Lacrimal sequelae of local and systemic therapies
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Outline
- Lacrical system overview
- Iatrogenic
- Topical medications
- Topical chemotherapeutics
- Radioactive iodine
- Systemic chemotherapeutics
- Others

Lacrimal drainage anatomy

Lacrimal Drainage Anatomy
- Puncta
  - Keratinized squamous epithelium
  - Approximately 0.3 mm in diameter
  - Sits atop the papilla lacrimalis
- Canaliculi
  - Lined by non-keratinized, stratified squamous epithelium
  - Surrounded by elastic tissue

Lacrimal Drainage Anatomy
- Lacrimal sac
  - Lined by superficial columnar epithelium
  - Deeper there is a pseudostratified epithelium
- Nasolacrimal duct
  - Approximately 1 mm in diameter
  - Similar epithelium as in the lacrimal sac

Induced Lacrical Abnormalities
- Malposition of the eyelid
• Blockage of the lacrimal drainage system
  – Stenosis
  – Occlusion
• Can occur at a variety of levels
  – Punctum
  – Canaliculus
  – Lacrimal sac
  – Nasolacrimal duct

8 iatrogenic causes

9 Iatrogenic Causes
  ■ Lacrimal plugs
    ■ Function by occluding the lacrimal punctum or the canaliculus

10 Punctal Plugs
  • Have a flange and anchor
  • Spontaneous loss can result in punctal or canalicular stenosis – with or without epiphora (Boldin et al. AJO 2008)
  • Canaliculitis, dacryocystitis, orbital cellulitis have been described

11 Intracanalicular Plug - SmartPLUG
  • SmartPLUG – acrylic
    – Placed in the vertical potion of canaliculus
    – Body temperature causes it to expand and occlude
    – Manufacturer claims can be removed by irrigating through the lacrimal system
  • Hill et al. OPRS 2009.
    – 7.23% (17/235) patients developed canaliculitis
    – 4.73% prevalence of canaliculitis per SmartPLUG

12 Intracanalicular Plug
  • Believed to have a higher incidence of complication than punctal plugs (Mazow et al OPRS 2007)
• Epiphora, canaliculitis, or dacryocystitis
• Surgery may not be effective (26% had residual post-operative symptoms)

13 Botulinum Toxin
  ▪ Has been used to reduce lacrimal drainage in patients with dry eyes (Sahlin et al. AJO 2000)
  ▪ Reduced tear drainage by 30% with just lower eyelid, and by 60% with upper and lower injection
  ▪ May result in epiphora

14 Topical medications

15 Glaucoma Drops
  • Can cause canicular obstruction (McNab Aust N Z J 1998)
  • Prospective comparison of patients taking glaucoma drops compared to controls (Kashkouli et al. OPRS 2008.)
  • 20% vs. 8.57% of controls had lacrimal drainage obstruction
  • 9.2% vs. 3.2% of controls were symptomatic
  • Primarily upper obstructions (punctum and canaliculus)
  • Possible scarring of punctal and canicular epithelium, as occurs in conjunctiva

16 Glaucoma Drops
  ▪ From the ophthalmic plastic surgery perspective:
    ▪ 23% of patients with primary acquired NLDO had POAG
    ▪ Compared to 6% having cataract surgery

17 Other Topical Medicines
  ▪ Epinephrine
    ▪ 2 patients with tearing, irrigation passed melanin-laden casts

18 Other Topical Medicines
  • Idoxuridine
• Phospholine iodide (echothiophate)
• Fortified antibiotics
  – Canalicular obstruction (Weston and Loveless Can J Ophthalmol 2000)

19 **Topical chemotherapeutics**

20 **Mitomycin C**

• DNA crosslinker
• Decreases fibroblast production and scar tissue
• May also induce scarring as toxicity

• Topical MMC 0.04% QID for 2-12 weeks for conjunctival neoplasia
  – Epiphora in 9 of 14 patients, 3 with punctal stenosis, 1 with common canaliculus obstruction, 1 with both, 1 with lower canaliculus obstruction (Kopp and Seregard BJO 2004)
• 14 of 100 patients with similar regimen developed punctal stenosis (Khong and Muecke BJO 2006)

21 **Mitomycin C**

  ▪ Interestingly...

22 **Systemic medications**

23 **Radioactive Iodine**

• Used for treatment of hyperthyroidism or thyroid malignancies
• Iodine concentrated in thyroid by sodium-iodine symporter
• Evidence of this symporter in lacrimal sac (Morgenstern et al. OPRS 2005)

24 **Radioactive Iodine**

  ▪ Therefore, patients have nasolacrimal duct obstruction more
commonly than canalicular/punctal obstruction
- Overall, incidence is 3.4% and is dose-dependent (Burns et al. OPRS 2004)
- Consider monitoring patients for tearing

25 **5-Fluorouracil (5-FU)**
- Inhibitor of DNA and RNA synthesis
- Used originally as an IV anti-cancer medication
- First report of tearing was 1978
- May be reversible if medication stopped early
- Primarily canalicular stenosis/obstruction
- Have found punctal and nasolacrimal scarring/stenosis/occlusion with systemic use

26 **5-Fluorouracil (5-FU)**
- In 52 patients with at least 3 months of systemic 5-FU:
  - 27% had tearing
  - 5.8% had punctal-canalicular stenosis
  - Overall, 93% had an ocular abnormality that caused tearing (Eiseman et al. OPRS 2003)

- No reports related to topical 5-FU

27 **Docetaxel (Taxotere)**
- Treatment for metastatic breast cancer and other malignancies
- Acts by stabilizing microtubules to halt cell division

- Association with tearing first described in 2001 in 3 patients (Esmaeli et al. Ophthalmol)
- Primarily from canalicular stenosis
- Mechanism unclear

28 **Docetaxel (Taxotere)**
- Prevention:
Some patients had reversal of stenosis with discontinuation of medication.

Phase II randomized double blind study showed no difference in topical corticosteroids vs. artificial tears.

Treatment:
- Some try bicanalicular intubation with success.
- If complete canalicular obstruction → Jones tube.
- Early referral!

**Paclitaxel (Taxol)**
- In the same class as docetaxel – inhibits microtubule function.
- Case report of a patient with epiphora 8 weeks after treatment (McCartney et al. OPRS 2007).
- Had stenosis of all 4 puncta, canaliculi, and valve of Hasner.
- Improved with lacrimal intubation, but still present.

**S-1**
- Prodrug of 5-FU combined with 2 modulators.
- More active and less toxic than IV 5-FU.
- Oral administration.
- Used for gastric, colon, pancreatic, and lung carcinomas.
- Up to 18% develop epiphora (Kim et al. Ann Oncol 2012).

**Imatinib Mesylate (Gleevec)**
- Oral anti-cancer medication.
- Acts by inhibiting tyrosine kinase.
- Used for CML, GI tumors, amongst others.

- 18% of 104 patients developed epiphora, although direct link is unclear (Fraunfelder et al. J Ocul Pharmacol Ther 2003).

**Others**

**Radiation**
- Well-known cause of lacrimal drainage stenosis/obstruction.
- Prophylactic lacrimal intubation can help (Lovato et al. Am J...
34 Summary

- Many local and systemic medications or treatments have effects on the lacrimal drainage system
- Can recognize these with thorough history
- May be reversible with discontinuation of drug
- Some may be treated with lacrimal intubation

35 Thank you!