Ophthalmology Grand Rounds

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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

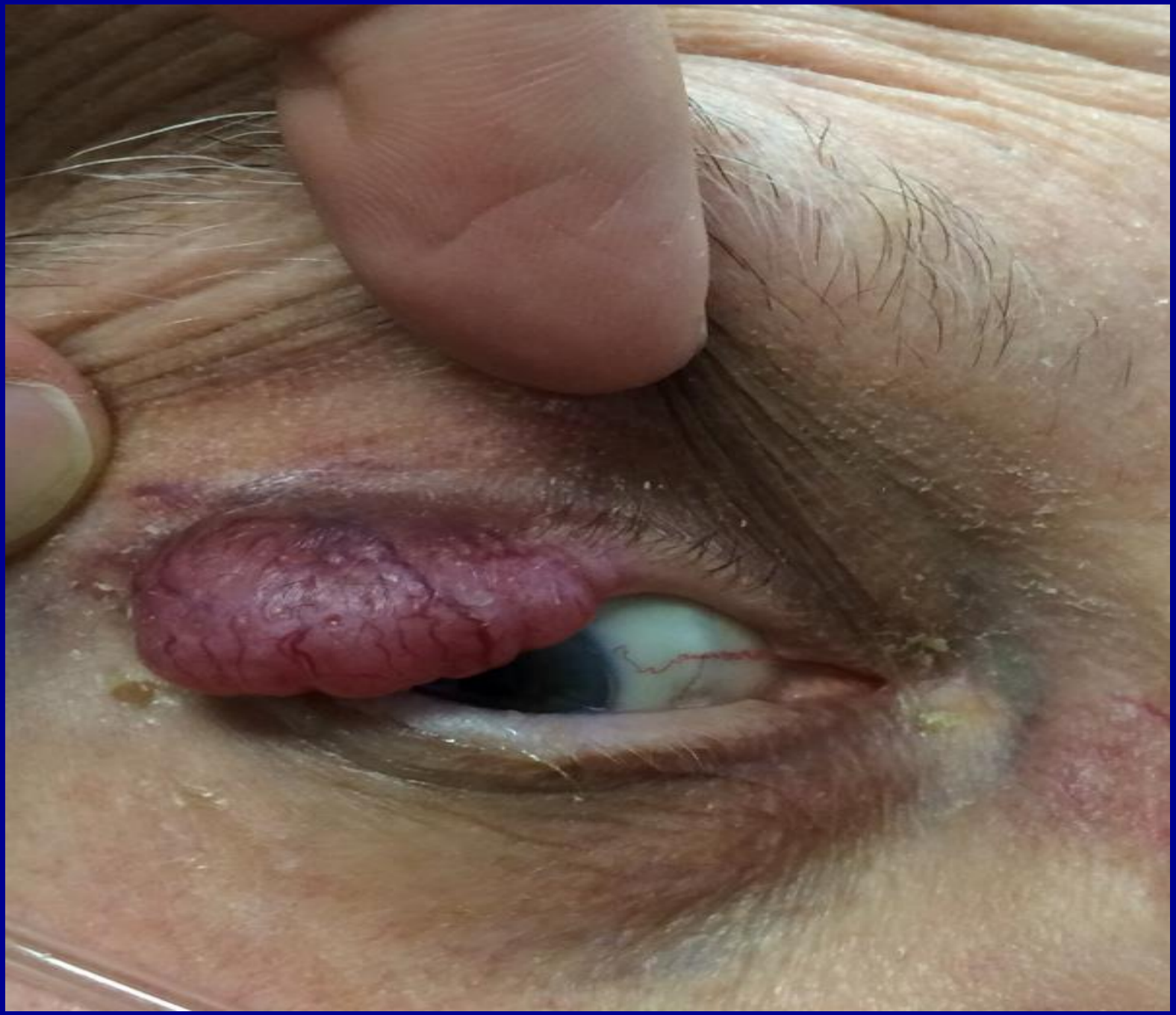
- PMHx: CAD s/p stenting, COPD w/ supplemental oxygen, HTN, DM2, atrial fibrillation; wheelchair bound pt
- POHx: CE/PCIOL ou
- FHx: not significant
- SocHx: +past tobacco use
- Meds: extensive medication list
- Allergies: NKMA
- Currently using tobradex ung qid od

