Presentation

- 53 F presents for routine eye exam
  - Last exam 1/25/2005

- C/O decrease in vision OS x 1 month
  - Left eye looks “smaller”
  - Temporal pain on left

- Denies LOC, flashes, floaters, veils, or curtains
History and Exam

- PMHx: HTN
- PSHx: none
- POHx: denies surgery or trauma
- FHx: (-)
- SHx: (-) x 3
- Meds: Norvasc, HCTZ
- Gtts: none
- All: NKDA

- dVAsc:
  - OD: 20/60- ph 20/30
  - OS: 20/400 ph ni
- Pupils: 4 to 2, no APD, hippus OS
- EOMs: full OD, -1 supraduction and adduction OS
- CVF: ftfc OU
- Tapp 17/20 @ 10:30 am
- Color: + control OU, 8/12 OU
- Gonio: open to SS 360 OU
Exam

- Photos from 1-2 years prior show equal globe position
What next?
Patient Care, Interpersonal and Communication Skills
Epithelial tumours of the lacrimal gland: a clinical, histopathological, surgical and oncological survey

Sarah Linéa von Holstein¹, Sarah E Coupland², Daniel Briscoe³, Christophe Le Tourneau⁴ and Steffen Heegaard¹,⁵

Table 1. Clinical characteristics of the most common epithelial tumours of the lacrimal gland.

<table>
<thead>
<tr>
<th>Tumour type</th>
<th>Mean age, gender (M:F)</th>
<th>Duration of symptoms</th>
<th>Symptoms and signs</th>
<th>Image analysis</th>
<th>Negative prognostic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign tumours</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleomorphic adenoma</td>
<td>40 years, (1:1)</td>
<td>2 years (mean)</td>
<td>Tumour signs - Pain</td>
<td>Circumscribed, round/oval, calcification, bone remodelling</td>
<td>Long duration, multiple recurrences, incomplete surgery, biopsy not settled.</td>
</tr>
<tr>
<td>Malignant tumours</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoid cystic</td>
<td>40 years, (1:1)</td>
<td>&lt; 1 year</td>
<td>Tumour signs - Pain</td>
<td>Irregular margins, nodularity, infiltration of adjacent tissue, calcification, bone destruction</td>
<td>Size &gt; 2.5 cm, histology: solid pattern</td>
</tr>
<tr>
<td>carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoma ex</td>
<td>52 years, (1:1)</td>
<td>&lt; 1 year</td>
<td>Tumour signs - Pain</td>
<td>Irregular margins, bone erosion/invasion, calcification</td>
<td>TNM stage †, histology: high proportion of carcinoma, extent of invasion, high proliferation index</td>
</tr>
<tr>
<td>pleomorphic adenoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>50 years, (1:1)</td>
<td>&lt; 1 year</td>
<td>Tumour signs - Pain</td>
<td>Irregular margins, bone erosion/invasion, calcification</td>
<td>Late detection and treatment</td>
</tr>
<tr>
<td>Mucopidermoid</td>
<td>50 years, (2:3)</td>
<td>1-2 years (mean)</td>
<td>Tumour signs - Pain</td>
<td>Irregular margins, bone erosion/invasion, calcification</td>
<td>Histological grading † (WHO)</td>
</tr>
<tr>
<td>carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tumour signs: Palpable tumour, proptosis, displacement of eyeball, retrobulbar resistance, restricted eye motility and diplopia.
Primary malignant neoplasms of the lacrimal gland

John E Wright, Geoffrey E Rose, Alec Garner

Figure 1. Age of patients at onset of the first symptom of a malignant lacrimal gland tumour.

Figure 8. Survival intervals and status after first treatment of 48 patients with lacrimal gland carcinomas. A mass, both clinical and radiological, is often present after treatment. Although such a mass might contain active tumour cells, such patients are categorised as "without tumour" until the onset of definitive signs of tumour growth.
Patient Care, Interpersonal and Communication Skills
Cribriform pattern
Trabecular pattern
Linear pattern
Mitosis
CA invading fat

Ductal formation with oncocytic features

Pleomorphic adenoma with stromal hyalinization

IHC highlighting ductal cells

Patient Care, Interpersonal and Communication Skills
Calponin IHC showing myoepithelial cells
Necrosis

Myoepithelial features
Perineural invasion

Patient Care, Interpersonal and Communication Skills
Pathology

- carcinoma ex pleomorphic adenoma
  - +necrosis
  - +perineural invasion
  - -vascular invasion
- Intermediate grade
- Positive margin
- >50% of lesion is malignant
- Mitoses seen but not a very high proliferation index
  - 2 mitoses per HPF
- Clear cell & myoepithelial differentiation
# Survey of 1264 Patients with Orbital Tumors and Simulating Lesions

