The Case of the Cute Congenital Coccygeal Curiosity

**Poll:**
Which element of the differential diagnosis do you favor based off the clinical and dermoscopic images alone?

A. Sacrococcygeal skin tag  
B. Occult spinal dysraphism  
C. Subcutaneous myxopapillary ependymal rest  
D. Coccygeal polypoid eccrine nevus  
E. Caudal appendage “Human tail”

Neonates with sacrococcygeal skin tags should be evaluated for spinal dysraphism.

**Things it was not...**
Sacrococcygeal skin tag

**Things it was not...**
Subcutaneous myxopapillary ependymal rest
Things it was not...
Caudal appendage
AKA “Human tail”

Spinal cord extending up to lower sacral region ending with a lipoma

There is associated syrinx of the spinal cord

(d and e) the clinical photograph of the lesion

It was a...
Coccygeal polypoid eccrine nevus

Healthy 4-month-old male infant with the congenital lesion shown and no other significant clinical findings and a normal ultrasound of the spine
Poll:
How does a Coccygeal polypoid eccrine nevus differ from a traditional Eccrine nevus?
A. Presence of hyperplastic eccrine glands
B. Prevalence
C. Location
D. Absence of hyperhidrosis
E. Both C and D
Poll:
How does a Coccygeal polypoid eccrine nevus differ from a traditional Eccrine nevus?

A. Presence of hyperplastic eccrine glands
B. Commonality
C. Location
D. Absence of hyperhidrosis
E. Both C and D

Coccygeal polypoid eccrine nevi (CPEN)
- Rare, benign, cutaneous polypoid lesions
- Localized to the coccyx region
- Hyperplastic eccrine ducts
- No hyperhidrosis

Eccrine nevus - rare, benign hamartoma
- Hyperplastic eccrine glands
- Commonly found on forearms
- Often have associated hyperhidrosis

Eccrine Nevus Affecting the Forearm of an 11-Year-Old Girl Successfully Controlled with Topical Glycopyrrolate

Hidradenocarcinoma of the Back

Hidradenocarcinoma
- AKA:
  - Clear cell eccrine carcinoma
  - Malignant nodular hidradenoma
  - Malignant clear cell acrospiroma
  - Malignant clear cell hidradenoma
  - Malignant eccrine spiradenoma
  - Primary mucoepidermoid cutaneous carcinoma
Hidradenocarcinoma

- An extremely rare tumor
- It is a rare version of a rare class of tumors
- Eccrine carcinomas make up less than 0.01% of all skin cancers
- Hidradenocarcinomas account for ≈ 6% of cancerous eccrine tumors
- Malignant neoplasm arising from the intradermal duct of eccrine sweat glands
- Head and neck are the most common sites
- Also occurs on extremities and trunk
- Cases have been reported on the eyelid, scalp, finger and the perianal region

Hidradenocarcinoma - Presentation

- Has a notoriously unimpressive clinical appearance until they are advanced
  - "impressively unimpressive"
- Typically a solitary, subcutaneous, firm nodule
- Less commonly is an erythematous plaque with telangiectasia +/- ulceration
- May mimic "benign" solitary skin lesions – i.e. EIC or pilar cyst
- May slowly expand circumferentially
- May maintain a stable size of 1–5 cm for several years
- May also appear fleshy red, gray, or violet with normal overlying
- May arise from pre-existing hidradenoma
- Clinical diagnosis on path submissions is almost always "cyst"

Poll – What is the Prognosis of a Hidradenocarcinoma

A. Similar to a basal cell carcinoma of similar size
B. Similar to squamous cell carcinoma of similar size
C. Similar to a porocarcinoma of similar size
D. Similar to a Merkel cell carcinoma of similar size
E. It depends who you ask

Hidradenocarcinoma Prognosis

- The most widely cited postsurgical survival rate at five years is < 30% especially on informational sites directed at the lay public
- This is understandably worrisome to patients and their families.
- Citations provided for this statistic in various publications include:
  - Granter et al recently suggested that the prognosis of patients with MES is generally not as grave as previously reported.

Cystic-solid tumor with irregular borders originating in the dermis and extending through the subcutaneous tissue. Clear cells and squamoid cells.
Hidradenocarcinoma Prognosis

- Mirza et al reported that out of 40 cases, lymph node metastases developed in 16 (40%) after approximately 3 years of follow up.
- 7 out of 40 patients (17.5%) developed distant metastases and died of disease.
- More recently published data indicate that if metastatic disease is diagnosed 5-year survival drops to less than 50%.
- Survival data for isolated lesions without metastatic disease is difficult to find.

For reference: Prognosis of Merkel Cell Carcinoma

<table>
<thead>
<tr>
<th>SEER stage</th>
<th>5-year relative survival rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>78%</td>
</tr>
<tr>
<td>Regional</td>
<td>51%</td>
</tr>
<tr>
<td>Distant</td>
<td>17%</td>
</tr>
<tr>
<td>All SEER stages combined</td>
<td>63%</td>
</tr>
</tbody>
</table>

American Cancer Society - Information from the SEER* database, maintained by the National Cancer Institute (NCI)

Hidradenocarcinoma

- May metastasize to regional lymph nodes and distant viscera:
  - Lungs
  - Liver
  - Brain
- The postsurgical recurrence rate is 50%

Our Patient

- 70-year-old man presented to our clinic in March 2018 as a new patient.
- Chief complaint – blister on finger and itchy brown spot on face. No other complaints at time of visit.
- On exam a 3 mm pink subcutaneous nodule was found on the mid back consistent with an epidermal inclusion cyst which was incised and drained, producing material consistent with keratin debris.
- Patient also had a digital mucous cyst which was drained with typical mucoid material and > 20 actinic keratoses.
- He was instructed to follow up in 6 months due significant sun damage.

