United States and Canadian Academy of Pathology
Seattle, WA 2016

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Genitourinary Specialty Conference
Uncommon lesions with papillary and/or comedo-like architecture

52 year old man who consulted for a long-standing mass on the distal penis

ACCME/Disclosures

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Dr. Elsa Velazquez declares she has no conflict(s) of interest to disclose.
• **Clinical examination**
  - 6.5 cm
  - Exophytic white-gray tumor
  - Glans and coronal sulcus
  - Bilateral inguinal lymphadenopathies

• **Partial penectomy and bilateral lymphadenectomy**
Diagnosis

Clear cell squamous cell carcinoma, poorly differentiated, infiltrating corpus cavernosum and urethra with lymphovascular and perineural invasion (pT3)

Inguinal lymph nodes
Metastatic carcinoma with clear cell features

Follow-up
Patient died with distant metastasis 12 months after diagnosis
### Table 1: Histopathologic Features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>52</td>
<td>68</td>
<td>90</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Size (cm)</td>
<td>0.6</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Margin of resection</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Depth of invasion</td>
<td>T1b</td>
<td>T1b</td>
<td>T1b</td>
</tr>
<tr>
<td>Surgical margins</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Tumor grade</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>WHO classification of tumors</td>
<td>Warty/basaloid PeIN</td>
<td>Warty/basaloid SCC</td>
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</tbody>
</table>

Differential diagnosis

- Other HPV-related SCC (Warty/basaloid SCC)
- Skin adnexal tumors
- Urethral clear cell adenocarcinoma
- Metastatic clear cell carcinoma (e.g. renal cell carcinoma)

Warty (condylomatous) carcinoma

- Glans
- Slowly growing
- Condylomatous/Papillary
- HPV 16, 18, 35
- Younger patients
- Immunosuppression

Warty Carcinoma

- 30% regional metastasis
- Survival 92%

Warty PeIN

p16 overexpression is strongly associated with high-risk HPV (16-18) related penile carcinomas and their precursor lesions


Basaloid carcinoma

- HPV-related (HPV 16)
- Glans
- Younger patients
- Solid w/ comedonecrosis
- Aggressive tumor
Basaloid carcinoma

- Aggressive behavior
- High incidence of metastasis
- 50% Mortality
Basaloid PeIN

- HPV-related
- Aggressive tumor
- Mixed warty/basaloid features

Warty-basaloid carcinoma

Basaloid PeIN

p16 expression “block” positivity
Warty-basaloid PeIN
**Warty/Basaloid and Clear cell SCC**

**Differences**

**Warty:** Predominantly papillary  
No comedonecrosis

**Basaloid:** No clear cell features

**Similarities**

**Warty SCC:** May show clear cell features

**Basaloid SCC:** Comedonecrosis

**Warty-basaloid (mixed):** Clear cells and comedonecrosis

**Clear cell SCC:** Clear cells and comedonecrosis
Warty-Basaloid and Clear cell SCC
Similarities (2)

- HPV-related
- Aggressive behavior
- Precursor lesions (warty/basaloid PeIN)
- Clear cell carcinoma may show small foci of classic warty/basaloid SCC
- Warty/basaloid SCC may show clear cells

Clear cell variant of SCC is most likely related to basaloid and warty carcinoma

Differential diagnosis

- Other HPV-related SCC (Warty/basaloid SCC)
- Skin adnexal tumors
- Urethral clear cell adenocarcinoma
- Metastatic clear cell carcinoma (e.g. renal cell carcinoma)

Adnexal tumors with clear cell features

- Trichilemmal carcinoma
- Sebaceous gland carcinoma
- Hidradenocarcinoma
- Clear cell carcinoma
Penile Clear Cell Carcinoma
A Report of 5 Cases of a Distinct Entity
Lielg et al. MD and Lajugal Ragan MD

Abstract: We present a series of 5 adult clear cell carcinoma, which were histologically distinguished from other entities. Clear cell carcinoma is a rare type of tumor that arises in the skin and mucous membranes. The tumors are characterized by the presence of clear cells, which are thought to be derived from epidermal and mucosal stem cells. There is no known risk factors for developing clear cell carcinoma.

The most frequent site of occurrence is the foreskin, no papillary features considered as adnexal carcinoma.

Differences
Lielg et al.
foreskin
no papillary features
considered as adnexal carcinoma
intraductal carcinoma (1/5 cases)

Sanchez et al.
glands
focal papillary features
considered a variant of SCC

<table>
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Clear cell carcinoma

Similarities

Lielg et al. & Sanchez et al.
• Penile tumors
• Clear epithelial cells
• Solid and comedo-like features
• HPV associated
• Aggressive behavior
• Associated with warty basaloid PeIN (1/5 cases and 2/3 cases)

Differential diagnosis

• Other HPV-related SCC (Warty/basaloid SCC)
• Skin adnexal tumors
• Urethral clear cell adenocarcinoma
• Metastatic clear cell carcinoma (e.g. renal cell carcinoma)

Clear cell adenocarcinoma of the urethra

• Exceptional in men
• Different anatomical location
• Tubular, papillary, hobnail, clear cells

Differential diagnosis

• Other HPV-related SCC (Warty/basaloid SCC)
• Skin adnexal tumors
• Urethral clear cell adenocarcinoma
• Metastatic clear cell carcinoma (e.g. renal cell carcinoma)
Primary vs. metastatic

- Tumor location
- Concomitant squamous cell carcinoma in situ (warts/basaloid PeIN)
- HPV positivity

In conclusion

Clear cell SCC

Unusual variant of penile SCC
HPV-related
Solid
Comedo-like
Focal papillary features
Aggressive behavior
Consider a distinct entity (WHO 2016)

Thank you