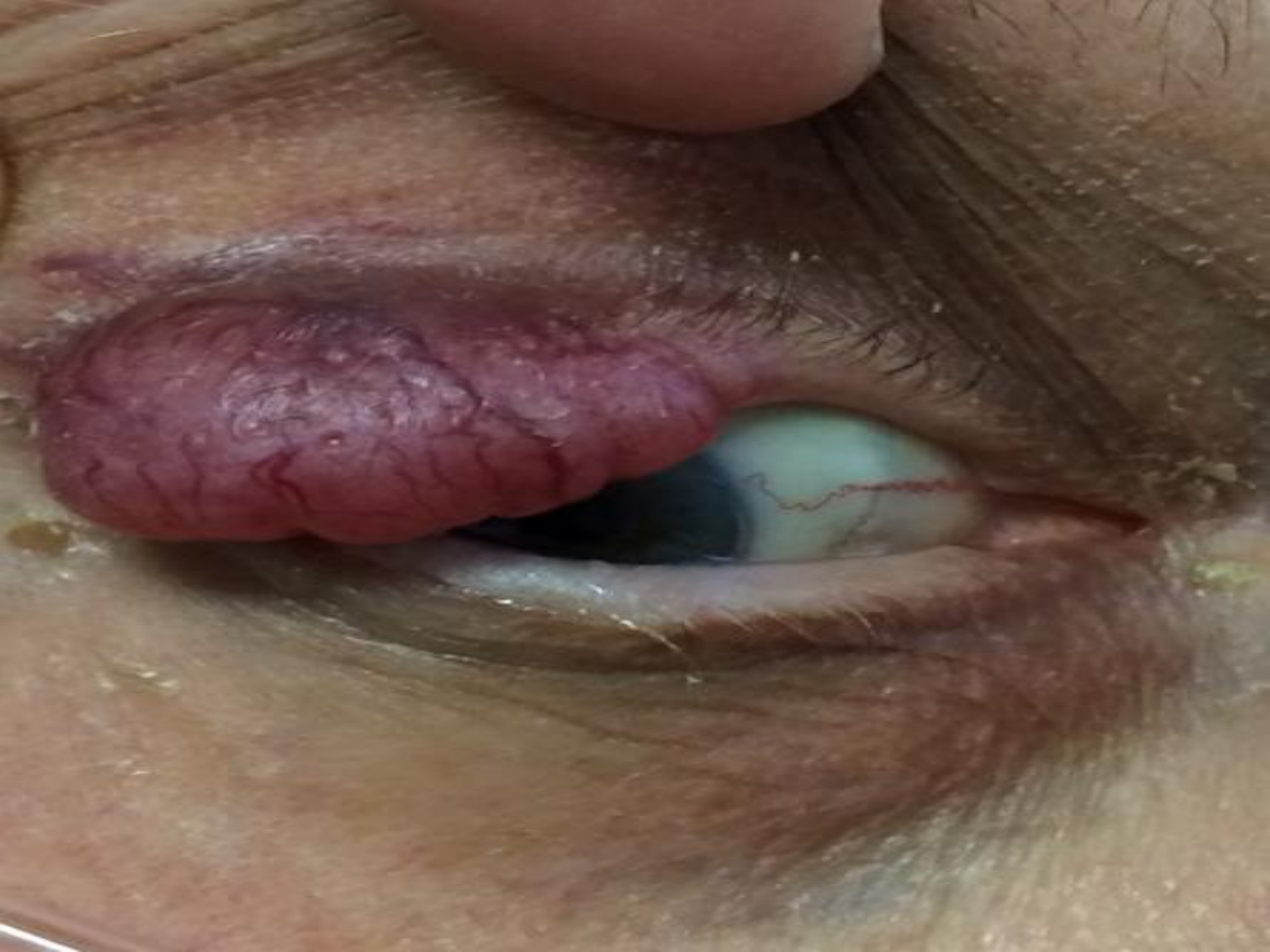
Exam Findings

- 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

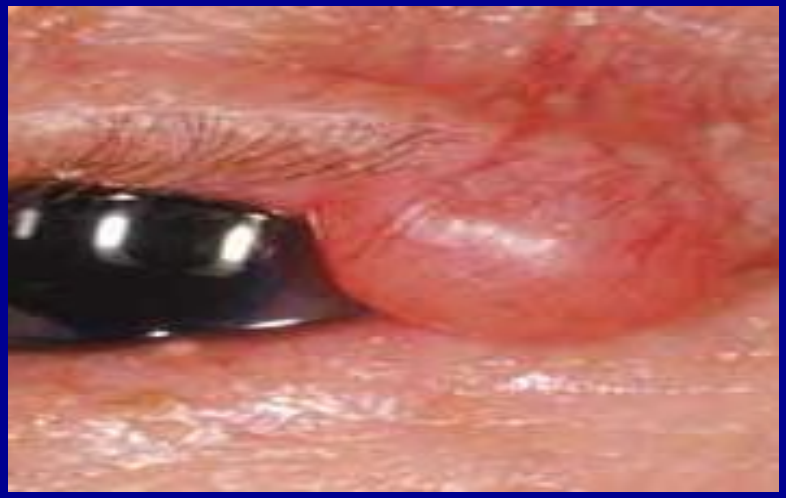
Vascularized

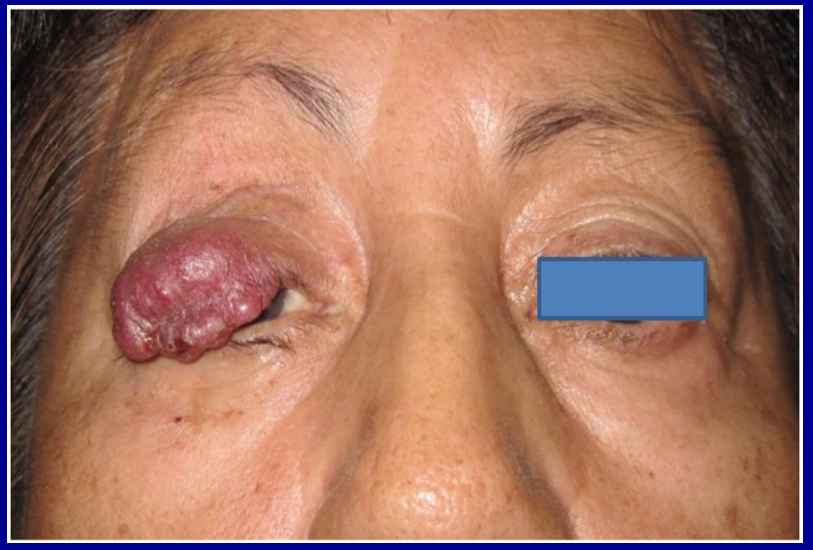