## The 2002 Montgomery Lecture, Part 1

Jerry A. Shields, MD, Carol L. Shields, MD, Richard Scartozzi, MD

---

### Table 11. Subclassification of 114 Patients with Lacrimal Gland Lesions among 1264 Consecutive Patients with Orbital Lesions

<table>
<thead>
<tr>
<th>Subcategory</th>
<th>Number of Patients (%)</th>
<th>% of Total Orbital Lesions*</th>
<th>Number Biopsy Proven (%)</th>
<th>Mean Age in Years (median, range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelial lesions</td>
<td>51 (45)</td>
<td>4</td>
<td>33 (65)</td>
<td>47 (47, 0–90)</td>
</tr>
<tr>
<td>Dacryops</td>
<td>19 (17)</td>
<td>2</td>
<td>4 (21)</td>
<td>49 (51, 0–74)</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>14 (12)</td>
<td>1</td>
<td>14 (100)</td>
<td>39 (32, 9–80)</td>
</tr>
<tr>
<td>Pleomorphic adenoma</td>
<td>11 (10)</td>
<td>&lt;1</td>
<td>10 (91)</td>
<td>48 (47, 15–90)</td>
</tr>
<tr>
<td>Pleomorphic adenocarcinoma</td>
<td>4 (4)</td>
<td>&lt;1</td>
<td>4 (100)</td>
<td>62 (67, 29–84)</td>
</tr>
<tr>
<td>Prolapsed lacrimal gland</td>
<td>2 (2)</td>
<td>&lt;1</td>
<td>0 (0)</td>
<td>55 (55, 50–60)</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>1 (1)</td>
<td>&lt;1</td>
<td>1 (100)</td>
<td>48 (40, 40–40)</td>
</tr>
<tr>
<td>Nonepithelial lesions</td>
<td>63 (55)</td>
<td>5</td>
<td>44 (70)</td>
<td>50 (51, 2–90)</td>
</tr>
<tr>
<td>Dacryadenitis (pseudotumor)</td>
<td>37 (33)</td>
<td>3</td>
<td>20 (54)</td>
<td>42 (40, 2–90)</td>
</tr>
<tr>
<td>Non-Hodgkin’s lymphoma</td>
<td>16 (14)</td>
<td>1</td>
<td>15 (94)</td>
<td>62 (66, 33–83)</td>
</tr>
<tr>
<td>Benign reactive lymphoid hyperplasia</td>
<td>7 (6)</td>
<td>1</td>
<td>7 (100)</td>
<td>63 (59, 50–76)</td>
</tr>
<tr>
<td>Atypical lymphoid hyperplasia</td>
<td>1 (1)</td>
<td>&lt;1</td>
<td>1 (100)</td>
<td>38 (38, 38–38)</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td>1 (1)</td>
<td>&lt;1</td>
<td>1 (100)</td>
<td>72 (72, 72–72)</td>
</tr>
<tr>
<td>Lymphoepithelial hyperplasia</td>
<td>1 (1)</td>
<td>&lt;1</td>
<td>0 (0)</td>
<td>49 (49, 49–49)</td>
</tr>
<tr>
<td>Total lacrimal gland fossa lesions</td>
<td>114 (100)</td>
<td>9</td>
<td>77 (68)</td>
<td>49 (51, 0–90)</td>
</tr>
</tbody>
</table>

*Percent are rounded.
Pleomorphic Adenoma

- AKA Benign Mixed Tumor
- Most common epithelial tumor of lacrimal gland (~50%)
- Adults, 4th-5th decade, men > women
- Slow growing (usually > 12 months)
- Firm, lobular mass; Well-circumscribed and nodular on imaging
- Treat with excision
  - 32% recur
- In recurrence 10% risk of malignant degeneration per decade
Adenoid Cystic Carcinoma

- AKA Cylindroma
- Most common primary malignant epithelial tumor of lacrimal gland (60%)
- Highly malignant
- Pain secondary to perineural invasion and bone destruction
- Rapid course and early pain (vs. pleomorphic adenoma)
- Lack of encapsulation

Comparison

(A)  

(B)  

(C)  

(D)  

(E)  

(F)  

Malignant Mixed Tumor

- AKA carcinoma ex pleomorphic adenoma, pleomorphic adenocarcinoma
- Histology similar to benign mixed tumors but with areas of malignant transformation, usually poorly differentiated adenocarcinomas
- Occur from:
  - Incomplete excision or incisional biopsy of pleomorphic adenoma (most common)
  - Previously unidentified pleomorphic adenoma with rapid lacrimal gland enlargement
  - Transformation of pleomorphic adenoma over decades
Salivary Gland Histology

- Similar morphologic and clinical characteristics
- 2006 AFIP classification of lacrimal tumors based on 1992 WHO classification of salivary tumors

