Ophthalmic pathology and oncology

Objective

Understanding the pathophysiology and oncology of the eye and in systemic diseases and their presentations. Differentiation of benign and malignant eye diseases, understanding the pathology and examination techniques with focus on the main risk factors of the disease. Recognising signs and symptoms of the disease with diagnostic tests at the slit lamp as well as functional and structural analysis. Management of presentation, including various therapeutic options (medical and surgical) and follow-up. Psychology and management of patients presenting with a potentially blinding and life-threatening disease.

A) Pathology

Anatomy and pathophysiology of:

-Ocular anatomy and histology of the major structures of the eye and its adnexa:

- Conjunctiva
- Cornea
- Sclera
- Anterior chamber
- Posterior chamber
- Iris
- Ciliary body
- Lens
- Vitreous
- Retina and retinal pigment epithelium
- Choroid
- Optic nerve
- Visual pathway
- Eyelids
- Extraocular muscles
- Lacrimal system
- Orbit

Disease process

- Congenital anomaly
- Choristoma versus hamartoma

Inflammation

- Acute versus chronic
- Focal versus diffuse
- Granulomatus versus nongranulomatous

Degeneration (includes dystrophy)

Neoplasia

- Benign versus malignant

- Epithelial versus soft tissue versus haematopoietic

-Basic pathophysiology of the common disease processes of the eye and its adnexa, and identify the major histologic findings:

a. Degeneration (e.g., pterygium, keratoconus)
b. Dystrophy (e.g., Fuchs' dystrophy, TGFBI-associated dystrophies)
c. Infection (e.g., fungal keratitis, bacterial endophthalmitis)
d. Inflammation (e.g., chalazion, idiopathic orbital inflammation)
e. Neoplasm and proliferation (e.g., basal and squamous cell carcinoma, uveal melanoma, retinoblastoma)

- Pathophysiology and identify the major histologic findings of common diseases of the eye (e.g., keratitis, exfoliation syndrome, corneal and retinal dystrophies and degenerations, frequent neoplasms, oculoplastics, cornea, glaucoma, retina, ophthalmic oncology).
- Pathophysiology and histology of potentially vision or life-threatening diseases (e.g., temporal arteritis, endophthalmitis, retinoblastoma, ocular melanoma, extraocular or orbital spread of an intraocular or periorbital tumour, metastasis to the eye and orbit).
- Less common ocular anatomy (e.g., pars plana cysts), and identify the histology of the minor structures (e.g., ciliary sulcus) of the eye and its adnexa.
- Pathophysiology of the disease processes of the eye, and identify major histologic findings of each (e.g., inflammatory pseudotumor, lymphoma, artifacts of tissue processing, virus particles).
- Histology of the less common but potentially vision- or life-threatening ocular and adnexal diseases (e.g., healed giant cell arteritis, mimics and masqueraders of inflammation and neoplasm, less common benign and malignant neoplasms).

Clinical knowledge of examination and ancillary testing:

- Common methods of specimen acquisition and handling for ophthalmic pathology, especial handling methods that avoid artifacts and ensure representative sampling:

Specimen Handling:

Communication (Communication with pathologist is important because specimens are small and require special handling.)
Orientation (Globes may be orientated according to the location of extraocular muscles.)
Transillumination (The shadow found with transillumination can be outlined with a marking pencil.)
Gross dissection
Processing and Staining (The most common fixative is Formalin 10%, Common Stains used in Ophthalmic Pathology, e.g., haematoxylin and eosin [H&E)], Periodic acid-Schiff [PAS])

Special Procedures:

Immunohistochemistry
Flow Cytometry
Molecular Pathology
Diagnostic Electron Microscopy

Special techniques:

Fine-Needle Aspiration Biopsy
Frozen section

- Ancillary procedures for oncology (eg, bone marrow aspiration, cerebrospinal fluid cytology).

Oncology

Knowledge to be gained

Anatomy and pathophysiology of:

- Conjunctival and intraocular tumours.
- Major types of ocular tumour.
- Epidemiology of the more common tumours (e.g., melanoma).
- Anatomy, histology, and physiology of the eye and ocular adnexa with relevance to ocular oncology.