Madarosis

Differential Diagnosis

- Merkel cell CA
- Lymphoma
- Sebaceous cell CA
- Squamous cell CA
- Basal cell CA
- Amelanotic melanoma

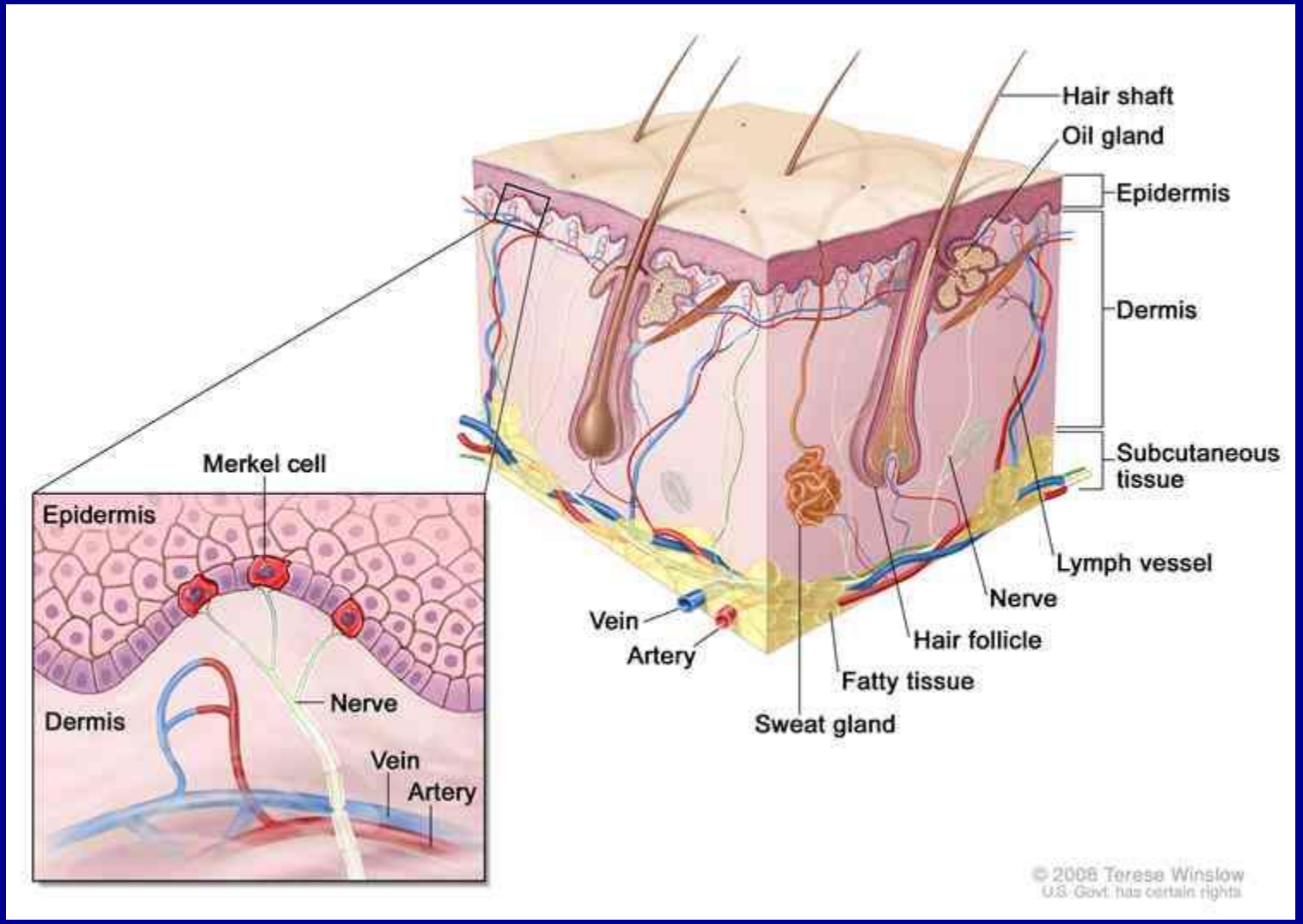
Diagnosis?