**Table 5. Pathologic Prognostic Factors in 66 Cases of Primary CxPA**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Overall Survival ($P^*$)</th>
<th>Determinate Survival ($P^*$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic T stage (1-4)</td>
<td>.040</td>
<td>.040</td>
</tr>
<tr>
<td>Pathologic T stage (a vs b)</td>
<td>.014</td>
<td>.002</td>
</tr>
<tr>
<td>Pathologic N stage (NO vs N+)</td>
<td>.004</td>
<td>.003</td>
</tr>
<tr>
<td>Overall pathologic stage (1-4)</td>
<td>.009</td>
<td>.006</td>
</tr>
<tr>
<td>Size</td>
<td>.012</td>
<td>.025</td>
</tr>
<tr>
<td>Histologic subtype</td>
<td>.349</td>
<td>.596</td>
</tr>
<tr>
<td>Grade</td>
<td>.005</td>
<td>.004</td>
</tr>
<tr>
<td>Proportion of carcinoma</td>
<td>.004</td>
<td>.005</td>
</tr>
<tr>
<td>Invasion (&gt;1.5 cm or &lt;1.5 cm)</td>
<td>.002</td>
<td>.004</td>
</tr>
<tr>
<td>p53 positivity</td>
<td>.552</td>
<td>.646</td>
</tr>
<tr>
<td>c-erbB-2 positivity</td>
<td>.809</td>
<td>.913</td>
</tr>
<tr>
<td>DNA content</td>
<td>.505</td>
<td>.575</td>
</tr>
<tr>
<td>Proliferation index of carcinoma</td>
<td>.032</td>
<td>.024</td>
</tr>
</tbody>
</table>

*Significant $P$ values are in boldface.

Malignant Mixed Tumor

- Previous case of Dr. Shinder’s synonymous to spontaneous salivary duct carcinoma
- Overall 5 year survival 30% with carcinoma ex pleomorphic adenoma of the salivary gland in Mayo study
Previous Cases

- Four similar histological cases have been presented in the literature previously:

<table>
<thead>
<tr>
<th>Author (y)</th>
<th>Age/sex</th>
<th>Clinical features</th>
<th>Computed tomography</th>
<th>Histopathology</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present case</td>
<td>62/F</td>
<td>Right orbital swelling × 4 y, rapid progression × 6 mo</td>
<td>27 × 24 × 20-mm heterogeneously enhancing lobulated mass with thinning of the overlying bone</td>
<td>+</td>
<td>Right fronto-orbital craniotomy and gross total resection followed by RT</td>
<td>No recurrence or metastases at 3 mo</td>
</tr>
<tr>
<td>Wiwatwongwana et al [4]</td>
<td>86/M</td>
<td>Diplopia × 6 mo</td>
<td>25 × 18-mm moderately homogenous hyperattenuating mass with scalloping of the lacrimal fossa</td>
<td>-</td>
<td>Lateral orbitotomy, tumor excision with bone followed by RT</td>
<td>Died after 15 mo, no recurrence</td>
</tr>
<tr>
<td>Chen et al [3]</td>
<td>80/M</td>
<td>Left orbital palpable mass × 19 mo</td>
<td>24 × 15 × 18-mm mildly enhancing soft tissue mass. No bony erosion</td>
<td>+</td>
<td>Lateral orbitotomy and tumor excision (RT refused by patient)</td>
<td>No recurrence or metastases at 2 y</td>
</tr>
<tr>
<td>Ostrowski et al [2]</td>
<td>63/M</td>
<td>Painless proptosis × 8 y with sudden increase in size × 2 mo</td>
<td>25 × 15-mm oblong mass with sharply margined irregular borders and focal calcification. No bony erosion</td>
<td>+</td>
<td>Orbital exenteration</td>
<td>No recurrence or metastases at 2 1/2 y</td>
</tr>
</tbody>
</table>

M indicates male; F, female; RT, radiotherapy.
Clear Cell Epithelial–myoepithelial Carcinoma Arising in Pleomorphic Adenoma of the Lacrimal Gland

Mary L. Ostrowski, MD, Ramon L. Font, MD, Jesse Halpern, MD, Ernst Nicolitz, MD, Robert Barnes, MD

Background: A 63-year-old man had an 8-year history of painless proptosis, which had noticeably increased over the last 2 months. A mass was palpable in the left lateral canthus. Computed tomographic studies showed a globular mass with small foci of calcification involving the lacrimal gland. After an incisional biopsy, a histologic diagnosis of clear cell epithelial–myoepithelial carcinoma was made and an orbital exenteration was performed.

Findings: Results of histologic examination of the mass showed a partially encapsulated, clear cell epithelial–myoepithelial carcinoma with an associated pleomorphic adenoma (benign mixed tumor). Immunohistochemical studies disclosed strong immunoreactivity to cytokeratin (AE1/AE3), epithelial membrane antigen, S-100 protein, and alpha-actin.