Epidemiology of tumours
Classification of the disease
Risks of the disease

Clinical knowledge of ancillary and diagnostic testing:

- Examinations and tests by which ocular tumours are diagnosed.
- Diagnostic techniques for ocular tumours (e.g., examination under anaesthesia for paediatric tumours, imaging, biopsy, laboratory tests, oncology referral).

- Indications (e.g., biopsy for lymphoma) and contraindications (e.g., biopsy for retinoblastoma) for the various diagnostic techniques.

- Fine Needle Aspiration Biopsy for Diagnosis, Prognosis (e.g. monosomy 3) and confirmation of choroidal metastasis.

- Examination techniques:
    a. Slit-lamp examination, gonioscopy, fundus examination with various lenses, indirect ophthalmoscopy
    b. Transillumination
    c. Colour photography
    d. Optical coherence tomography
    e. Autofluorescence
    f. Angiography (indocyanine green and fluorescein) and Angio-OCT
    g. Ultrasonography (A and B scan)
    h. Magnetic resonance imaging
    i. Computerised tomography
    j. Positron emission tomography
    k. Biopsy
        I. Aspiration
        II. Incisional
        III. Excisional
        IV. Impression cytology
- Systemic investigation according to ocular tumour diagnosis
    a) History
    b) Clinical examination
    c) Haematology and biochemistry
    d) Radiography
    e) Ultrasonography
    f) Computerised tomography

g) Magnetic resonance imaging
h) Genetic testing

Clinical knowledge of diagnosis, aetiology and pathology:

Following pathological conditions:

a. Non-neoplastic tumours
    i. Hamartoma
    ii. Choristoma
    iii. Granuloma
    iv. Cyst
    v. Hyperplasia
    vi. Metaplasia
b. Neoplastic tumours
    i. Benign
    ii. Malignant
        1.1. Proliferation
        2.1. Invasion
        3.1. Seeding
        4.1. Metastasis
    iii. Iatrogenic disease
        1.1. Radiation
        2.1. Pharmacology
        3.1. Surgery
        4.1. Phototherapy

Pathological techniques, such as:

a. Fixatives
b. Immunohistochemistry
c. Flow cytometry
d. Molecular pathology (e.g., Polymerase chain reaction)
e. Fine Needle Aspiration Biopsy
f. Frozen sections

Genetic abnormalities and techniques:

a. Germinal mutations relevant to oncology
b. Somatic mutations in tumours
c. Genetic techniques
    i. Karyotyping
    ii. Polymerase chain reaction
    iii. Fluorescence in situ hybridisation
    iv. Multiplex ligation-dependent probe amplification
    v. Gene expression profiling
    vi. Comparative genomic hybridisation
    vii. Other

Symptoms and clinical manifestations indicating the presence of an ocular tumour (e.g., leukocoria, sentinel vessels).

Following clinical diagnoses and pathological and genetic aspects of malignant tumours:

Conjunctiva Neoplasia

Squamous lesions
Melanocytic lesions
Lymphocytic Lesions
Granular lesions

Scleral

Fibrous Histiocytoma
Nodular fasciitis

Vitreous

Intraocular lymphoma

Retina and Retinal Pigment Epithelium

Retinoblastoma
Retinocytoma
Medulloepithelioma
Fuchs adenoma
Combined hamartoma of the retina and RPE
Adenomas and Adenocarcinomas of the RPE

Uveal tract

Neoplasia iris, choroid and Ciliary body
Metastatic Tumours

Eyelids

Epithermal neoplasms
Dermal neoplasms
Appendage neoplasms
Melanocytic neoplasms

Orbit

Lacrimal sac neoplasia
Lacrimal gland neoplasia
Lymphoproliferative lesions
Soft tissue tumours
Vascular tumours
Tumours with Fibrous Differentiation
Tumours with Muscle differentiation
Nerve Sheath tumours
Adipose tumours
Bony lesions of the Orbit
Metastatic tumours

Optic nerve

Melanocytoma
Glioma
meningioma

- Systemic features of ocular tumours and how these features are detected.

Differential diagnosis (DD) for each of the ocular tumours:

DD for pigmented lesions in Ocular fundus.