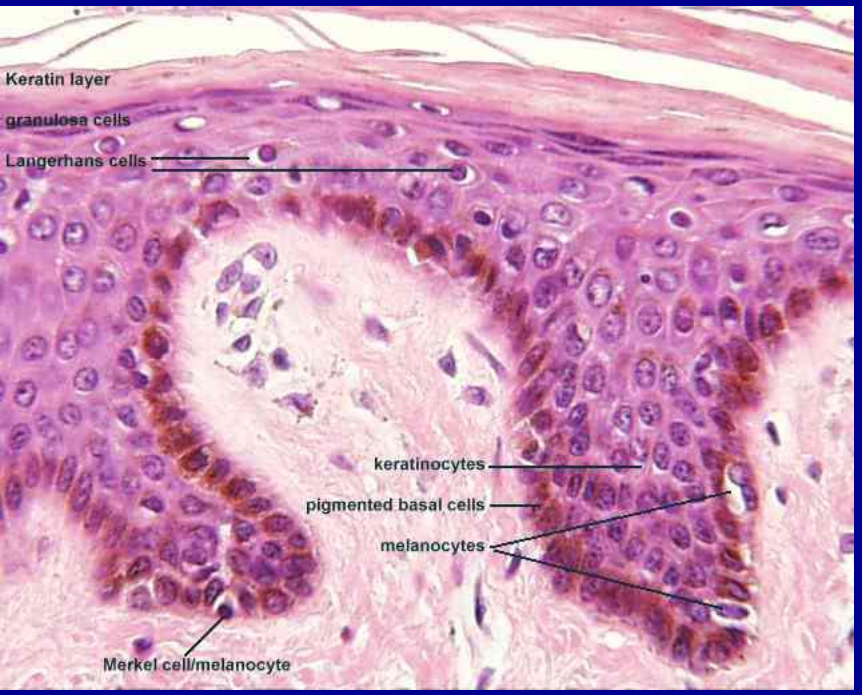


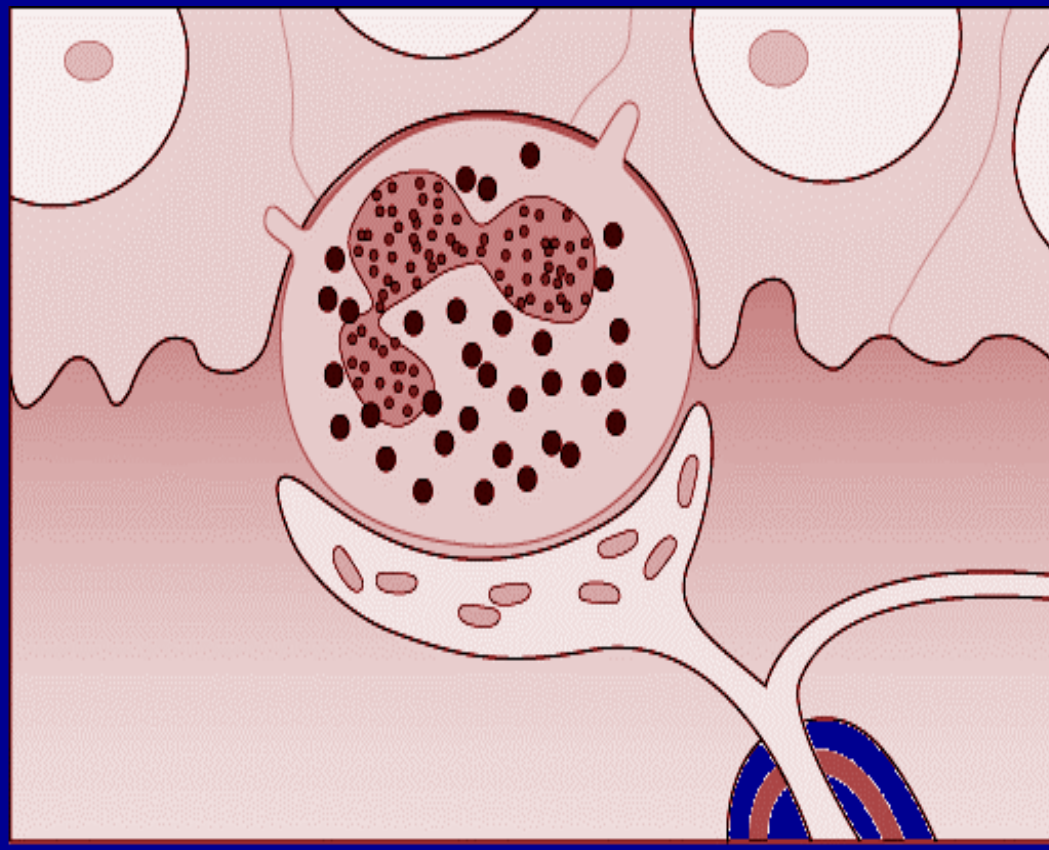
Merkel Cell Carcinoma

- 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



Medical Knowledge

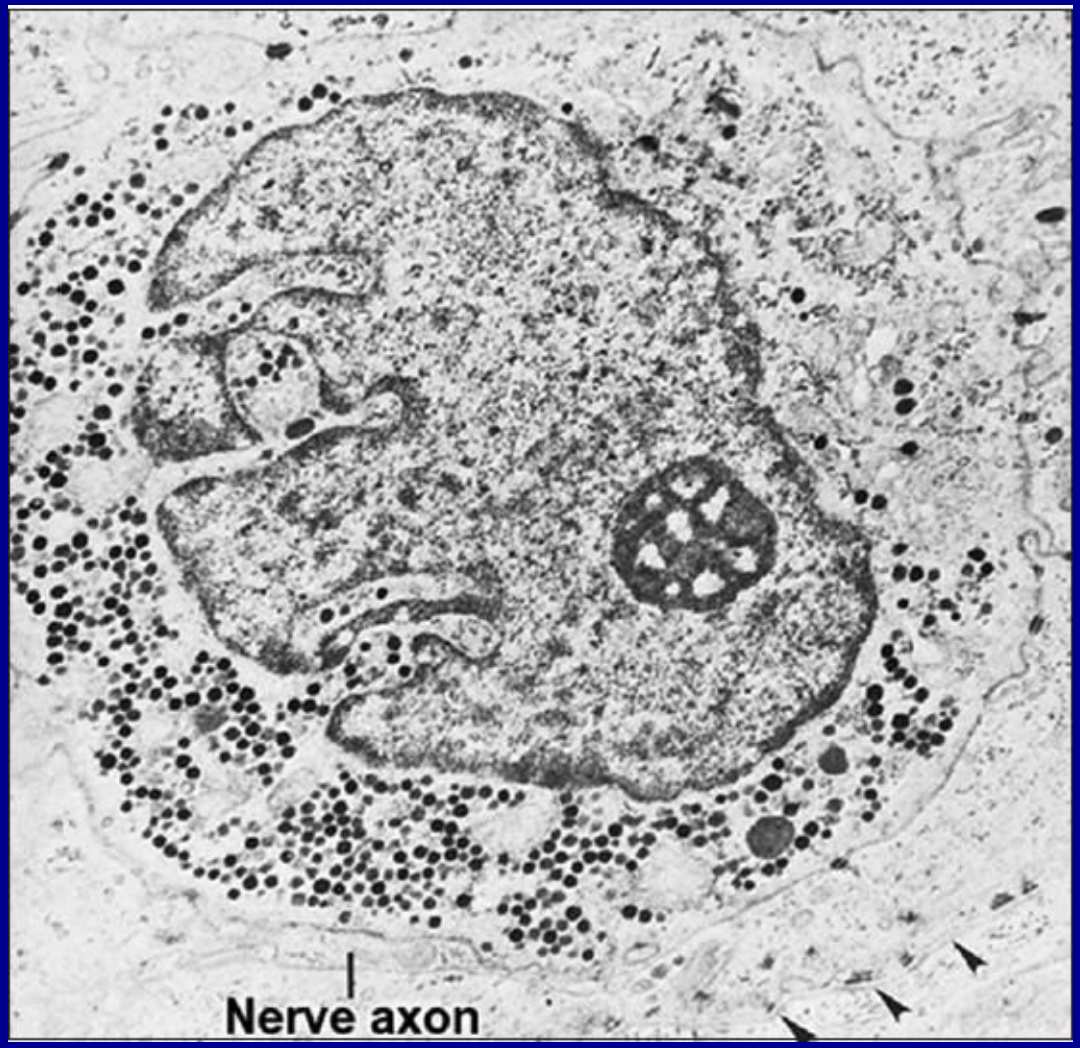




The nucleus of the cell is lobulated and the cytoplasm contains granules of unknown function similar to secretory granules. The axon terminal is filled with mitochondria and covered by a Schwann cell until it enters the Merkel cells.

