Impact of Variant Histology on Response to Neoadjuvant Chemotherapy for Bladder Cancer

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Materials and Methods

- We identified 1,440 patients from our prospectively maintained database with urothelial carcinoma of the bladder who underwent radical cystectomy at our tertiary referral center between 2003 and 2016
- Histology was categorized as pure urothelial carcinoma (PUC) or variant histology (VH)
- Neuroendocrine variants were excluded
- Multivariable Cox proportional hazards model was used to analyze impact of VH on overall survival (OS)

Results

- 1,171 (81.3%) patients were PUC, 269 (18.7%) were VH
- Variant histology was more likely to:
  - Present with extravesical extension (20.8%) vs PUC (13.3%), p<0.01
  - Receive NAC (27.7%) vs PUC (16.4%), p<0.01
  - Be downstaged after receiving NAC (62.3%) vs PUC (54.4%), p<0.01
- On multivariable Cox regression, extravesical extension (HR=2.3, p<0.01), positive lymph node (HR=4.7, p<0.01), LVI (HR=1.6, p<0.01), and age (HR=1.03, p<0.01) were associated with worse OS
- Clinical VH (HR=1.04, p=0.76) and pathologic VH (HR=0.79, p=0.70) had no effect on OS
- 5-year overall survival for VH + NAC was 55% and VH - NAC was 57%, p=0.33

Table 1. Variant histology characteristics

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>269</th>
</tr>
</thead>
<tbody>
<tr>
<td>Squamous</td>
<td>121 (44.9)</td>
</tr>
<tr>
<td>Nested</td>
<td>10 (3.7)</td>
</tr>
<tr>
<td>Glandular</td>
<td>54 (20.0)</td>
</tr>
<tr>
<td>Clear cell</td>
<td>5 (1.9)</td>
</tr>
<tr>
<td>Micropapillary</td>
<td>30 (11.2)</td>
</tr>
<tr>
<td>Rhabdoid</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Sarcomatoid</td>
<td>14 (5.2)</td>
</tr>
<tr>
<td>&gt;1 variant</td>
<td>28 (10.4)</td>
</tr>
</tbody>
</table>

Conclusions

- Variant histology was more likely to present with extravesical disease, receive neoadjuvant chemotherapy, and be downstaged at cystectomy compared to pure urothelial carcinoma
- Despite the tumor response to NAC, there was no effect on overall survival
- Within variant histology, there are differences in clinical characteristics. Future directions include assessing each variant histology’s response to neoadjuvant chemotherapy

Background

- Neoadjuvant chemotherapy (NAC) provides a survival benefit for muscle-invasive bladder cancer
- Variant histology (VH) of urothelial carcinoma has gained attention for its aberrant characteristics
- Our objective was to assess the ability of NAC to downstage VH and pure urothelial carcinoma (PUC) and to quantify variant subtypes and overall survival

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