Retinoblastoma

- Retinoblastoma is an intraocular malignancy with primitive neuroendocrine origins that primarily affects young children.

- Commonest age presentation - 18 months (usually within 5 yrs)
- Transmission can be

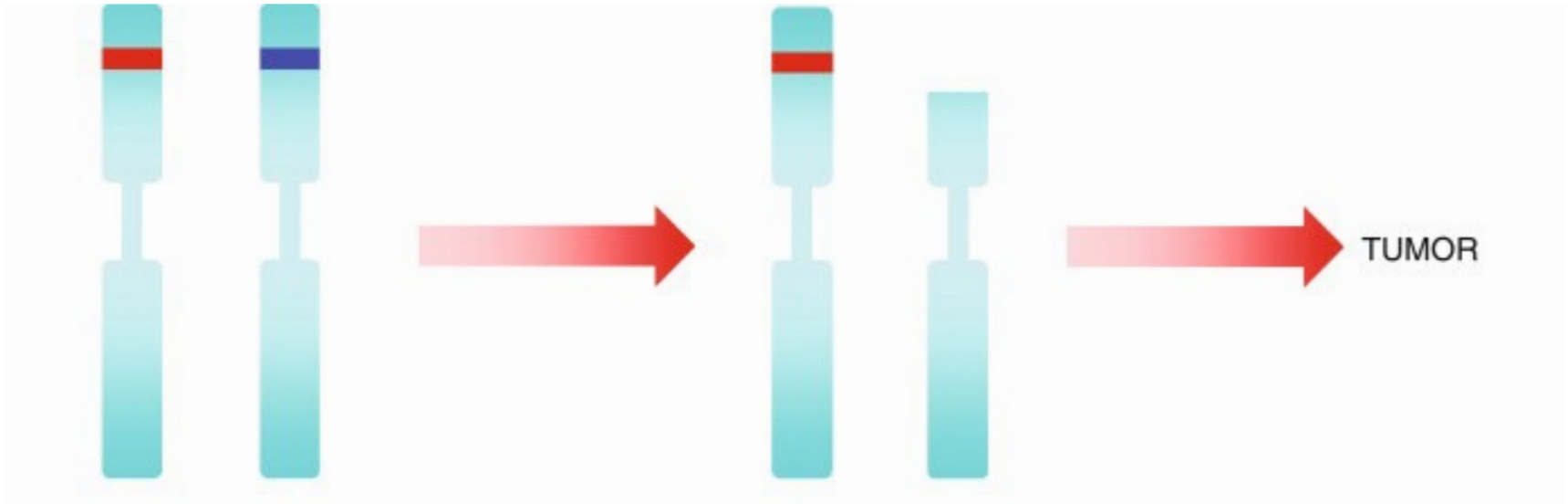
(a) Non-hereditary (60%)

(b) Hereditary (40%) —— Familial (7-10%)
                        Non-familial (30-33%)

- Unilateral (70%)
  Bilateral (30%)

Genetics:

- RB-1 gene (It is a tumor suppressor gene located in 13q14)
- Follows Knudson's 2 hit hypothesis.