Medical Knowledge

Dykes et al. 2011



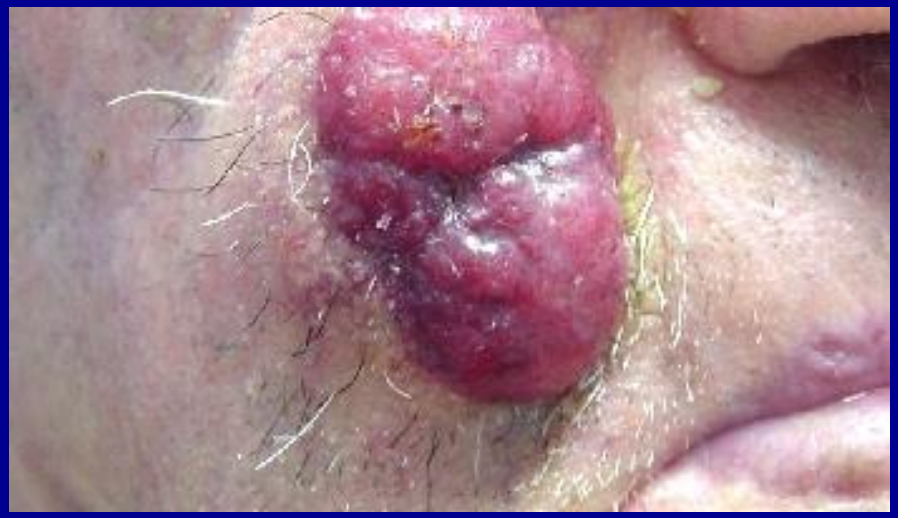
Medical Knowledge

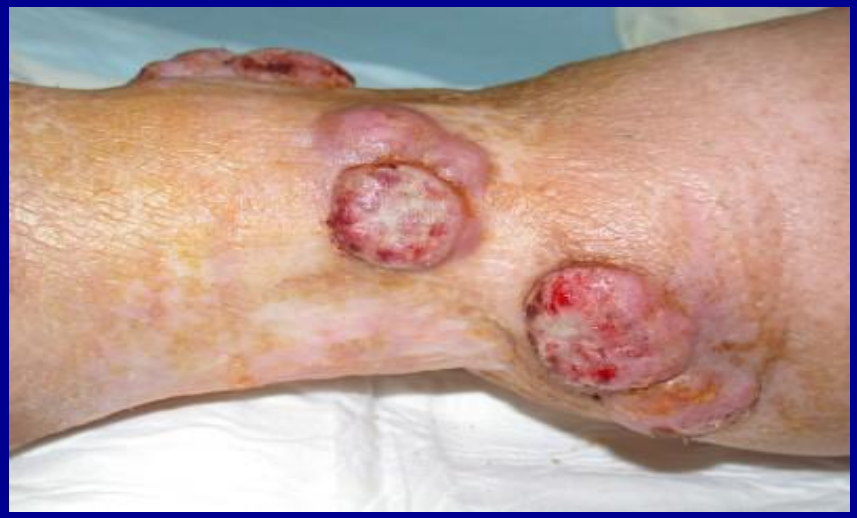
Munde et al. 2011

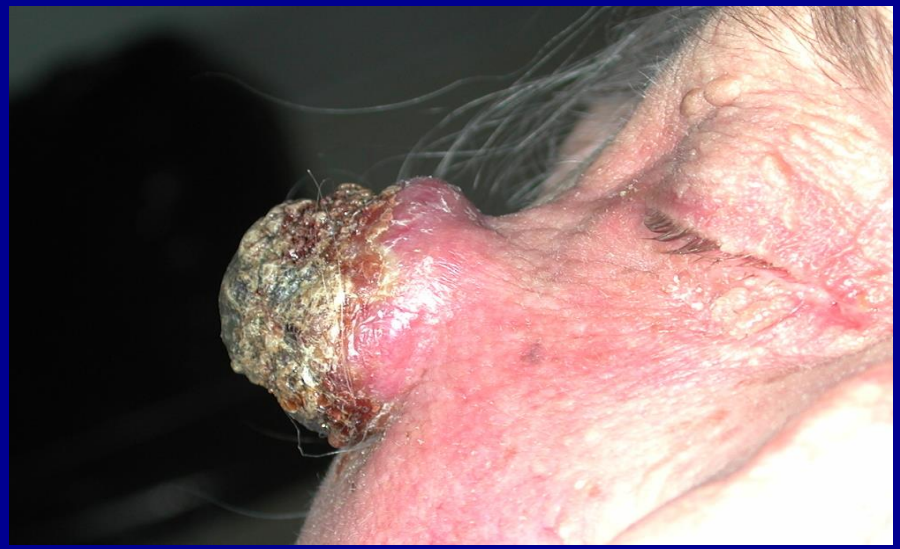
Clinical Features

- 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 6th 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 *Merritt et al. 2014*







