Case #6
Dina R. Mody, MD

71 year old male
FNA biopsy of a right pelvic bony lesion
Case 6 What is your diagnosis?
Case 6 Answer

Mixed Adenocarcinoma (with Papillary Villoglandular Features) and Small Cell Carcinoma of the cervix

Small Cell Undifferentiated Carcinoma of the Cervix

- Uncommon malignancy of cervix
- Age range 25-40
- Coexist with adenocarcinoma (more frequently) or Squamous cell ca or SIL
- Type 18 or 16 in almost all cases
- Falls in the family of Neuroendocrine carcinoma of the cervix (Carcinoid, atyp carcinoid, small cell ca, large cell NE ca)
Small Cell Undifferentiated Carcinoma of the Cervix

- Cytologic diagnosis difficult and dd includes HSIL and lymphoma
- Moulding may be difficult to see on liquid based
- Chromogranin, synaptophysin, CD56, NSE +, Keratin -, LCA-
- Propensity for lymphovascular invasion and poor prognosis

Differential Diagnosis of Small Cell Undifferentiated Carcinoma of the Cervix

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Immunohistochem</th>
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<tbody>
<tr>
<td>Sm cell ca</td>
<td>Chr, Syn+, P63-</td>
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<tr>
<td>Sq cell ca</td>
<td>P63++, chr, syn –</td>
</tr>
<tr>
<td>Basaloid ca</td>
<td>same as above</td>
</tr>
<tr>
<td>PNET</td>
<td>O13/Cd99</td>
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<tr>
<td>Lymphoma</td>
<td>LCA, B&amp;T markers</td>
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<tr>
<td>Melanoma</td>
<td>S100, HMB45, MelanA+</td>
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</tbody>
</table>

Differential Diagnostic Considerations

- Endometrial cells
- Follicular Cervicitis
- Deep atrophy
- High Grade SIL
- Squamous cell carcinoma
- Adenocarcinoma
- Small cell Carcinoma
- Others…
Small Cell Ca of Cx: P16 and HPV Types

In a series of 9 cases, 100% P16+
- P53 neg 7/9
- HPV 16 4/9
- HPV18 1/9
- HPV68 1/9
- HPV 3 1/9
- HPV neg 1/9

Horn LC, Linder K et al. Int J of Gynecol Pathol. 25(2) 182-186, 2006
Small Cell Ca of Cx: HPV mRNA (in a series of 20 cases)

<table>
<thead>
<tr>
<th>Neuroend mks</th>
<th>HPV Type</th>
<th></th>
<th>16</th>
<th>18</th>
<th>neg</th>
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<tr>
<td>Neg</td>
<td></td>
<td>2</td>
<td>2</td>
<td>0</td>
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<tr>
<td>NSE</td>
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<td>0</td>
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<tr>
<td>NSE+Ch</td>
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<td>8</td>
<td>1</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>NSE+Ch+Syn</td>
<td></td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>0</td>
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<tr>
<td>Total</td>
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<td>20</td>
<td>3</td>
<td>14</td>
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</table>


High Risk HPV and Cervical Adenocarcinomas

<table>
<thead>
<tr>
<th>Author</th>
<th>Positive</th>
<th>Method</th>
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</thead>
<tbody>
<tr>
<td>Andersson</td>
<td>71%</td>
<td>PCR L1&amp;E6</td>
</tr>
<tr>
<td>Casellsague</td>
<td>87.4%</td>
<td>PCR G5+/6+</td>
</tr>
</tbody>
</table>

Casellsague et al. JNCI 2006; 303-315

High Risk HPV Positive Cervical Adenocarcinomas and Age

HPV Vaccines (Prophylactic)

- Gardasil (HPV 16, 18, 6, 11) (Merck)
- Cervarix (HPV 16, 18 not FDA approved yet in the US) (Glaxo SK)
- Manufacturers plan to extend current Virus-like particle vaccines to approx 6 carcinogenic types that collectively cause >90% of cervical Ca worldwide. Timeline not known.

What Does a Drop In prevalence of Disease Do to the Screening Program?

Predictions for the Future of Cervical Cancer Screening

- Since the other carcinogenic types (non 16/18) are less threatening, cost effectiveness analyses support raising the age of first cervical screening to approx 24 yrs
- If durability is truly long term (may need boosters), then stretch out screening intervals
Predictions for the Future of Cervical Cancer Screening (Generation)

• Best fit for the future would be a combination of a molecular test such as type specific HPV-DNA and computer assisted cytology
• 3-5 yr intervals
• If all goes as planned and in the perfectly implemented scenario, Pap volumes would drop by 50%. But.........

HPV Vaccination

• Timelines and strategies
• Payment
• Acceptance
• How long before we will see results
• Cross protection
• Duration of protection
Selected References

Small Cell Carcinoma of Cervix


Glandular references

General References


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Glandulars and HPV typing


**ThinPrep and Glandulars**


SurePath


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