Where's the bleeding coming from? A case of recurrent basal cell carcinoma

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Abstract:
A 95 year old male with a history of basal cell carcinoma of the right eyelids and orbit, and squamous cell carcinoma of the forehead presents with bleeding of unknown origin and severe eye pain.

I. Case History:
- 95 year old Caucasian male
- Chief complaint: bleeding, mucous discharge, and very painful aching, stinging eye pain OD x 2 weeks. Denies fever or trauma
- Ocular History:
  - Pseudophakia OS with secondary corneal edema
    - Poor vision OS likely due to corneal edema, distortion from limbal sutures, and macular drusen
  - Phthisis bulbi OD
  - Locally advanced basal cell carcinoma OD involving right eyelids, orbit, and ocular surface
    - s/p radiation Vismodegib oral chemo (2013)
    - s/p multiple eyelid resection surgeries with grafts (2006)
  - s/p partial permanent tarsorrhaphy OD
  - H/o secondary open angle glaucoma s/p complications with cataract surgery OD
- Medical History:
  - Basal cell carcinoma
  - Squamous cell carcinoma of skin of eyelid
  - Squamous cell carcinoma of ear
  - Seborrheic dermatitis
  - Seborrheic keratosis
  - Actinic keratosis
  - Chronic atrial fibrillation
  - Bronchial asthma
  - Vitamin B12 deficiency
  - Enlarged prostate
  - Benign essential hypertension
  - Hyperlipidemia
  - Coronary artery disease
  - MRSA infection
  - Peripheral vascular disease
  - Hearing loss
  - Dermatophytosis of nail
  - Breast mass
  - Adjustment disorder with anxiety
Medications:
- Artificial tears OS tid
- Pred Forte OS qd
- Brimonidine OS bid
- Neomycin-polymyxin-bacitracin ointment OD tid
- Losartan 100mg po qd
- Simvastatin 10mg po qd
- Mometasone 220mcg oral inhaler bid
- Fluorouracil 5% topical cream qpm
- Isosorbide mononitrate 30mg po qam
- Finasteride 5mg po qd
- Imiquimod 5% topical cream qd
- Amlodipine besylate 10mg po qd
- Cyanocobalamin 1000mcg po qd

Other salient information:
- Patient is not ambulatory and unable to transfer into exam chair. He is accompanied by his caretaker who repeats conversation for patient, as he suffers from severe hearing loss.
- s/p complicated cataract surgery OS 05/2016 with secondary corneal edema
- Patient has 30+ year history of nodular and infiltrative basal cell carcinoma of his right temple and right eyelid, and most recently was treated with Vismodegib, an oral chemotherapy agent for basal cell carcinoma, for 3 months in 2013 but elected to discontinue therapy and treat conservatively due to 40 lb weight loss, significant loss of appetite, malnutrition, and impact on quality of life
- Patient had invasive squamous cell carcinoma of his forehead which was treated with Mohs micrographic surgery

II. Pertinent Findings:
- Clinical:
  - OD: NLP
  - OS: 20/200, PH: 20/70
  - External exam: narrow right palpebral fissure with erythema of RUL and RLL, extending down toward cheek.
- Anterior segment:
  - Lids/Lashes:
    - OD: Partial lateral and medial tarsorrhaphy, crusts of dried blood along nasal canthus region, scalloped lid margins with mucous crusting; no tenderness with palpation. Erythema of RUL and RLL, extending from nasal canthus down toward upper cheek
    - OS: 1+ scurf/blepharitis
  - Conjunctiva:
    - OD: phthisis bulbi – unable to assess
    - OS: trace hyperemia 360; superior limbal sutures
  - Cornea:
    - OS: mucous strand, no corneal edema appreciated
  - Anterior chamber:
    - OS: no cells/flare
Iris:
- OS: mechanically dilated, peaked superiorly, minimal reaction to light

- Histology of RUL and RLL (2005) revealed multicentric invasive basal cell carcinoma extending to deep and lateral surgical margins

III. Differential Diagnosis:
- Preseptal cellulitis in the presence of suspected recurrent basal cell carcinoma
- Atypical dacryocystitis with associated preseptal cellulitis
- Recurrent squamous cell carcinoma
- Sebaceous gland carcinoma
- Severe blepharitis

IV. Diagnosis:

Patient’s treatment and follow-up for Preseptal Cellulitis:
- For preseptal cellulitis, systemic oral antibiotics are therapy of choice. Augmentin and Keflex are preferred; however contraindicated in this patient due to penicillin allergy. Bactrim DS second choice, but also contraindicated due to possible severe drug interaction with Losartan.
- Ordered doxycycline 100mg po bid x 10 days due to good penetration of soft tissue
- Continue neomycin-polymyxin-bacitracin ointment OD as previously prescribed
- Referred patient to see an oculoplastic surgeon for evaluation within one week
- 10 days after initial presentation, patient returned for follow-up reporting that his right eye felt much better. However, he never went to his consultation with an oculoplastic surgeon. Bleeding and mucous have ceased and he is in no apparent discomfort
  - Follow-up exam findings:
    - MRx: OD BALANCE, OS: -4.75 +2.00 x 035, VA: 20/50
    - EOMs: full and smooth OS
    - Confrontation fields: Full OS
    - Applanation tonometry OS: 15 mmHg
    - Biomicroscopy revealed a presumed human hair within eye socket OD
      - As hair within eye socket was removed with a sterile cotton tipped applicator, tissue within eye socket began to bleed. Socket was irrigated and gauze was applied. Bleeding subsided quickly. Patient did not experience any pain and left in good condition
      - Stat referral was again placed for evaluation with an oculoplastic surgeon
  - 6 days after follow-up, patient was seen by an oculoplastic ophthalmologist. Impression/plan was as follows:
    - Orbital invasive BCC right eyelids/orbit/ocular surface s/p radiation Vismodegib oral chemo. Previously discussed repeat radiation with radiation oncologist and patient is not a candidate. Also, pt did not tolerate Vismodegib oral chemo. Discussed with patient’s daughter that mass is not resectable short of radical exenteration. Will discuss case with dermatology and call daughter. F/u one month