Medical Knowledge

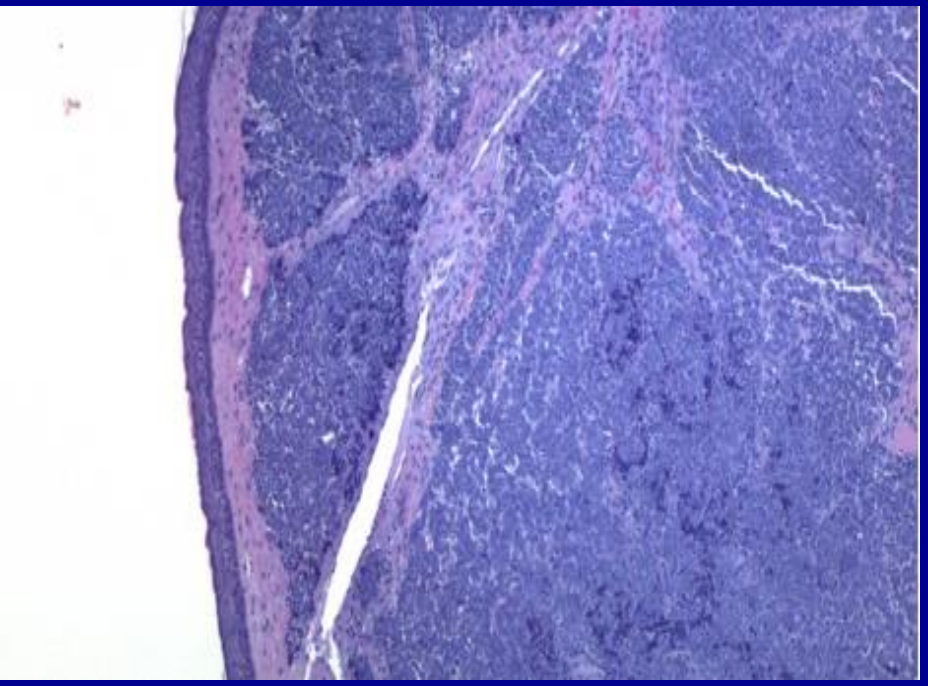
http://www.meb.uni-bonn.de/cancer.gov

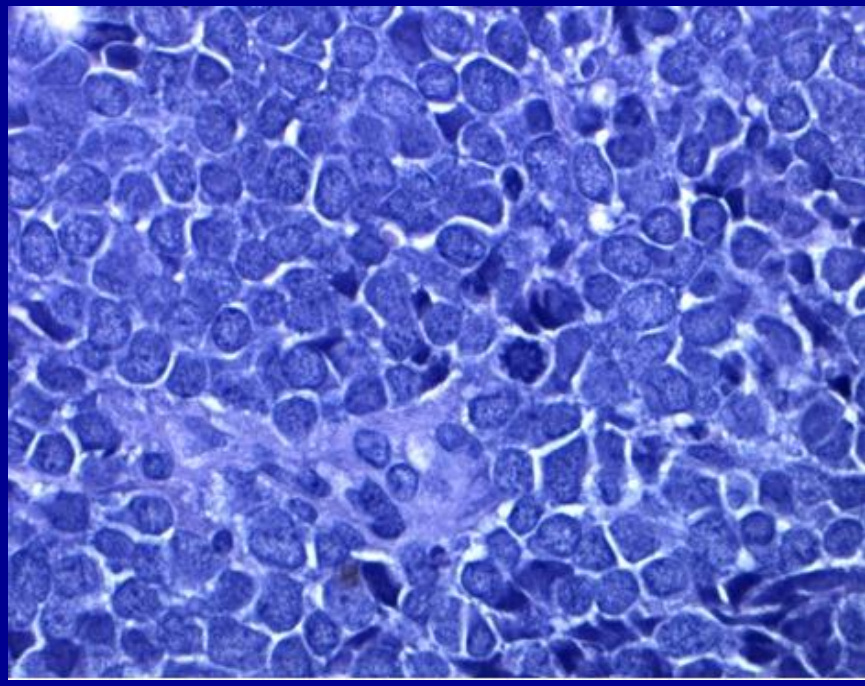
Pathology

- 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





Our Patient

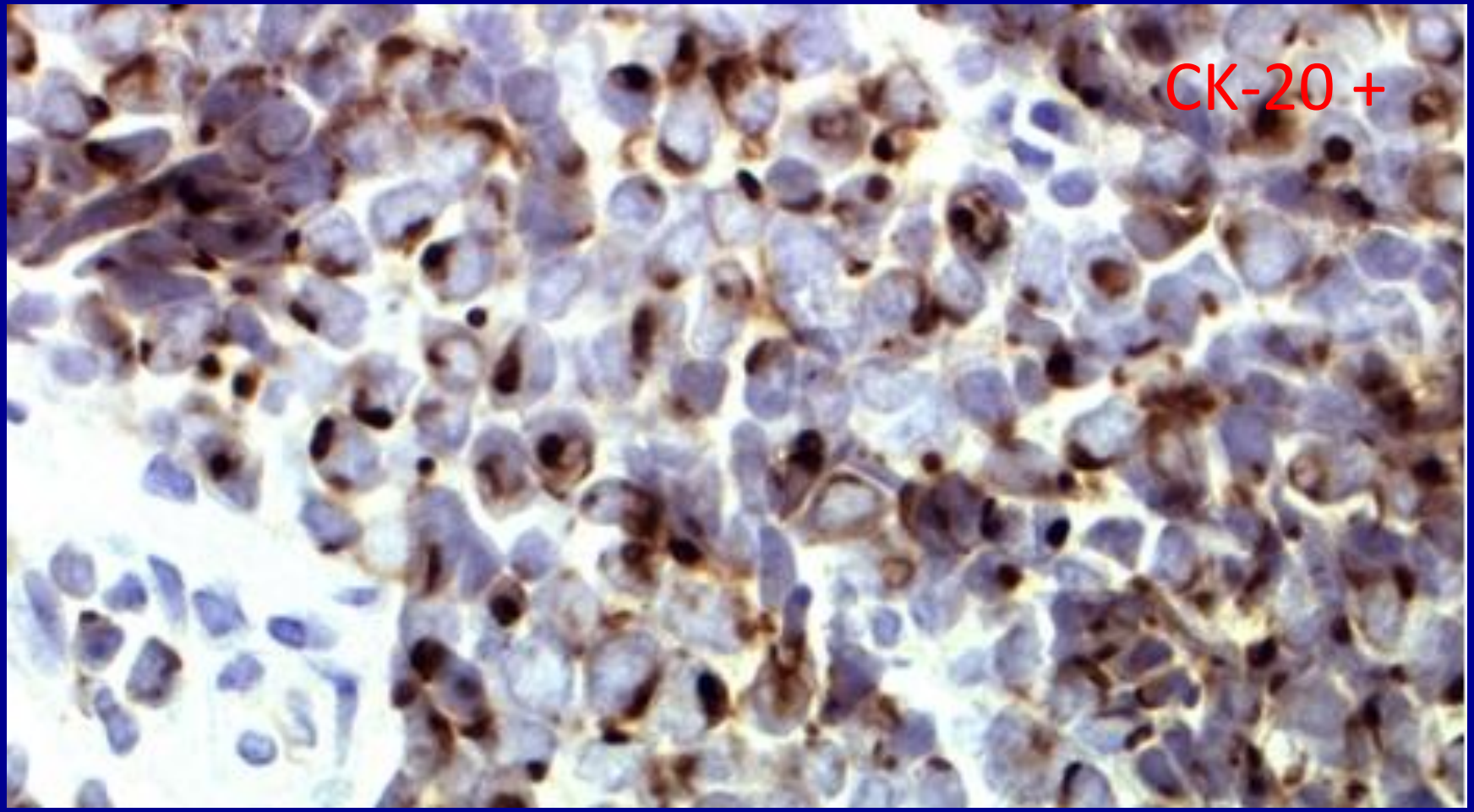


Table 1. Comparison of American Joint Committee on Cancer, 7th edition, T Categories for Eyelid Carcinoma and Merkel Cell Carcinoma.

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

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

Sniegowski et al. 2014

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?

Merritt et al. 2014

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 w/ 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 w/ distant mets or those w/ extensive regional nodal metastasis
- Sensitive to cisplatin, cyclphosphamide, 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 w/ locally advanced or metastatic MCC showed 61% overall clinical response to chemotherapy; however, associated w/ high toxicity-related mortality

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

- Dykes, Robert W.; Mcbain Daniel. *11. Sensory Systems*, Savolainen, Heikki, Editor, *Encyclopedia of Occupational Health and Safety*, Jeanne Mager Stellman, Editor-in-Chief. International Labor Organization, Geneva. © 2011.
