract was excluded by intravenous pyelography.

Spontaneously voided urine and barbotage bladder washings specimens were analysed by conventional cytology. In each patient an aliquot of 10 ml of the entire collected urine sample was centrifuged with 1700g for 10 min and the sediment was resuspended in Saccomanos fixative. In this condition the samples were transported to the laboratory and were there centrifuged for 10 min with 2000 g in a Hettich centrifuge directly on glass slides. The obtained slides were re-fixed using an ethanol-polyethylene-glycol spray. Staining was as described by Papanicolaou. Urinary cytology was performed independently by different members of our pathology department using standard diagnostic criteria.³ After collection of the voided urines and bladder wash specimens, respectively, all patients underwent transurethral resection of suspicious bladder areas as first line therapy if cystoscopy and/or preceding biopsy was

positive. Histopathological staging was performed according to the International Union Against Cancer criteria.

Statistical analysis

Statistical analyses were performed using computer software to calculate overall sensitivity, specificity, positive and negative predictive value. Values are presented as mean \pm standard deviation. Differences were analysed using the two-sided Fisher's exact test and Cochran's test. A *p*-value <0.05 was considered significant.

Results

There were 57 cases of pTa, 27 pT1, 21 pT2, 26 pT3 and 9 pT4 transitional cell carcinoma, two cases of carcinoma in situ and 10 cases of concomitant carcinoma in situ of the bladder. Urothelial carcinoma of the bladder was grade 1 in 42 cases, grade 2 in 55 and grade 3 in 45. Histology revealed a urothelial carcinoma of the urinary bladder in 142 patients. Three hundred and fifty-three patients had no history of bladder cancer and bladder cancer was excluded by cystoscopy and randomised biopsies in all patients.

The results regarding sensitivity and specificity of urinary cytology are summarized in [Tables 1 and 2](#). In a total of 495 patients urinary cytology had a sensitivity of 38.0% and a specificity of 98.3% with a positive and negative predictive value of 90.6 and 78.6, respectively. Sensitivity increased significantly with malignancy grade from 11.9% up to 57.8% for G1 and G3 tumours ($p < 0.05$). Multiple samples from a completely different void or bladder wash could not improve sensitivity in detecting low grade tumours. In high grade tumours sensitivity improved from initial 52.2% up to 78.3% after the third sample. In sensitivity and specificity of spontaneously voided urine and barbotage washing samples no statistically significant difference was detected. Sensitivity of urinary cytology in detecting carcinoma in situ (Cis) was 67%, superficial bladder cancer 22% and invasive bladder cancer 52%.

Discussion

Sensitivity and specificity of urinary cytology

Early detection of new tumours and effective surveillance for recurrences could reduce morbidity

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