Ophthalmology Grand Rounds

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April 23, 2015
Case Presentation

- 86yo white female presents with one month history of a rapidly growing right upper eyelid lesion previously diagnosed as a chalazion...
Case Presentation

- **PMHx:** CAD s/p stenting, COPD w/ supplemental oxygen, HTN, DM2, atrial fibrillation; wheelchair bound pt
- **POHx:** CE/PCIOL ou
- **FHx:** not significant
- **SocHx:** +past tobacco use
- **Meds:** extensive medication list
- **Allergies:** NKMA
- **Currently using tobradex ung qid od**
Exam Findings

- Nvacc: 20/40- OD; 20/25- OS
- Pupils: errl ou, no apd
- EOM: full od/os
- CVF: ftfc od/os
- Tapp: 17/17 @1600
- L/L/A: RUL lesion as shown in photo; +dermatochalasis b/l, +steatoblepharon b/l
- C/S: w+q ou
- K: clear ou
- AC: d+q ou
- I/P: wnl ou
- Lens: pciol ou
- DFE wnl ou
Violaceous
Vascularized
Madarosis
Differential Diagnosis

- Merkel cell CA
- Lymphoma
- Sebaceous cell CA
- Squamous cell CA
- Basal cell CA
- Amelanotic melanoma
Diagnosis?
Merkel Cell Carcinoma

- Cutaneous neuroendocrine carcinoma
- 1,500 new cases diagnosed each year
- M>F, Caucasians > other ethnicities
- Sparse literature
- Aggressive, malignant
- High likelihood of recurrence and metastasis: ~50% pts develop regional and distant mets
- Associated w/ sun exposure, polyomavirus infection, immunosuppression: RR in HIV positive pts is 13.4 (Engels et al. 2002)
- Arises from “merkel cells”- specialized neuroendocrine receptor cells of skin and mucous membranes
  - Mediate light touch sensation and discrimination
The nucleus of the cell is labulated and the cytoplasm contains granules of unknown function similar to secretory granules. The axon terminal is filled with mitochondria and covered by a Schwann cell until it enters the Merkel cells.

Medical Knowledge
Clinical Features

• Occurs on trunk, extremities, face
  • 46-48% cases occur in head and neck region
  • ~10% cases affect eyelid and periocular skin
    • F>M (?)
    • Of these cases, upper eyelid (64%) > lower eyelid (13%) > canthi (11%) involvement
• Painless, progressive, red or violaceous nodule
• Telangiectasias present near surface of lesion
• Madarosis
• Diagnosis most commonly occurs after 6\textsuperscript{th} decade in Caucasians
  • One study shows Merkel cell CA has been diagnosed in 22 year old female
• Masquerades as chalazion leading to serious delay in diagnosis
Medical Knowledge

http://www.meb.uni-bonn.de/cancer.gov
Pathology

- Lobules of poorly differentiated malignant cells
- Scant cytoplasm
- Nuclei w/ finely dispersed chromatin ("salt and pepper")
- Tumor cells involve dermis and spare epidermis
- EM: neurosecretory granules in cytoplasm
- IHC:
  - presence of neurofilament protein, cytokeratin 20, neuron-specific enolase, synaptophysin
  - Absence of leukocyte common Ag, S100 protein

Medical Knowledge  Merritt et al. 2014
Our Patient
### Table 1. Comparison of American Joint Committee on Cancer, 7th edition, T Categories for Eyelid Carcinoma and Merkel Cell Carcinoma.

<table>
<thead>
<tr>
<th>Merkel Cell Carcinoma</th>
<th>Eyelid Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX  Primary tumor cannot be assessed</td>
<td>TX  Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0  No evidence of primary tumor (e.g., nodal/metastatic</td>
<td>T0  No evidence of primary tumor</td>
</tr>
<tr>
<td>presentation without associated primary)</td>
<td></td>
</tr>
<tr>
<td>Tis In situ primary tumor</td>
<td>Tis Carcinoma in situ</td>
</tr>
<tr>
<td>T1  Less than or equal to 2 cm maximum tumor dimension</td>
<td>T1  Tumor 5 mm or less in greatest dimension, not</td>
</tr>
<tr>
<td>T2  Greater than 2 cm but not more than 5 cm maximum</td>
<td>invading the tarsal plate or eyelid margin.</td>
</tr>
<tr>
<td>tumor dimension</td>
<td>T2a Tumor more than 5 mm, but not more than 10 mm in</td>
</tr>
<tr>
<td>T3  Over 5 cm maximum tumor dimension</td>
<td>greatest dimension, or, any tumor that invades the</td>
</tr>
<tr>
<td>T4  Primary tumor invades bone, muscle, fascia, or</td>
<td>tarsal plate or eyelid margin</td>
</tr>
<tr>
<td>cartilage</td>
<td>T2b Tumor more than 10 mm, but not more than 20 mm in</td>
</tr>
<tr>
<td></td>
<td>greatest dimension, or, involves full thickness</td>
</tr>
<tr>
<td></td>
<td>eyelid</td>
</tr>
<tr>
<td></td>
<td>T3a Tumor more than 20 mm in greatest dimension, or,</td>
</tr>
<tr>
<td></td>
<td>any tumor that invades adjacent ocular or orbital</td>
</tr>
<tr>
<td></td>
<td>structures. Any T with perineural tumor invasion.</td>
</tr>
<tr>
<td></td>
<td>T3b Complete tumor resection requires enucleation,</td>
</tr>
<tr>
<td></td>
<td>exenteration, or bone resection</td>
</tr>
<tr>
<td></td>
<td>T4 Tumor is not resectable due to extensive invasion</td>
</tr>
<tr>
<td></td>
<td>of ocular, orbital, craniofacial structures, or</td>
</tr>
<tr>
<td></td>
<td>brain</td>
</tr>
</tbody>
</table>
Sentinel Lymph Node Biopsy

