

Urinary cytology in bladder cancers

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A prospective study was done to explore the reliability of urinary cytologic examination of 40 cases of transitional cell carcinoma seen at this institution for the period 1991 to 1993. A specificity of 97% sensitivity of 80%, false negative rate of 12.5% were obtained. A single blind review of cytologic and histologic material from 24 of the cases was also performed for evaluation of the cytologic criteria employed for the grading of tumors. Cytohistologic results of grade 1 lesions was unreliable, whereas the results of grades 2 and 3 lesions were reasonably good. [Turk J Med Res 1994; 12(6): 232-235]

Key Words: Cytology, Bladder cancer

Urinary cytologic examination is an accepted laboratory test for screening and follow up of patients with bladder tumors. Because of a lack of morphologic alterations in the low grade tumor, this tumor is not easily identifiable by cytologic examination. Several studies have demonstrated a good correlation between histologic grade and stage, underscoring the necessity of accurate grading (1,2).

We have prospectively explored the sensitivity and specificity of urinary cytologic examination as done in our institution on 40 cases of bladder cancers. Because we routinely perform cytologic grading for correlation with histologic grading, we reviewed our grading system in 24 cases in which cytologic and histologic examination could be simultaneously performed in a blind fashion. Our cytologic criteria for grading are shown in Table 1. The histologic features were graded according to the World Health Organization (WHO) classification. The results of urinary cytologic examination in a total of 40 cases of bladder cancers along with cytohistologic correlation of 24 cases were presented.

MATERIALS AND METHODS

Between the years 1991 and 1993, cytology was performed in 40 bladder cancers, all of which have been included in this study. The urinary cytologic examination was performed at the cytopathology laboratory. During the same period urinary cytologic examination was performed on 247 other urologic cases, of which 240 cases were correctly identified as benign and were false positives.

All of the 40 cases of transitional cell carcinoma (TCC) were located in the bladder. The cytologic examination was performed on voided urine specimens and bladder washing specimens.

Fresh or refrigerated voided urine specimens were prepared with standardized semiquantitative cytocentrifugation preparations as described previously and stained with the hematoxylin-eosin (3). Millipore membrane filter preparations were made in a few instances, when the specimen was hypocellular at the time of initial diagnosis.

The cytologic material was screened by a cytotechnologist and reviewed by a pathologist. Urothelial neoplasms were identified and graded according to criteria in Table 1. The sensitivity and specificity were calculated.

Cytologic materials from 24 cases were reviewed and graded by a pathologist with the criteria listed in Table 1. Representative cytologic and histologic findings are shown in Figures 1 to 3. In some cases, intermediate grades I to II and II to III were more ap-

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Table 1. Criteria for cytologic grading of bladder cancer

| Morphologic Features | Cytologic Grading | | |
|----------------------|--|--|--|
| | I | II | III |
| Background | Clean | Clean | Dirty, tumor diathesis |
| Cellular arrangement | Large fragments of transitional epithelium | Large fragments of transitional epithelium single cells Nuclear crowding and overlap | Large fragments and numerous single cells Syncytia* Cannibalism" |
| Nuclear features | | | |
| Nuclear membrane | Regular, round and oval | Minimal membrane irregularity | Marked membrane irregularity |
| Chromatine | Finely granular | Finely granular, evenly distributed | Increased chromatin coarsely granular, unevenly distributed |
| Nucleolus | Occasional micro nucleoli | Variable micro nucleoli | Macronucleoli |
| Cytoplasmic features | Cell maturation present | Moderate degree of maturation | Maturation absent Squamoid feat Glandular feature |

Loss of cell borders
Cell in cell arrangement

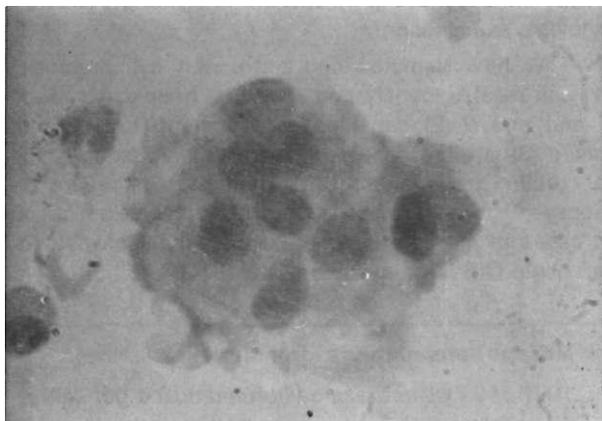


Figure 1. Grade 1 TCC with slightly hyperchromatic (H.E.x1 000)

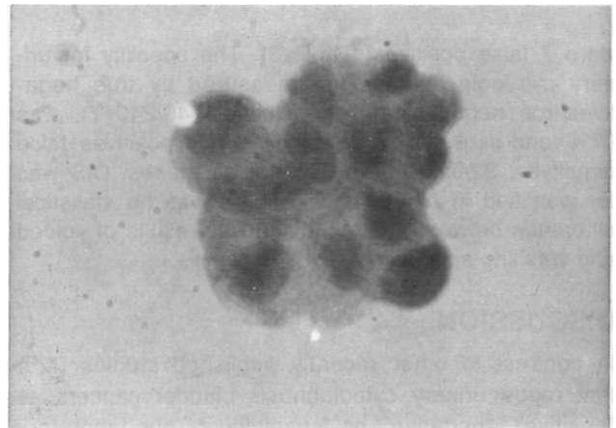


Figure 2. Grade 2 TCC with pleomorphic and moderate hyperchromatic (H.E.x1 000)

appropriate when there was a mixture of cellular patterns.

