Ocular Surface Squamous Neoplasia (OSSN)

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## Major types of conjunctival tumor

<table>
<thead>
<tr>
<th>Category</th>
<th>Subtype</th>
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</thead>
<tbody>
<tr>
<td>Epithelial tumors</td>
<td>Non-melanocytic tumors, Melanocytic tumors</td>
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<tr>
<td>Stromal tumors</td>
<td>Vascular tumors, Neural tumors, Myxoid tumors, Lipomatous, Hamartoma, Fibrous tissue tumors, Histiocytic tumors, Myogenic, Lymphoproliferative, Choristoma</td>
</tr>
<tr>
<td>Congenital</td>
<td></td>
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<tr>
<td>Secondary tumors</td>
<td></td>
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<tr>
<td>Metastatic tumors</td>
<td></td>
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<tr>
<td>Infectious and inflammatory lesions that simulate neoplasms</td>
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</table>
Introduction

✓ Precancerous and cancerous epithelial lesions of the conjunctiva and cornea: dysplasia, CIN, and SCC
✓ Prevalence → 0.13-1.9 cases/100,000 population
✓ The highest incidence of OSSN: male, 50 - 75 years old
✓ Common risk factors: older age, UV exposure, HIV
✓ A slow growing tumour of low-grade malignancy, which rarely metastasize
Risk factors

1. Fair skin, pale irises, high propensity to sunburn, and a past history of skin cancer
2. Chronic infection by HPV, trachoma, vitamin A deficiency, chronic irritants, xeroderma pigmentosa
3. Immunosuppression, whether due to organ transplantation or secondary to HIV/AIDS
Signs and Symptoms

- Usually asymptomatic and are detected by chance
- Redness, irritation or foreign body sensation
- Visual acuity is usually not reduced, unless the center of the cornea is affected
- May grow within weeks to years
- Details such as history of growth, the patient’s demographic features, the existence of systemic diseases, and specific tumor features should be assessed
Clinical Examination

- Conjunctival and corneal involvement
- Fluorescein or rose Bengal stains
- Evaluate all possible extension
- A cotton tipped applicator to evaluate it moves
- Ultrasonography → if tumor is thick /adheres to its surroundings
Clinical features

Gelatinous
- the commonest, circumscribed, propensity for rapid growth and diffuse variety, with superficial vessels as a result of acanthosis and dysplasia

Leukoplakic
- caused by hyperkeratosis, parakeratosis, and dyskeratosis

Papilliform
- type a sessile papilloma harbors dysplastic cell

Nodular lesion, especially when it is invasive SCC
Diffuse lesion masquerading as chronic conjunctivitis
Documentation

- Color of the lesion – pigmented or non-pigmented, red, pink, white, or yellow
- Consistency – hard, soft, rubbery, or gelatinous
- Composition – solid or cystic
- Number of tumors – solitary or multiple
- Surface – smooth, irregular, granular, papillary, ulcerated, covered by keratin
- Shape – flat or raised, pedunculated or papillary
- Thickness – thin or thick
- Location – bulbar, palpebral, forniceal conjunctiva or caruncle
- Mobility – movement with conjunctiva or fixation to globe
Simulating tumors

- Such as pinguecula, pterygium, and papilloma
- Unsuspected OSSN was found incidentally in 9.8% of 538 consecutive samples of pterygia (Hirst LW, et al, 2009)
- Not neoplastic in origin → can be confused with tumors when covered by keratin plaque or have a gelatinous appearance
When → Malignant

- Leukoplakia (ekstensif leukoplakia)
- Feeder vessels
- Intrinsic vascularity
- Pigmentation
- Unusual place in conjunctiva (contoh: bukan didaerah bukan intra palpebralis). Posisi di superior/ inferior…
- Rapid growth
- Immunocompromised patient
- Young adult or very old patient
• Membuktikan itu adalah vedder vessel: (bukan injeksi silier /crock crew):
• feeder vessel mengarah kearah tumor:
• dibuktikan dengan cotton tip. Ikut bergerak saat menggerakkan tumor.
• Arah berbeda dg injeksi konjungtiva
• Warna lebih kelam (seperti injeksi silier)
• Ukuran lebih besar
Intrinsik vaskularity