Choroidal naevus
Choroidal melanoma
Atypical disciform scar associated with age-related macular degeneration
Suprachoroidal haemorrhage
RPE hyperplasia
Congenital hypertrophy of the retinal pigment epithelium
Choroidal hemangioma with RPE hyperpigmentation
Melanocytoma
Metastatic carcinoma with RPE hyperpigmentation
Choroidal osteoma

DD Features of iris Nodules

Brushfield spots
Epithelial invasion
Foreign body retained
Fungal endophthalmitis
Iridocyclitis
Iris freckle
Iris naevus
Iris naevus syndrome
Iris pigmented epithelial cysts
Iris pigmented epithelial proliferation
Juvenile xanthogranuloma
Leiomyoma
Leukaemia
Lisch nodules
Melanocytosis
Melanoma
Metastatic carcinoma
Retinoblastoma

DD Amelanotic choroidal mass

Amelanotic melanoma
Choroidal metastasis
Choroidal hemangioma
Choroidal osteoma
Sclerochoroidal calcification
AMD
Choroidal detachment
Posterior scleritis
Chorioretinal granuloma
Neurilemoma
Leiomyoma

DD of Retinoblastoma

Persistent Foetal Vasculature
Retinopathy of prematurity
Posterior Cataract
Coloboma of Choroid or Optic disc
Uveitis
Toxocara

Congenital retinal fold
Coats disease
Organising Vitreous haemorrhage
Retinal dysplasia

- Epidemiology of the more common tumours (e.g., melanoma and retinoblastoma, angiomatous tumours).
- Pathological conditions, such as:
  a. Nonneoplastic tumours (e.g., hamartomas)
  b. Neoplastic tumours
     i. Benign (e.g., naevus, hemangiomas: Choroidal Hemangiomas, Retinal Angiomas Arteriovenous malformation)
     ii. Malignant (e.g., melanoma, carcinoma, metastasis)
  c. Traumatic lesions (e.g., implantation cysts, haemorrhages)
  d. Degenerative lesions (e.g., disciforms, sclerochoroidal calcification)
  e. Idiopathic disease (e.g., juvenile xanthogranuloma, vasoproliferative tumour)
  f. Paraneoplastic disease (e.g., Bilateral diffuse uveal melanocytic proliferation)
  g. Iatrogenic disease (e.g., radiation-induced disease)

- Ocular Involvement in Systemic Malignancies
  Secondary tumours of the eye: Metastatic carcinoma
  Lymphomatous Tumours: Primary Intraocular Lymphoma
  Ocular manifestations of Leukaemia

- Genetic abnormalities and techniques:
  - Germinal and somatic mutations relevant to oncology (e.g., retinoblastoma)
  - Important genetic techniques (e.g., fluorescence in situ hybridisation)
- Environmental factors (e.g., conjunctival squamous cell carcinoma)
- Genetic factors (e.g., retinoblastoma)
- Syndromes (e.g., Von Hippel-Lindau disease)
- Malformations (e.g., choroidal osteoma)

- Genetic Counselling mainly for retinoblastoma

- Staging systems for ocular tumours:
  a. TNM Classification of Malignant Tumours cancer staging system
     i. Uveal melanoma
     ii. Retinoblastoma
     iii. Conjunctival melanoma
     iv. Conjunctival carcinoma
     v. Ocular adnexal lymphoma
  b. International retinoblastoma staging system
  c. Reese-Ellsworth staging system for retinoblastoma
  d. Other staging systems (e.g., Collaborative Ocular Melanoma Study)

Pathology of the following:

a. Ocular tumours and pseudotumours
   i. Congenital/developmental
      1.1. Conjunctiva

a. Dermoid
b. Dermolipoma
c. Choristoma (simple and complex)

2.1. Uvea
a. Lisch nodules
b. Stromal iris cyst
c. Lacrimal gland choristoma

3.1. Retina
a. Multiple congenital hypertrophy of the retinal pigment epithelium (CHRPE)
b. Astrocytic hamartoma
c. Hemangioblastoma
d. Cavernous angioma
e. Dominant exudative vitreoretinopathy
f. Norrie disease
g. Incontinentia pigmenti
h. Solitary CHRPE
i. Grouped pigmentation
j. Arteriovenous malformation (racemose angioma)
k. Posterior primary hyperplastic vitreous (PPHV)
l. Glioneuroma

ii. Inflammatory (infectious, non-infectious)