Our Patient

- Personal Skin History
  - No history of skin cancer.
- Family Skin History:
  - Melanoma.
  - Father.
- Past Medical History:
  - CVD, HTN, Hypercholesterolemia,
  - Family History:
  - Sister - Breast cancer and Ovarian cancer – BRCA2 positive
Our Patient

• Patient returned to clinic in late May 2019
  • (a year and two months later than recommended)
• He had cardiovascular issues since last visit that precluded earlier follow up.
• Chief complaint: Bump on finger, itchy brown spot on face, no other complaints
• On exam he had a 3 mm pink non-descript papule on the mid back
• At this visit it was not typical dermoscopically for an epidermal inclusion cyst, the lesion was pink and non-descript, and the decision was made to punch excise it

(A,B) Original lesion predominantly composed of clear cells with only minor cytological pleomorphism, whereas a metastatic lesion (C, D) shows smaller rounded nuclei of epithelial cells, eliciting a desmoplastic stromal reaction. Note the low-grade cytology of the tumor despite aggressive behavior and intralymphatic propagation.
Hidradenocarcinoma

- Multilobulated, with solid aggregates of neoplastic cells that vary in shape and size and may infiltrate the dermis
- Neoplastic cells may be clear cells, pale cells, squamous cells, polygonal cells, oncocytoid cells, or mucinous cells
- Nuclear pleomorphism, mitotic figures, and the degree of atypia may be very striking or may be low grade
- The stroma is composed of sclerotic collagen bundles

Hidradenocarcinoma Immunohistochemistry

Reported positive immunohistochemical stains
- AE1/AE3
- CK5/CK6
- EMA, CEA, S-100 protein
- bcl-1, bcl-2, p63
- Androgen receptor, EGFR, estrogen receptor
- MUC5AC, and p53
- A high Ki-67 expression helps distinguish hidradenocarcinoma from atypical hidradenoma

Hidradenocarcinoma Histopathologic Differential

- Hidradenoma
- Metastatic clear cell carcinomas
  - Thyroid
  - Lung
    - TTF-1 may be helpful in differentiating hidradenocarcinoma from lung and thyroid carcinomas
  - Kidney
    - CD10 and epithelial membrane antigen (EMA) positivity would help differentiate
- Clear cell variant of Squamous Cell Carcinoma
- Clear cell variant of Basal Cell Carcinoma

Hidradenocarcinoma Genetic Basis

- Mutations in PTCH1 and TCF7L1 have been reported
- Mastermind-like transcriptional coactivator 2 (MAML2) translocation has been reported
  - MAML2 is known as a molecular marker unique to mucoepidermoid carcinoma (MEC)
- Her2 gene amplification has been reported


Angela J. Wyatt, Klaus J. Busam, in Dermatopathology, 2010

Clear cell squamous cell carcinoma

Clear cell basal cell carcinoma
Hidradenoma Genetic Basis

- No cases have been reported associated with BRCA2 mutations to date
- Our patient’s sister has a BRCA2 mutation with a history of breast and ovarian cancer.
- For this reason he underwent genetic testing and was also found to carry a BRCA2 mutation
- The role of hormones in this neoplasm is incompletely understood but AR positivity has been reported

Translocation of the MAML2 gene in hidradenocarcinoma

(a) A granular, pale pink, hard tumor on the right axilla
(b) The tumor presented in the dermis to subcutaneous, formed multilobulated irregular nests. The tumor was mainly composed of
(c) clear cells,
(d) squamous cells,
(e) mucinous cells
(f) cells that lined ductal structures
(g) The probe marks the distal portion of the MAML2 gene with green fluorochrome and marks the proximal portion of the MAML2 gene with orange fluorochrome. The separate green and orange signals reveal rearrangement of the MAML2 gene.

Poll:
What is the recommended treatment for Hidradenocarcinoma

A. Wide local excision with Sentinel Lymph Node exam
B. MOHS surgery
C. Radiotherapy
D. Antiandrogens such as Tamoxifen
E. No uniform treatment guidelines have been established

Hidradenocarcinoma Management

- Due to its rarity, no uniform treatment guidelines have been established
- Wide local excision with Sentinel Lymph Node exam is the mainstay of the treatment in most case series
- MOHS surgery has been used with significant success
- For metastatic lesions:
  - Radiotherapy in a dose of 50Gy–70Gy
  - 5-fluorouracil and capcitabine-based combination chemotherapy
  - Trastuzumab, EGFR inhibitors, PI3K/Akt/mTOR pathway inhibitors
  - Electrochemotherapy
  - Clinical trials
  - Antiandrogens especially Tamoxifen — requires hormone receptor status evaluation

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Our Patient

- Following presentation to tumor board and consultation with tertiary referral centers our patient underwent wide local excision with SLNB
- All nodes were negative
- No residual tumor was found on re-excision
- Currently doing well
- Further workup is planned
Support and Advocacy

- Organizations Providing General Support
  - American Cancer Society
    250 Williams Street NW
    Atlanta, GA 30329
    Toll-free: 1-800-227-2345
    Website: https://www.cancer.org
  - Rare Cancer Alliance
    5649 North Pacana Way
    Green Valley, AZ 85614
    Telephone: 520-625-5499
    Website: http://www.rare-cancer.org

References


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