- Pada tumor yang papilary??
- Didalam tumor ada pembuluh darah
Drawings/photography externally or via the slit lamp

palpate the preauricular and submandibular areas for enlarged lymph nodes → rule out regional metastases

Pre operative

Systemic evaluation (Pemeriksaan pada: Paru utamanya)

Impression / Exfoliative Cytology
CARA MENGAMBAR
Pre operative diagnosis

Impression cytology

- obtaining cells from the surface of the conjunctival lesion
- good accuracy but can miss about 20% of cases
- definite role in follow-up of lesions

Exfoliative cytology

- obtained by platinum spatula, brush, and cotton-tip
- advantages: mainly in differentiating between benign and malignant lesions, to sample multiple sites, and in easy follow-up evaluation
- disadvantage is the superficial nature of the samples obtained
<table>
<thead>
<tr>
<th>Clinical stage</th>
<th>Definition</th>
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<tbody>
<tr>
<td><strong>Primary tumor (T)</strong></td>
<td></td>
</tr>
<tr>
<td>Tx</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>Tumor absent</td>
</tr>
<tr>
<td>T (is)</td>
<td>Tumor present as carcinoma in situ/GIN</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor present with largest basal diameter &lt;5 mm</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor present with largest basal diameter &gt;5 mm, without invasion of adjacent structures</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades adjacent structures excluding the orbit</td>
</tr>
<tr>
<td>T4</td>
<td>Tumor invades orbit with or without further extension</td>
</tr>
<tr>
<td>T4a</td>
<td>Tumor invades orbital soft tissues, without bone invasion</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades bone</td>
</tr>
<tr>
<td>T4c</td>
<td>Tumor invades adjacent paranasal sinuses</td>
</tr>
<tr>
<td>T4d</td>
<td>Tumor invades brain</td>
</tr>
<tr>
<td><strong>Regional lymph node (N)</strong></td>
<td></td>
</tr>
<tr>
<td>Nx</td>
<td>Regional lymph node cannot be assessed</td>
</tr>
<tr>
<td>N0a</td>
<td>No regional lymph node metastasis, biopsy done</td>
</tr>
<tr>
<td>N0b</td>
<td>No regional lymph node metastasis, no biopsy done</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastasis</td>
</tr>
<tr>
<td><strong>Distant metastasis (M)</strong></td>
<td></td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
</tbody>
</table>

Surgical Excision

Tumor outlined with 3 – 4 mm margins

Conjunctival tumor being excised using Westcott scissors with “no-touch technique”
Surgical Excision

Absolute dehydrated alcohol applied to corneal surface for 60 seconds
AKE

AKE dilakukan selama 60 detik. Yang diambil 2 mm dari tepi tumor yg terkena alkohol

Post excision
Surgical Excision

Application of double freeze-thaw cryotherapy to conjunctival base and conjunctival edge double freeze: tepi konjungtiva. Tepi tumor, 2x putaran, tepi basis (tidak lama2, ditempel sebentar karena ada resiko trjdi limbal stem cell diefisiensi).
Surgical excision principal

- Complete excision with tumor free margin (4-6 mm)
- No-touch technique
- Alcohol-assisted keratoepitheliectomy with 2 mm margin
- Lamellar keratectomy/sclerectomy (0.2-0.3 mm depth)
- Double freeze-thaw cryotherapy to resection edge and base
- Amniotic membrane grafting
Histopathology