Conclusion: Although a clear cell myoepithelial carcinoma rarely has been reported in association with a pleomorphic adenoma of the submandibular gland, to the authors' knowledge, this combination has never been reported in the lacrimal gland. Nor has a clear cell epithelial–myoepithelial carcinoma ever been reported in this anatomic location. The differential diagnosis of lesions with prominent clear cells involving the lacrimal gland is extensive and includes clear cell variants of acinic cell carcinoma and oncocytoma, mucoepidermoid carcinoma, and others. Ophthalmology 1994;101:925–930
Wiwatwongwana, et al. 


Chan, et al.

“Biphasic” architecture in the form of tubular structures lined by ductal epithelial cells surrounded by a layer of clear myoepithelial cells further enveloped by a well-defined basement membrane is noted at the periphery of nodules (C, medium power). Frequent mitoses were identified in the myoepithelial nodules along with prominent perineural invasion (H and I, high power).
What to do?

- Observe with serial imaging?
- Further surgery?
  - Bone & orbital Bx’s?
  - Globe salvage?
  - Exenteration?
- Radiation therapy?
  - EBRT vs. IMRT vs Proton vs Orbital Plaque?
- Surgery & RT?
- Intra-arterial chemo?
Our Patient

- Systemic workup found possible residual tumor at site vs. post-operative changes, second opinion in progress
- Contralateral enlargement of sub-mandibular node, not thought to be related
- Seeing Dr. Shinder soon to discuss treatment options
Our Patient
References

1. BCSC Book 7: Orbits, Eyelid, and Lacrimal System
2. BCSC Book 4: Ophthalmic Pathology and Intraocular Tumors
Thank You

- Dr. Roman Shinder
- Dr. Valerie Elmalem
- Dr. Kenneth Olumba
- Dr. Michael Dattilo
- Dr. Jordan Spindle
- Dr. Renelle Lim
- Dr. Nora Katabi
Reflective Practice

• This case represents a serious and life-threatening condition. It is essential to understand the early signs and symptoms and include this diagnosis within the differential of a lacrimal mass.

• In this situation the department worked quickly and efficiently to treat our patient. Many different residents were involved and the department worked well as a unit to effect compassionate care.
Core Competencies

• Patient Care: The case involved thorough patient care, ability to explain findings, and need for treatment to the patient. Once diagnosed, the patient received proper management and care.
• Medical Knowledge: This presentation allowed us to review the presentations, proper evaluation/work up, and differential of a lacrimal mass.
• Practice-Based Learning and Improvement: This presentation included a current literature search of a lacrimal mass.
• Interpersonal and Communication Skills: The patient was treated with respect and every effort was made to communicate with the patient and treat in accordance with her wishes.
• Professionalism: The patient was treated in the proper manner.
• Systems-Based Practice: The patient was discussed with colleagues and treated appropriately.
Dear Dr. Chen,

I reviewed the submitted slides of Ms. from the lacrimal gland. The slides show a salivary gland type tumor with ductal and myoepithelial differentiations. Although the tumor is relatively well defined, it appears to be infiltrative. Multiple growth patterns are noted including cribriforming, solid, trabecular, and linear patterns. Discrete duct formations are identified with some of the ductal cells showing oncocytic features with eosinophilic cytoplasm and prominent nucleoli. These oncocytic ductal cells are highlighted by the immunostain for AR. In addition, myoepithelial differentiations are seen. The immunostains for cam5.2, s100, p63, calponin, and CEA-M show variable staining patterns, but in overall they highlight the ductal and myoepithelial differentiations in the tumor. CD117 shows a patchy immunostaining in the tumor. CD117 staining is not specific for adenoid cystic carcinoma and can be seen in many other salivary gland tumors especially tumors with ductal and myoepithelial differentiation. CK7 immunostain is diffusely positive in the tumor. Furthermore, there is a discrete stromal hyalinized areas with bland ductal formations noted which is highly suggestive of a pleomorphic adenoma component or a carcinoma ex pleomorphic adenoma. The extent of invasion beyond the pleomorphic adenoma capsule cannot be assessed in this material. The tumor demonstrates a spectrum of cytologic atypia with occasional mitotic activities identified (focal 2 mitoses/10 HPFs). There is focal tumor necrosis seen. The performed immunostain for Ki-67 shows a focal 10-20% staining in tumor cells. Despite the lack of a standard grading system for salivary gland tumors, in a three tiered grading system, this tumor is best graded as intermediate grade for the above mentioned reasons. Perineural invasion is noted. Tumor is identified at the inked margin.

Thank you for sharing with us this very interesting and challenging case.

Sincerely,

Nora Katabi, M.D.
Assistant Attending Pathologist