• Considered for periocular MCC, however, only 1 case report of MCC of eyelid w/ positive SLN (Esmaeli et al. 2002)

• Schwartz et al. 2014: Incidence of SLN positivity in large trials of patients w/ MCC of all sites ranges from 23% to 45%
SLN Biopsy

- Sniegowski et al. 2014:
  - Multidisciplinary management of eyelid MCC
  - Strong consideration for prophylactic radiation therapy OR SLN biopsy
  - SLN dissection in pts w/ either node positive disease or tumors that are T2b or more advanced at presentation
Metastasis

• MCC of eyelid
  – Overall metastatic rate ranging from 10% to 30%
  – Regional lymph node recurrence rate 20%
  – Distant mets rate 5%
  – Recent study showed that only statistically significant factor a/w decreased disease free survival was nodal involvement at presentation

• Most common sites of metastasis of all MCC: skin, bone, brain liver, lung

Merritt et al. 2014
Management

- Empiric treatment since no prospective, randomized studies investigating management in literature
- Surgical excision: more conservative approach than MCC excision at other sites w/ margins as small as 5mm
  - Mohs micrographic surgery vs wide excision w/ frozen section control of margins
- Postoperative adjuvant radiation therapy: Merkel cell CA is very radiosensitive!
- Prophylactic lymph node dissection?
Role of Prophylactic Radiotherapy

- Controversial
- No strong evidence that radiotherapy alone improves survival (Gillenwater et al. 2001)
- Radiotherapy to regional lymph nodes can be justified in all patients OR only in those with SLN positive status depending on practitioner perspective:
  - 24-68% risk of nodal metastasis from MCC
  - However, all draining lymph nodes must be included in prophylactic radiation field
Role of Chemotherapy

• Considered for patients with distant mets or those with extensive regional nodal metastasis
• Sensitive to cisplatin, cyclophosphamide, doxorubicin, vincristine, 5-FU (Ott et al.)
• However, adjuvant chemotherapy has not proven to decrease rates of recurrence nor improve survival
  – Voog et al: 107 patients with locally advanced or metastatic MCC showed 61% overall clinical response to chemotherapy; however, associated with high toxicity-related mortality

Practice Based Learning

Merritt et al. 2014
Question of Management

• If systemic workup proves negative, how should we treat this elderly wheelchair-bound patient? Surgery and radiation? Radiation alone?
• Does SLN biopsy make sense for our patient w/ regard to overall survival and quality of life?
Thoughts from Radiation Oncology

• If metastatic disease → chemotherapy vs supportive care (reserve radiation for palliative care)

• If no metastatic disease but positive nodes on imaging → FNA node for confirmation → radiation to primary tumor and lymph nodes VS resection followed by radiation

• If localized disease → resection of primary tumor +/- SLN biopsy followed by radiation to tumor bed VS radiation to primary tumor and nodes
Our Patient

- Pathologic diagnosis of Merkel cell carcinoma of eyelid
- SLN Bx not offered by SI treating physicians
- Pt started radiation therapy last Friday
- Full body workup is still pending
References

- http://www.meb.uni-bonn.de/cancer.gov
Reflective Practice

- This case demonstrated the importance of a thorough ophthalmic exam and diagnostic workup and allowed me to learn more about a few disease entities, their presentations, and their complications.

- This case also allowed me to evaluate the literature for the differential diagnoses of this disease entity while keeping in my mind my patient’s expectations.
Core Competencies

• Patient Care: The case involved thorough patient care and careful attention to the patient’s past medical history. Once diagnosed the patient received proper management and follow up care.

• Medical Knowledge: This presentation allowed me to review the presentation, differential diagnosis, proper evaluation/workup and different treatment options for merkel cell carcinoma (MCC) and involvement in orbital processes.

• Practice-Based Learning and Improvement: This presentation included a current literature search of current studies in the clinical and radiographic presentation of MCC and involvement in different orbital processes.

• Interpersonal and Communication Skills: The patient was treated with respect and every effort was made to communicate with the patient in a timely manner.

• Professionalism: The patient was diagnosed in a timely manner. She was informed of his diagnosis and explained current treatment options.

• Systems Based Practice: The patient was discussed with the Oculoplastics service about prognosis and treatment options.
Thank You!

- Patient
- Dr. Shinder