Introduction

Cytology is integral in the assessment of urothelial cell carcinoma (UCC). However, upper urinary tract (UUT) specimens are cytologically challenging due to limited tissue and reactive atypia. At our institution UUT biopsies are processed as cell blocks (CB). We compared our institution’s reporting system (IRS) with the recently proposed Paris System for Reporting Urine Cytology (PRS) (Table 1) in UUT specimens and correlated the findings with CB and follow-up resections.

Methods

85 UUT ThinPrep (TP) slides were randomly selected from 64 patients for double-blinded group consensus review. Cytologic assessment was based on guidelines provided by institutional morphologic criteria (IRS) and The Paris System for Reporting Urine Cytology (PRS) (Table 1). Twenty-six of the 85 CBs had follow-up resections, which were separately reviewed and compared using 1973 and 2004 WHO Classification of Tumors of the Urinary System (LGUC, low grade 1, 2; HGUC, grades 2,3). Cytologic concordance between IRS and PRS was evaluated and cytohistologic correlation using CB and resections as the gold standard was also examined.

Table 1: Institutional Reporting System (IRS) and Paris System for Reporting Upper Tract Urothelial Lesions (PRS)

<table>
<thead>
<tr>
<th>Category</th>
<th>Features (IRS)</th>
<th>Features (PRS)</th>
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<tbody>
<tr>
<td>Negative for malignancy</td>
<td>Normal urothelial cells with no features for LGUC and HGUC</td>
<td>N/A</td>
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<tr>
<td>Negative for high grade urothelial carcinoma</td>
<td>N/A</td>
<td>Specimen does not contain cells with features concerning for or diagnostic of high grade UCC.</td>
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<tr>
<td>AUC</td>
<td>Mildly atypical cells, however, insufficient for LGUC or HGUC diagnosis</td>
<td>Some features suggestive of high grade UCC are present but not as pronounced as high grade UCC.</td>
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<tr>
<td>Suspicious for LGUC</td>
<td>Papillary-like clusters lacking fibrovascular cores or limited by preservation issues, obscuring factors, or low cellularity</td>
<td>N/A</td>
</tr>
<tr>
<td>Suspicious for HGUC</td>
<td>Cells with features suggestive of HGUC but limited by preservation issues, low cellularity, or obscuring factors</td>
<td>Unreliable diagnosis of high grade limited by: - Quantitative or qualitative features of abnormal cell morphology. (Note: a single cell meeting these criteria can qualify as suspect)</td>
</tr>
<tr>
<td>Suspicious for urothelial carcinoma, NOS</td>
<td>Urothelial cells with mild to moderate atypia not diagnostic for LGUC or HGUC due to low cellularity, preservation issues, or obscuring factors</td>
<td>N/A</td>
</tr>
<tr>
<td>LGUC</td>
<td>Papillary clusters with fibrovascular cores and mild grade non-urothelial malignancy, scrambling and crowding</td>
<td>No features of high grade UCC and true papillary carcinoma are present.</td>
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<tr>
<td>HGUC</td>
<td>Cells with severe atypical nuclear irregularities, enlargement, hemorrhrosis, scrambling and crowding</td>
<td>At least 10 high power (HP) preserved urothelial cells diagnostic of high grade UCC. (Note: a single cell meeting these criteria can qualify as HGUC)</td>
</tr>
<tr>
<td>Other</td>
<td>Other malignant non-urothelial neoplasms, squamous cell carcinoma, adenocarcinoma, synovial sarcoma, small cell carcinoma.</td>
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</table>

Results

- IRS and PRS had similar rate of HGUC (7.0%, 8.2%, respectively).
- AUC was higher for IRS (31.8%) compared to PRS (11.8%).
- Diagnostic yield of CB was 87% with 9 cases interpreted as HGUC and 17 cases as LGUC.
- CB interpreted with TP specimens increased the overall neoplastic rate in 27% (n=18) of negative, indeterminate (AUC) and suspicious (SUSP) cases (Figure 2).
- PRS-IRS-CB concordance for HGUC was 56% (Figure 1).
- All IRS and PRS HGUC cases were confirmed on biopsy and resection (100% positive predictive value, PPV), and only 2 CB were falsely negative.
- 64% of LGUC on CB were HGUC on resection (Figures 2, 3).
- Of the 24 HGUC CB and resection cases, PRS and IRS correlation was only 21%. PRS reported 32%, [n=8] as negative; and IRS reported 40% as AUC [n=10].
- Using resections as the gold standard, the overall sensitivity of IRS and PRS for HGUC was 75% and 33%, respectively.
- The PPV of IRS, PRS and CB for HGUC was 100%. PRS had more false negative as IRS, which had a higher sensitivity for HGUC. UUT biopsies processed as cell blocks had 87% diagnostic rate and improved the neoplastic rate of TP cases. However, small biopsies may be falsely negative or undergo sample high grade areas.

Discussion

The PPV of IRS, PRS and CB for HGUC was 100%. PRS had more false negative cases than IRS, which had a higher sensitivity for HGUC. UUT biopsies processed as cell blocks had 87% diagnostic rate and improved the neoplastic rate of TP cases. However, small biopsies may be falsely negative or undergo sample high grade areas.

References