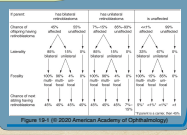
4.19.1. Retinoblastoma (I)

Genetic counseling

- 13q14 — long arm of chromosome 13 locus 14 — RB1 tumor suppressor gene
- mutation of both copies of RB1 gene is needed for tumor formation
- 98% germline — bilateral RB
- germline mutation — 5% familial
- present at an earlier age — 15% of unilateral cases have germline mutation
- 60% unilateral
  - no germline mutation
  - new germline mutation — 30% multiple/bilateral
- 95% sporadic
- 50% chance of inheriting
- 90% chance of penetrance
- 45% — chance of RB in children of RB survivor with hereditary RB
- genetic testing
  - gene sequencing via quantitative PCR
  - karyotyping
  - fluorescent in situ hybridization
  - multiplex ligation-dependent probe amplification
  - RNA analysis
  - 95% chance of finding a new mutation
- 45% bilateral (germline) RB survivor — 15% chance of being germline
- 7% unilateral RB survivor
- <5% normal parents of a child with bilateral RB
- 45% normal parents of a2 siblings with RB
- chance of having an affected child for



Demographics

- most common primary intraocular malignant tumor of childhood
- second most common primary intraocular malignant tumor in all age groups
- 3rd most common intraocular cancer overall after melanoma and metastasis
- incidence = 1/14,000-1/20,000 — 250-300 new cases in US/year
- M=F
- R eye = L eye
- no racial predilection
- 90% <3 years of age
- 30-40% bilateral
- age at diagnosis
  - (+) family history — 4 months
  - bilateral disease — 12 months
  - unilateral disease — 24 months
- geographic variation
  - highest incidence in — Africa, India
  - Mexico-US
  - recent increased incidence in Central America

presenting signs/symptoms

- 60%
- leukocoria

Figure 19-2 (© 2020 American Academy of Ophthalmology)

- strabismus — 20%
- ocular inflammation — 5%
- iris heterochromia
- spontaneous hyphema/hypopyon
- orbital inflammation/cellulitis

clinical appearance

- RB is a clinical diagnosis
- translucent gray-white intraretinal tumor

Figure 19-4 (© 2020 American Academy of Ophthalmology)

- fed & drained by dilated tortuous retinal vessels

Figure 19-3 (© 2020 American Academy of Ophthalmology)

- calcification — chalky white appearance

Figure 19-5 (© 2020 American Academy of Ophthalmology)

- exophytic — serous retinal detachment

Figure 19-6 (© 2020 American Academy of Ophthalmology)

- subretinal seeds
- growth pattern
  - may enter anterior chamber
    - iris nodules
    - pseudo-hypopyon

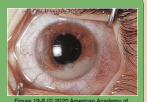


Figure 19-8 (© 2020 American Academy of Ophthalmology)

    - secondary glaucoma
    - rubeosis iridis
    - 50%
  - endophytic — vitreous seeds

Figure 19-7 (© 2020 American Academy of Ophthalmology)

- diffuse infiltrating RB
  - later age (>5 years)
  - unilateral
  - dense vitreous cells
  - misdiagnosed as intermediate uveitis

Differential diagnosis

Persistent fetal vasculature (PFV)

- recognized within days/weeks of birth
- 2/3 unilateral
- microphthalmos
- shallow/flat AC
- hypoplastic iris with prominent vessels
- inward drawing of ciliary processes — retrolenticular fibrovascular mass
- attached to posterior lens capsule — vascular stalk arising from optic nerve head
- closed funnel retinal detachment
- short axial length
- +- calcification
- in selected cases — combined lensectomy & vitrectomy — treatment

Coats disease

- 1st decade
- M>F
- unilateral
- yellow exudation
- no distinct mass
- exudative retinal detachment
- neovascular glaucoma
- no retinal tumor — ultrasonography
- cholesterol convection in subretinal fluid
- telangiectatic vessels — fluorescein angiography
- laser photocoagulation
- cryotherapy — treatment
- +- subretinal fluid drainage

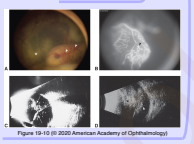


Figure 19-10 (© 2020 American Academy of Ophthalmology)

Ocular toxocariasis

- older children
- soil ingestion
- exposure to puppies — predisposing factors
- posterior granuloma
- peripheral granuloma
- uveitis — clinical
- exudative RD
- cataract
- no calcium — ultrasonography

Astrocytoma/Astrocytic hamartoma

- small smooth white glistening tumor
- larger
- calcified — +- mulberry appearance
- located in the nerve fiber layer
- giant drusen — optic disc astrocytoma
- single or multiple
- unilateral or bilateral
- clinical

Figure 19-11 (© 2020 American Academy of Ophthalmology)

- most common — isolated
- tuberous sclerosis — predisposing conditions
- neurofibromatosis

Medulloepithelioma

- derived from inner layer of optic cup (medullary epithelium)
- benign & malignant forms
- also in adults — children aged 4-12 years
- most common — ciliary body
- retina — arises from
- optic disc
- variably pigmented
- large cysts
- iris heterochromia — neovascular glaucoma
- +- erode into the anterior chamber
- observation
- enucleation
- iodine 125 plaque radiotherapy — treatment
- specifically avoided — surgical resection
- metastasis is rare

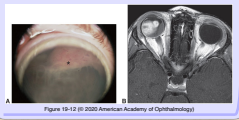


Figure 19-12 (© 2020 American Academy of Ophthalmology)

Diagnostic evaluation

- examination under anesthesia needed in all patients
  - IOP
  - corneal diameter
  - location of all tumors should be documented
- examination of parents and siblings
- complete history & physical examination by pediatric oncologist
- systemic metastatic evaluation
  - lumbar puncture
  - bone marrow aspiration
  - optic nerve invasion — extension into subarachnoid space
  - orbital invasion
    - preceded by massive choroidal invasion
    - proptosis

Figure 19-9 (© 2020 American Academy of Ophthalmology)

  - anterior chamber/trabecular meshwork invasion
  - lymphatic spread — preauricular lymph nodes, cervical lymph nodes
  - metastasis sites
    - skull bones
    - distal bones
    - brain
    - spinal cord
    - lymph nodes
    - abdominal viscera
  - indicated if
    - neurologic abnormalities
    - extraocular extension — optic nerve invasion — lumbar puncture
- imaging
  - ultrasonography — calcification
  - CT scan
    - calcification
    - potentially harmful radiation exposure
  - preferred diagnostic modality
  - MRI
    - optic nerve
    - better soft tissue resolution — orbit

Ophthalmology Mind Maps/Arman Mashayekhi, MD