- placed flat on filter paper and allowed to dry for 30–60 seconds
- Mark 2 adjacent margins include a diagram depicting this orientation on the pathology requisition form
- The status of the lateral and deep margins is important for prognosis
<table>
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<th>Condition</th>
<th>Description</th>
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| Dysplasia                              | - Mild, moderate, or severe degrees of cellular atypia that may involve various thicknesses of the epithelium, starting from the basal layer outwards  
  - Severe dysplastic changes → difficult to distinguish the lesion from carcinoma in situ |
| Carcinoma in situ                      | - May exhibit all the histological features of SCC  
  - Remains confined to the epithelium, respecting the basement membrane  
  - Affecting the full thickness of the epithelium |
| Invasive squamous cell carcinoma       | - The basement membrane of the epithelium is breached and the subepithelial tissue of the conjunctiva is invaded.  
  - Well differentiated and often show surface keratinization  
  - Can be pigmented → owing to abnormal proliferation of melanocytes |
PERBEDAAN

• Displasia:
• Dari membran basalnya.
Topical Chemotherapy

- **Rule of 4**: 0.04% MMC, 4 times a day, 4 days a week, 4 weeks (2 weeks of treatment-free interval)

- **Indications**:
  - >2 quadrants of conjunctival involvement
  - >180° of limbal involvement
  - Clear corneal extension encroaching the papillary axis
  - Positive margin after excision
  - Patient not fit for surgery

OSSN in XP
Modified Enucleation/Exenteration

Pasien seperti ini (sudah invasif) cek PKGB dan metastasis paru

Butuh insisional biopsi
SCC tipe ganas
- Mukoepidermoid ca
- Spindel sell ca

- Inisisonal biopsi: sebagian saja
- Eksisional biopsi: semuanya

Tepi tumor licin umumnya citologi impresi hasilnya negatif, butuh insisional biopsi
Sc konjungtiva recurrent infiltrasi orbita: Eksenterasi

Massa konjungtiva medila tipe: noduler. Dengan leukopiakia ekstensif.
Pdx: exfoliatif citologi—tindakan seperti insisional biopsi. Konjungtiva ditutup sedikit, dalam diambl. Kemudian ditutup kembali
Jika ada leukopiakia ekstensif: kemungkinan CIN
Ptx: AKE, wide excision, cryoterapi, AMT (u/ menutup defek), pemberian MMC paska operasi (jika durante op bersih dari tumor, dan tidak ada infiltrasi akss)
Diagnosa: OSSN (CIN)

Tumor dilimbus bentukan gelatinous. Dengan pemeriksaan rose bengal didapatkan gambaran + di konjungtiva
Pdx: sitologi impesi
Hasil : displasia sedang berat;
Dx OSSN, Ptx: wide ekstsi. Jika tumor smapai fornixsulit untuk mengambil bersih sehingga butuh mmc

Massa berbentuk papiliform dengan intrinsik vaskularity dan feeder vessel
Cytologi impesi: hasil PA: SCC invansif (adafeeder vessel dan intrinsik vaskularity)
DX: OS konjungtival kornea (tumors cel carsinoma)
Ptx: kira kira pengambilan tidak bisa bersih (sudah SCC), sehingga dapat dilakukan pemberian MMC dahulu, sifh mengicil di eksisi.
Jika PKGB + preaurikula: modified enucleation
Conclusion

• Diagnosis can often be made using thorough clinical examination
• Recognized and diagnosed at a relatively early stage
• Histopathology is the gold standard
• Surgical excision (alone) often inadequate to determine tumor’s edges and deep margins
• Added with alcohol exposure (AKE) or cryotherapy of the tumor bed (sclera and adjacent conjunctiva) → improved local control
• Role of topical chemotherapy for OSSN : MMC, IFN α 2b
Acknowledgement

Successful treatment of cancer depends upon its early detection and intervention.

The goals of therapy in ophthalmic oncology are:

1. to eradicate the tumors in order to save the life of the patient
2. preserve as much vision as possible
3. minimize the risk of late sequelae from treatment

Take home messages
Thank You
Kecurigaan Ke intra okuler

- Tanda awal adalah terjadi uveitis
  Konfirmasi dg USG

Kecurigaan ke intraorbita:
Okular motiliti terhambat. Globe displacement +, konjungtiva terkena hingga ke fornix → hal ini semua indikasi dilakukan CT Scan
Gambaran tersering:
- Gelatinous
- Leukoplakia (sering juga ditemui pada pterigium)
- Papiliform