- Engels, E.A.; Frisch, M.; Goedert, J.J.; Biggar, R.J.; Miller, R.W. Merkel cell carcinoma and HIV infection. Lancet **2002**, 359, 497–498.
- Esmaeli, B.; Naderi, A.; Hidaji, L.; Blumenschein, G.; Prieto, V.G. Merkel cell carcinoma of the eyelid with a positive sentinel node. Arch. Ophthalmol. **2002**, 120, 646–648.
- Gillenwater, A.M.; Hessel, A.C.; Morrison, W.H.; Burgess, M.; Silva, E.G.; Roberts, D.; Goepfert, H. Merkel cell carcinoma of the head and neck: Effect of surgical excision and radiation on recurrence and survival. Arch. Otolaryngol. Head Neck Surg. **2001**, 127, 149–154.
- Munde PB, Khandekar SP, Dive AM, Sharma A. Pathophysiology of merkel cell. *Journal of Oral and Maxillofacial Pathology : JOMFP*. 2013;17(3):408-412.
- Sniegowski, M.C.; Warneke, C.L.; Morrison, W.H.; Nasser, Q.J.; Frank, S.J.; Pfeiffer, M.L.; El Sawy, T; Esmaeli, B. Correlation of American joint committee on cancer T category for eyelid carcinoma with patient outcomes in eyelid Merkel cell carcinoma. Ophthalmic Plast. Reconstr. Surg. **2014**. in press.
- Voog, E.; Biron, P.; Martin, J.P.; Blay, J.Y. Chemotherapy for patients with locally advanced or metastatic merkel cell carcinoma. Cancer **1999**, 85, 2589–2595.
- 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