Discussion:
- Basal cell carcinoma (BCC) is the most prevalent form of skin cancer, and the most common malignant eyelid tumor in Caucasians. Most commonly affected regions are the lower eyelid, followed by the medial canthus.
Along with squamous cell carcinoma, it is classified as a non-melanoma skin cancer (NMSC), which has a very low mortality rate. Metastasis of BCC is rare.

Incidence of NMSC increases with age, and it is found more often in men than in women. It has a high recurrence rate of almost 50%.

Definitive cell of origin for BCC is still unknown due to conflicting evidence. Current data indicates that BCCs may originate from hair follicle stem cells, or from basal keratinocytes of the interfollicular epidermis – both cell types exist in the lower layer of the epidermis.

Largest risk factor is long-term exposure to ultraviolet radiation, although BCC can also be found in non-exposed parts of the body.

Pathogenesis: aberrant Hedgehog pathway signaling and mutations of Patched-1 and Smoothened genes.

Main clinical subtypes: nodular, superficial, and morpheaform – all painless in early stages of presentation.

- Nodular: most common: 50-79% of all BCC
  - Lesions are described as pearly with small arborizing telangiectasias. Crusting may appear over a central umbilication. Bleeding with minor trauma occurs frequently
- Superficial: second most common, up to 15% of cases
  - Lesion is described as well-circumscribed, scaly, pink-to-red macule, patch, thin papule, or thin plaque. May have crusting or a rolled border. Favored location is the trunk and extremities
- Morpheaform/Sclerosing:
  - Lesion is pink-to-white, smooth, shiny, and scar-like with ill-defined borders. Morpheaform BCCs are notorious for subtlety in presentation, but are more aggressive than the other subtypes, tending to spread

Only definitive means of diagnosis is via biopsy.

- Biopsy techniques include excision, incision, shave, and punch biopsies

Retrospective review of 147 eyelid lesions (Tzoutzos et. al 2016)

- 119 specimens were BCC, from 43 men and 66 women. The difference in sex proportions was statistically significant
- Mean age of the afflicted patients was 70
- Main histological appearance was solid subtype, followed by solid-cystic, superficial, adenoid subtype, and basosquamous cell carcinoma
- Probability of ulceration was positively correlated with increased age of BCC patients, though this did not reach statistical significance
- Relationship of inflammation of BCC with age was statistically significant
- Mean tumor diameter was 0.70cm, and correlated positively with probability of inflammation, but not ulceration
- In all patients with recurrences, tumors were always solid type

V. Treatment and management

- Treatment is mainly comprised of complete excision, which may include electrodessication and curettage, cryosurgery, or Mohs surgery. Surgical reconstruction of eyelids is required to maintain structure and function of eyelids after surgical interventions.
- Nonsurgical treatment options may be desirable in select populations such as the immunosuppressed, elderly, in cases of minimal involvement, or advanced or recalcitrant BCC.
  - Localized therapies include topical medications or light and radiation-based treatments
- **Topical Therapies:**
  - Imiquimod: immunomodulatory drug that stimulates the immune system while exhibiting pro-apoptotic effects on malignant cells. Also inhibits the Hedgehog signaling pathway
  - 5-Fluorouracil: selectively affects DNA synthesis in neoplastic cells, reserved for treatment of superficial BCCs
  - Ingenol mebutate: induces cell necrosis and an inflammatory response
  - Tazarotene: disrupts the differentiation and proliferation of keratinocytes in BCC and activates apoptosis.
  - Solasodine glycoalkaloids: hypothesized to disrupt cellular membranes or to increase tissue necrosis factor
- **Light-based treatment:**
  - Photodynamic Therapy (PDT): chemical reactions catalyzed by light generate reactive oxygen species for destruction of tumor cells. Resultant inflammation enhances immune responses in immunocompetent patients
  - Laser therapy: not yet FDA-approved, but used off-label. Laser ablation of superficial skin
- **Radiation treatment:**
  - Radiotherapy uses radiation source applied to treated area induces genetic damage to affected area, causing tumor cell lysis and destruction of offending BCC
- **Systemic therapies:**
  - Hedgehog pathway inhibitors: Vismodegib, approved for use in metastatic BCC, recurrent BCC, or BCC in patients who are not good candidates for radiation or surgery
  - Chemotherapy: widely variable clinical outcomes with significant adverse events. Reserved treatment for nonresponsive or resistant BCCs

**VI. Conclusion**
- Overall incidence of basal cell carcinoma is rising. Though mortality rates are low and metastasis is rare, eyelid BCCs can be disfiguring. Reconstructive surgery is often necessary to maintain functionality of eyelids as a protective anatomical barrier to the ocular surface. Early detection may lead to more favorable outcomes. Optometrists skilled in identification of suspicious eyelid malignancies such as basal cell carcinomas will be more likely to detect these often seemingly-innocuous lesions.
References


