Clinical History:

- 41 year old female with a right parotid “lump” apparently present since childhood but with a recent increase in size over the past year.
- By clinical and radiologic examination, the lesion surrounded the facial nerve and involved the digastic and stylopharyngeus muscles.
- A right parotidectomy, soft tissue resection in the region of the styloid, and a selective level IIB neck dissection were performed.
Summary of Findings

- Parotid – Bland but infiltrative keratinizing squamous proliferation with minor squamoglandular component
- Styloid - Bland but infiltrative squamoglandular proliferation with focal keratinization and mucus extravasation

One or Two Lesions?

Differential Diagnoses

Single Lesion?
- Branchial cleft anomaly
- Squamous cell carcinoma (SCC) involving duct
- Adenosquamous carcinoma
- Keratocystoma +MEC hybrid
- Keratocystoma with mucus metaplasia
- Metaplastic Warthin tumor or pleomorphic adenoma
- Skin adnexal tumor

Collision? (two lesions)
- Branchial cyst and SCC or MEC
- SCC + MEC
- Keratocystoma +MEC

What is wrong with MEC here?
- Classic MEC phenotype:
  - Intermediate cell
  - Clear cell or oncocyte
  - Mucous cell or columnar (mucin poor) glandular cell
  - Epidermoid cell
  - Squamous cell
- Overt keratinization is rare and focal
- Too much keratinization... think adenosquamous carcinoma

Whats wrong with adenosquamous carcinoma (AsqCA) here?
- SCC variant with glandular differentiation
- Prototypically high grade and keratinizing
- Key features
  - Surface dysplasia
  - Pronounced keratinization
  - Infiltrative growth
  - Discrete glandular foci
  - Pronounced nuclear atypia
- Well differentiated variants exist but...
- Pronounced keratinization and infiltration is all we have so far here

Flashback: 2011 USCAP evening conference Case 3... in San Antonio: A well differentiated AsqCA
- Ciliated adenosquamous carcinoma – often bland, largely non-keratinizing and HPV driven
- Current case no ciliated components and tumor is heavily keratinizing
What about Keratocystoma?
- Exceptionally rare, bland keratinizing multicystic proliferation
- M:F – 5:2, mean age: 37 years (range: 8-49 years), all parotid
- No recurrences (mean f/u: 33 months, range 18-48 months; n=6)
- No malignant transformation or glandular components to date
- Our case shows infiltration and PNI and glandular components

Let’s try 1st Branchial cleft anomalies
- Typically 1st to 2nd decade of age (patient had a lesion since childhood…) – can be a sinus, fistula or cyst
- Two types (Work 1972)
  - Type I – ectodermal – reduplication of external auditory canal
  - Type II – ectodermal and mesodermal – contains adnexae and cartilage
- Histologically bland and architecturally unilocular and recapitulates skin

Let’s try again… 1st Branchiogenic carcinoma??
Mythos of Branchiogenic Carcinoma Revisited

Best to be skeptical given our "stellar" track record with 2nd branchiogenic carcinomas (AKA misclassified cystic HPV related SCC metastases)

Problems with Other Options
- Metaplastic Warthin tumor (WT)
- Metaplastic Pemphigoid adenoma (PA)
- Current case: infiltrative and no evidence for residual PA or WT

Summary of Diagnostic Considerations....
- Bland but infiltrative squamoglandular lesion of parotid
- Does not fit cleanly into MEC or AsqCA
- Some problems with other considerations like keratocystoma, 1st branchial cleft cyst (or carcinoma), and metaplastic WT and PA
- Still not clear whether this is one lesion (variant/hybrid tumor) or a collision of two of these previously mentioned entities

Further Classification Concepts

Incorporation of Molecular Phenotype

Immunohistochemistry
Other Immunostains

- CK 5/6 - positive
- Cam 5.2 - positive
- P16 - negative (as a surrogate marker of high risk HPV)
- HPV ISH - negative
- ER - negative
- PR - negative
- AR - negative
- P53 - rare cells ("wild type")
- Ki-67 - low (~2-3%)
- CD34 - focal stromal staining

Differential Diagnoses

Single Lesion?
- Branchial cleft anomaly
- Squamous cell carcinoma (SCC) involving a duct
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- Keratoctystoma MEC hybrid
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Collision? (two lesions)
- Branchial cleft cyst and SCC or MEC
- SCC + MEC
- Keratoctystoma + MEC
Differential Diagnoses

Single Lesion?

- Keratinizing mucoepidermoid carcinoma (MEC)
- Keratocystoma MEC hybrid
- SCC + MEC

The Name Game

- Keratocystoma MEC hybrid
  - Somewhat reasonable, but keratinizing component is also malignant
- SCC-MEC hybrid
  - Also reasonable (what I called it in 2011) but misleading since 1st SCC of salivary gland is virtually non-existent, and usually higher grade
  - Keratinizing MEC
    - Respects the common clonal origin and somewhat reconciles the bland morphology of both components

Final Diagnostic Interpretation (ver 2011)

- MEC with SCC component (i.e. hybrid), Intermediate Grade
  - +PNI, Ø ALI
  - 0/12 neck LN

Final Diagnostic Interpretation (ver 2017)

- Keratinizing MEC, Intermediate Grade
  - +PNI, Ø ALI
  - 0/12 neck LN

- F/U
  - XRT 2011
  - Recurrence 2013 - chemo
  - NED as of 2/2017

Keratinizing MEC – Is this a thing???

- No similar molecularly confirmed cases to date.
- Most similar example – MEC associated with sialadenoma papilliferum (i.e. papilliferum like change)
Expanding the spectrum of MEC

• Common variants
  • Clear cell
  • Oncocytic
  • Sclerosing
• Unusual/putative variants
  • Sialadenoma Papilliferum like
  • ?Mucoacinar Carcinoma
  • ?Keratinizing

Unresolved Issues

• How to grade - ?Cystic and bland, but infiltrative with PNI (mostly keratinizing component)
  • Given discordant features – intermediate grade assigned
• Etiology if accepted as a variant - ?Infarcted/metaplastic MEC
• Does the childhood history of a mass mean anything or is it a red herring?

Summary

• Rare case of translocation proven MEC with keratinizing (SCC like) component
• Both components are bland but infiltrative and locally aggressive
• Both components share common molecular phenotype arguing against a collision.
• Forces a reassessment of morphologic possibilities for MEC
• Reasons for keratinization speculative

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The Online CME/Evaluations/SAMs claim process will only be available on the USCAP website until September 30, 2017.

No claims can be processed after that date!

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THANK YOU

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