1.1. Conjunctiva
a. Granuloma (e.g., syphilis, sarcoid)

2.1. Uvea
a. Granuloma (e.g., tuberculosis)
b. Uveal effusion
c. Posterior scleritis

3.1. Retina
a. Granuloma (e.g., toxocara)

iii. Neoplastic

1.1. Benign
a. Conjunctiva
i. Naevus
ii. Papilloma
iii. Oncocytoma
iv. Primary acquired melanosis
v. Reactive lymphoid hyperplasia
vi. Other
b. Uvea
i. Naevus/melanocytoma
ii. Hemangioma
iii. Osteoma
iv. Neurilemmoma
v. Neurofibroma
vi. Leiomyoma
vii. Mesectodermal leiomyoma
viii. Reactive lymphoid hyperplasia
ix. Bilateral diffuse uveal melanocytic proliferation
x. Other rare conditions
c. Retina
i. Retinoma/retinocytoma

ii. Adenoma
iii. Fuchs adenoma
iv. Benign medulloepithelioma
v. Other

2.1. Malignant
a. Conjunctiva
i. Melanoma
ii. Squamous cell carcinoma
iii. Sebaceous carcinoma
iv. Kaposi sarcoma
v. Lymphoma
vi. Extraocular tumour spread
vii. Metastasis
viii. Other
b. Uvea
i. Melanoma
ii. Lymphoma
iii. Intraocular tumour spread from conjunctiva
iv. Systemic lymphoma
v. Systemic leukaemia
vi. Metastasis
vii. Other
c. Retina
i. Retinoblastoma
ii. Adenocarcinoma
iii. Malignant medulloepithelioma
iv. Lymphoma
v. Leukaemia
vi. Metastasis
vii. Other

iv. Traumatic
1.1. Conjunctiva
a. Implantation cyst
b. Foreign body granuloma
c. Pyogenic granuloma
2.1. Uvea
a. Implantation cyst
b. Choroidal haemorrhage
c. Miotic cyst
3.1. Retina
a. Retinopathy of prematurity
b. Retinal detachment
c. Massive reactive gliosis

v. Degenerative
1.1. Conjunctiva
a. Lacrimal retention cyst
2.1. Uvea
a. Disciform lesion
b. Sclerochoroidal calcification
c. Vortex vein ampulla
3.1. Retina

a. Vasoproliferative tumour

vi. Idiopathic
   1.1. Conjunctiva
      a. Lymphangiectatic cyst
   2.1. Uvea
      a. Juvenile xanthogranuloma
   3.1. Retina
      a. Coats' disease
      b. Combined hamartoma of retina and retinal pigment epithelium
      c. Iris cyst
      d. Ciliary epithelial cyst

vii. Paraneoplastic disease
   1.1. Bilateral diffuse uveal melanocytic proliferation
   2.1. Carcinoma-associated retinopathy
   3.1. Melanoma-associated retinopathy
   4.1. Other

Clinical knowledge of management and therapy:

- Basic management principles of ocular tumours.
- Management options for ocular tumours with indications and contraindications for each form of management.
- Therapeutic modalities and their effects are relevant to ocular tumours:
   a. Radiotherapy (e.g., brachytherapy, external beam radiotherapy, proton beam)
   b. Chemotherapy (e.g., topical, intraocular, systemic)
   c. Phototherapy (e.g., photocoagulation, photodynamic therapy)
   d. Cryotherapy (e.g., liquid nitrogen, carbon dioxide)
   e. Surgical resection (e.g., local resection, enucleation)

- Complications of ocular therapy and their management.
- Basic histopathology of tumours, including immunohistochemistry.
- Prognosis of the different types of ocular tumour and prognostic factors.
- Methods, risks, and benefits of tumour biopsy.
- Therapeutic modalities and their effects are relevant to ocular tumours:
   a. Observation
   b. Photoablation and Hyperthermia (TTT)
   c. Brachytherapy – radioactive plaques (e.g., iodine, ruthenium)
   d. External beam Radiation
   e. Charged-particle radiation (protons and helium ions)
   f. Biological effects
   g. Cryotherapy
   h. Surgical resection
   i. Chemotherapy
   j. Immunotherapy
   k. Exenteration

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