Histologic material consisted of both biopsy and cystectomy specimens obtained within a year after the cytologic specimens. The slides were reviewed by a pathologist without knowledge of previous grade or clinical history. Patterns of growth and any associated atypia were noted in each case.

RESULTS

As presented in Table 2, 32 of 40 bladder cancers were correctly identified on cytologic examination. Three cases were suspicious, 5 cases had negative cytologic findings. The five negatives included one grade III, one grade II, and three grade I TCCs. There

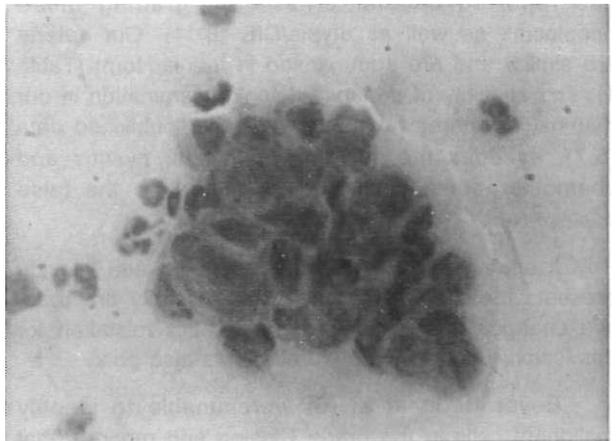


Figure 3. Grade 3 TCC with hyperchromatic macronucleoli and extremely pleomorphic (H.E.x1 000)

Table 2. Histologic diagnosis of 40 cases of bladder cancer

| Histologic diagnosis | Cytologic diagnosis | | |
|----------------------|---------------------|------------|----------|
| | Positive | Suspicious | Negative |
| Grade 1 | 10 | 1 | 3 |
| Grade 2 | 10 | 1 | 1 |
| Grade 3 | 12 | 1 | 1 |
| Total | 32 | 3 | 5 |

Table 3. False positive findings on cytologic examination

| No of cases | Cytologic diagnosis | Comments |
|-------------|---------------------|--|
| 2 | MI | Repeat cytologic examination negative, cystoscopy negative |
| 2 | MI | Cystoscopy negative, histologic examination negative |
| 1 | MI | Lithiasis |
| 1 | MI | Cystitis and lithiasis |
| 1 | MI | Chemotherapy |

were 7 false positives (Table 3). The specificity for urinary cytologic examination measured by true negatives/true negatives+false positives (240/240+7), was 97%, and sensitivity (true positives/true positives+false negatives, 32/32+8) was 80% for all grades. CIS was not identified in all instances. There was no statistical difference between the cytodiagnostic results of voided and washing specimens.

DISCUSSION

In contrast to other recently published studies (4,5) that report urinary cytodiagnosis bladder cancers as "positive", "negative" or "suspicious", our laboratory grades lesions for the purpose of correlating cytologic results with surgical pathological findings. The literature has reported cellular criteria for grading these neoplasms as well as atypia/CIS (8,11). Our criteria are similar and are summarized in tabular form (Table 1). The specificity of urinary cytologic examination in our material compares favorably with other published data (6,7), as does the sensitivity lithiasis, cystitis and chemotherapeutic changes contributed to the false positive rate.

It appears from our study that the grade I lesion presents the greatest problem, for not only are reactive changes due to lithiasis and cystitis mistaken for this lesion, but histologic correlation is also poor.

Beyer Boon et al (6) were unable to identify malignant cells in the grade I lesion and reported that the efficacy of urinary cytologic examination improved with the higher grades, Esposti and Zajicek (7,8) em-

phasized the same point. Our experience is similar to theirs.

Rubben et al (12) compared cytohistologic grading in 300 cases. Their results differ markedly from our own in that they considered 50% of histologic grade III lesions that were either grade II or grade I cytologically. In our data, grade II and III lesions showed good cytohistologic correlation.

The growth pattern of the various lesions demonstrated that practically all of our grade II to III and grade III lesions were infiltrative, which is similar to previously published data (1,2,4). There was either squamous or glandular differentiation in more than 50% of grade III and grade II to III lesions we studied, a feature first recognized by Suprun and Bitterman (11). If identified in urinary cytologic examination, this differentiation almost always indicates a grade III lesion.

There are various classifications (9,10) for cytologic grading, but the major advantage of our system to the clinician is that the cytologic report is similar to the surgical pathological report. In our experience the grade I TCC can only be suspected; grade II TCC is identified with more certainty, and there is no difficulty in diagnosing grade III lesions on urinary cytologic examination.

We have demonstrated that urinary cytodiagnosis: (1) can reliably identify and urothelial neoplasms grade II and above (2) can identify CIS in up to 100% of cases (3) is more sensitive than histologic examination in certain circumstances, eg., denuded epithelium on biopsy (4) is less sensitive than histologic examination in cases of multiple lesions and (5) cannot always differentiate CIS from invasive grade III TCC.

Mesane kanserlerinde idrar sitolojisi

1991-1993 yılları arasında kurumumuzda görülen 40 tranzisyonel hücreli karsinom vakasında idrarın sitolojik muayenesinin güvenilirliğini araştırmak için prospektif bir çalışma yapıldı. Spesifite %97, sensitive %80, false negatiflik oranı ise % 12.5 olarak bulundu. Tümör derecelemesi amacıyla tesis edilmiş olan sitolojik kriterlerin değerlendirilmesi için 24 vakada sitolojik ve histolojik materyal tek kor olarak gözden geçirildi. Grade I lezyonlarda sitoloji sonuçları güvenilir olmamasına karşın grade II ve III lezyonların sonuçları oldukça iyiydi [TurkJMedRes 1994; 12(6): 232-235]

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