Case # 48
Uterine Trophoblastic Tumor in a Cynomolgus Macaque

Sunish Mohanan DVM, MS
Jennifer Cann* DVM, PhD, Diplomate ACVP
Mark Cline DVM, PhD, Diplomate ACVP
Wake Forest University School of Medicine, Winston Salem, NC

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Signalment and Case history

- 15 year old, Female, Cynomolgus macaque
- Experimental study “hormone replacement therapy on cardiovascular disease risk in postmenopausal monkeys”
- Euthanized at the end of the experimental study
- Gross finding: Irregular thickening of the endometrium
Uterus: Trophoblastic tumor
Trophoblastic tumor
Trophoblastic tumor
Spiral arterioles of endometrium
Previous pregnancy associated vascular change
Pancytokeratin staining
Morphologic Diagnoses

- Trophoblastic tumor, Uterus
- Stromal Cell Hypertrophy and Hyperplasia (Endometrial pseudo-decidualization), Multifocal, Chronic, Moderate, Uterus
Trophoblastic Tumor

- Cellular pleomorphism, high degree of anaplasia and invasive or expansile growth patterns
- Three main types
  - Choriocarcinoma
  - Placental site trophoblastic tumor (PSTT)
  - Epithelioid trophoblastic tumor (ETT)
- Challenging to morphologically differentiate these subclasses
- Cytokeratin, Ki67, human chorionic gonadotropin, inhibin, human placental lactogen
- SRY (Sex Determining Region) antibody

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Immunohistochemistry

- Diffuse cytoplasmic staining for pancytokeratin; negative for vimentin
- 5-15 percent of the neoplastic cells are positive for human chorionic gonadotropin (hCG)
- 5-10 percent are positive for human placental lactogen (hPL)
- Negative for estrogen receptor expression
- 15-20 percent of the neoplastic cells positive for Anti-SRY (sex-determining region of the Y chromosome) antibody staining
# Immunohistochemical marker profile of PSTT, ETT, and choriocarcinoma

<table>
<thead>
<tr>
<th>Markers</th>
<th>PSTT</th>
<th>ETT</th>
<th>Choriocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>hPL</td>
<td>+++</td>
<td>-/+</td>
<td>+/++++</td>
</tr>
<tr>
<td>hCG</td>
<td>-</td>
<td>-/+</td>
<td>++/++++</td>
</tr>
<tr>
<td>Mel-CAM</td>
<td>+++</td>
<td>-/+</td>
<td>+/++++</td>
</tr>
<tr>
<td>PLAP</td>
<td>-</td>
<td>++</td>
<td>-/+</td>
</tr>
</tbody>
</table>

hPL – human placental lactogen  
hCG – human chorionic gonadotropin  
Mel-CAM – melanoma cell adhesion molecule (CD146)  
PLAP – placental alkaline phosphatase

Blaustein's Pathology of the Female Genital Tract, pp. 1230.
<table>
<thead>
<tr>
<th>Feature</th>
<th>Placental site TT</th>
<th>Epithelioid TT</th>
<th>Choriocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell population</td>
<td>Monomorphic</td>
<td>Monomorphic</td>
<td>Dimorphic, primitive previllous type</td>
</tr>
<tr>
<td>Cell size and shape</td>
<td>Large and pleomorphic</td>
<td>Small, round and uniform</td>
<td>Irregular, highly variable</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>Abundant and eosinophilic</td>
<td>Eosinophilic or clear</td>
<td>Eosinophilic to purple</td>
</tr>
<tr>
<td>Growth pattern</td>
<td>Infiltrating single cells or confluent sheets</td>
<td>Epithelioid nests, cords or solid masses</td>
<td>Dimorphic, mononucleate and syncitiotrophoblast</td>
</tr>
<tr>
<td>Margin</td>
<td>Infiltrating</td>
<td>Circumscribed, expansile</td>
<td>Circumscribed, expansile</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>Focal or haphazard</td>
<td>Usually present</td>
<td>Massive and central</td>
</tr>
<tr>
<td>Cellular necrosis</td>
<td>Usually absent</td>
<td>Extensive</td>
<td>Extensive</td>
</tr>
<tr>
<td>Vascular invasion</td>
<td>From periphery to lumen</td>
<td>Absent</td>
<td>From Lumen to periphery</td>
</tr>
<tr>
<td>Mitosis</td>
<td>Variable, 0-6/10 HPF</td>
<td>Variable, 1-10/10 HPF</td>
<td>High, 2-22/10 HPF</td>
</tr>
</tbody>
</table>

Blaustein’s Pathology of the Female Genital Tract, Chapter 24, pp. 1226.
Discussion

- Experimentally this macaque received
  - Combination of medroxyprogesterone acetate (MPA, 0.169 mg/kg body weight) and conjugated equine estrogens (CEE, 0.042 mg/kg body weight) for 12 months
  - Atherogenic diet
- Equivalent to a woman’s dose of 2.5 mg per day MPA and 0.625 mg per day CEE
- CEE causes approximately a 10X increase in endometrial cancer risk in women but that the addition of MPA removes this risk.
- Thus, in this macaque, the hormonal treatment is considered incidental to this specific tumor type.
Call for Cases:
2009 ACVP Mystery Slide Session - Female Reproductive Pathology

- 2009 ACVP Mystery Slide Session
  - Annual Meeting will be held on Monday, December 7, from 7:00 p.m.-10:00 p.m
- Focus on female reproductive pathology
- Members interested in submitting an interesting case for consideration are encouraged to contact the session chair, J. Mark Cline DVM, PhD, DACVP
  - by e-mail at jmcline@wfubmc.edu
  - Phone (336) 716 1564
  - Deadline: September 1, 2009
- Inquiries prior to case submission are encouraged
Literature


Text Book:

- Blaustein's Pathology of the Female Genital Tract