Clinical features

- Leukoplakia
- Papilliform
- Gelatinous with tufted vessels
- Velvety
- Nodular or diffuse
- Nasal or temporal limbus
- Present as a mass, redness or irritation
Differential diagnosis

- Papilloma (A)
  - Younger patient, anywhere on conj., vascular pattern
- Solar elastosis (B)
- Corneal conjunctival dysplasia (C)
- SCC (D)
- Pyogenic granuloma
- Limbal vernal
  - Suspect in younger patient
- Malignant melanoma (E)
  - Smooth surface, not gelatinous or leukoplakia

Rudkin et al BJO 95;350-354
Impression cytology

Useful to confirm diagnosis prior to topical chemotherapy
• Use of Biopore membrane
• High reliability >90% correlation rate with histology
• High degree of suspicion in heavily keratinized lesion
• Cannot identify SCC reliably
• Post MMC effect noticed

Tole et al BJO 2001;85:154-8
Pathology

- **Dysplasia**
  - Cellular atypia
    - mild <1/3 atypical cells
    - Moderate ¾ atypical cells
    - Severe nearly full thickness

- **Carcinoma in situ**
  - Full thickness atypia with loss of normal surface layer

- **SCC invasion of BM**
How do you distinguish SCC from dysplasia?
SCC of the Conjunctiva
Clinico-pathological review

- Identify clinical diagnostic features
- Establish reliability of impression cytology as an aid to diagnosis
- Outcome/ prognosis markers

McKelvie et al BJO 2002;86:168-173
Clinical diagnosis

- Correct pre-operative diagnosis in 35%
- Pre-operative diagnosis of OSSN 85%
- If lesion > 10mm correct 67%
- Sex: 77% male
- Age: 69% >60 years
- Presentation:
  - mass 80%
  - redness/ irritation 36%
  - Vision impaired 10%
- Size: 50% >10 mm
Follow-up

- Median follow-up 26 months
- 7/26 recurrence (27%)
- 4/6 positive margins recurred
- 4 deaths
- 2 died of metastatic disease (8%)
Risk factors for recurrence

- Positive margins $p=0.028$
- Size($>10\text{mm}$) $p=0.049$
- Ki 67 score $p=0.047$
- Increased age $p=0.0028$

Non significant factors: sex, shape, differentiation, invasion of orbit/cornea/sclera or intraocular extension
SCC Pathology

• All lesions keratinised
• Solar damage in all cases
• Invasive tumour arose from field of CIS in 7/26, dysplasia in 16/26
• Scleral/corneal invasion 30%
• Orbital invasion 15%
• Intraocular invasion 11%
Keratotic variant

- Most common 16/26
- Invasion varied from minimal to deep
- Minimal invasion 11/26
- Leukoplakia present
Endophytic variant

- 8/26 endophytic type
- lobules of invasive keratinising SCC in stroma
- Nodular or diffuse
Papillomatous SCC

- 2/26 papillomatous or exophytic
- velvety, papilloform
SCC invading angle

- Invasion AC/ trabecular mesh/ iris 2/26
- Ciliary body invasion 3/26
Impression cytology

- Using Biopore membrane 80+% accuracy in OSSN diagnosis
- No tumour diathesis seen in SCC
- 60% had CIN or partial thickness epithelial atypia that would not yield atypical cells
- Endophytic and orbital lesions not identified

Not a reliable method to exclude SCC
Summary

- Large lesions with hyperkeratotic plaques most correctly diagnosed
- CIC not reliable aid to diagnosis
- Proliferation index Ki-67 offers useful prognostic information
- Adequate margin at time of first surgery critical
Management of OSSN

- Excisional biopsy
- Cryotherapy
- Topical chemotherapy
  - MMC
  - 5 FU
  - Interferon
Surgical technique

- Wide resection of conjunctival tumour
  - Partial lamellar scleroconjunctivectomy
  - Conjunctival margin 2mm
  - 0.2mm thin scleral flap
  - Emerging into cornea, @ Bowmans
- Double freeze thaw cryotherapy
- Closure of conjunctival wound

Shields et al Arch Ophthalmol 1999
Long term results with surgery

- 15 year follow-up
- 79 cases, 52 dysplasia, 27 CIS
- Complete excision 33% recurrence
- Incomplete excision 56% recurrence
- 15% recurred more than 5 years after surgery
- 9% progressed to SCC

Tabin et al Ophthalmol 1997
Chemotherapy options

- Mitomycin
  Dose 0.02-0.04% QID for one-three weeks
- Interferon alpha 2B
  Topical QID until resolved
  Intra lesional injection
  Plus Retinoic acid
- 5-Fluorouracil 1%
  Topical QID daily for one week followed by drug holiday of 3 weeks
Mitomycin results

MMC 0.04% week on and week off
• Clinical resolution of disease 19/20
• Time to resolution 2-8 weeks (median 4)
• Number of cycles 1-5 (median 2)

MMC 0.04% 3 weeks
• 24/26 resolved


Hirst Ophthalmol 2007 976-982
Complications

Epithelial toxicity 34%
Epiphora 14%
Lid/skin toxicity
Limbal stem cell deficiency rare

Khong et al BJO 2006;90:819-22
Interferon results

IFN alpha2B (1x $10^6$ iu/ml) QID until resolved
- 27/28 resolved, median 3 months treatment

IFN alpha 2B QID topically plus retinoic acid 0.01% alternate days
- 87/89 resolved
- 98% resolution in 1-7 months
- Side effects papillary conjunctivitis

IFN alpha 2B 0.5ml intralesional 2 weekly (10 x $10^6$iu/ml)
- 13/15 resolved, median 6 injections
Current protocol

• Primary disease treated with surgical excision + cryotherapy (excisional biopsy)

• Recurrent/residual disease considered for interferon
• Interferon alpha 2a $1 \times 10^6$ IU/ml QID until resolves
• Work-up including impression cytology
• MMC 0.04% qid for one week for recalcitrant disease
  – One week off treatment and review
  – 2nd cycle of treatment and review
  – If not resolved by 8 weeks consider 3rd cycle
  – Punctal plug not required
• Long term follow up recommended
Comparison of costs of topical meds

The retail price at Slade Pharmacy (Richmond):

• MMC 0.04% - $247.90 (2 x 5 mL) or $192.95 (1 x 5 mL) – 28 days expiry from date of manufacture but 7 days expiry once opened.

• Interferon alpha 2b 1x10^6 IU - $269 (note 14 day expiry and interferon alpha 2b (IntronA) deleted from market 1 June 2018 – may not be able to be prepared in future)

• 5 FU 1% - $121 (4 x 3 mL)

Eye and Ear Pharmacy

• Interferon alpha 2a (Roferon A) $200 (14 day supply)
Management options

- **Amniotic membrane transplant**
  - Large conjunctival defect

- **Pre operative chemoreduction**
  - Extensive disease involving limbus
  - Consider subconj high dose monthly injections \(10 \times 10^6\)iu/ml

- **Post operative adjunctive therapy**
  - Incomplete margins
  - High grade disease
  - Immunoprevention in HIV
  - ? All cases (IFN QID for 2 months)

- **Long-term outcomes after adjunctive topical 5-fluorouracil or mitomycin C**
  153 eyes followed 3+ years. There was one recurrence in the 5-fluorouracil group and no recurrences in the mitomycin C group (but more side effects in MMC group)
Conclusion

• Difficult to make a clinical diagnosis, need to check pathology
• Primary disease treated with surgical excision + cryotherapy
• Exception is widespread disease, consider chemoreduction
• Recurrent/ residual disease considered for medical treatment