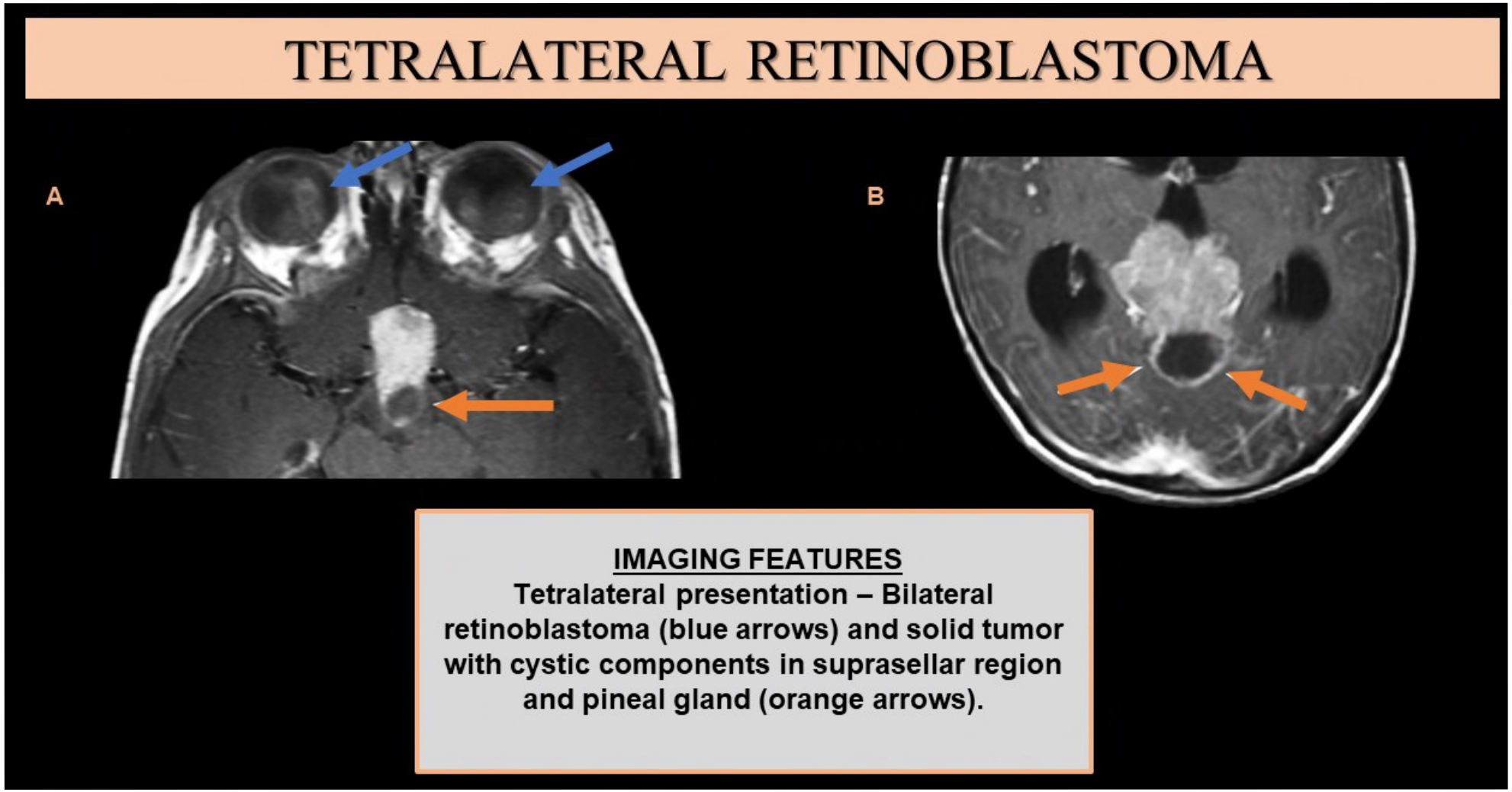


First 'hit' due to a germline mutation. Red line represents germline AIP mutation, blue line represents normal AIP allele

Second 'hit' due to a deletion in the normal AIP allele. Tumor tissue shows loss of heterozygocity around the AIP area

Gene and protein expression of the mutant allele can be detected in the tumor tissue depending on the size and the detection methoidd. Second 'hit' due to a deletion in the normal AIP allele. Tumor tissue shows loss of heterozygocity around the AIP area

- Most common associated malignancy = PNET
  (Primitive neuro endocrine tumor) (Pinealoblastoma)
- B/L retinoblastoma + Pinealoblastoma = Trilateral Retinoblastoma.



Clinical Features:

(i) Leucocoria (Amaurotic cat's eye pupil)
(White eye reflex) (most common sign)

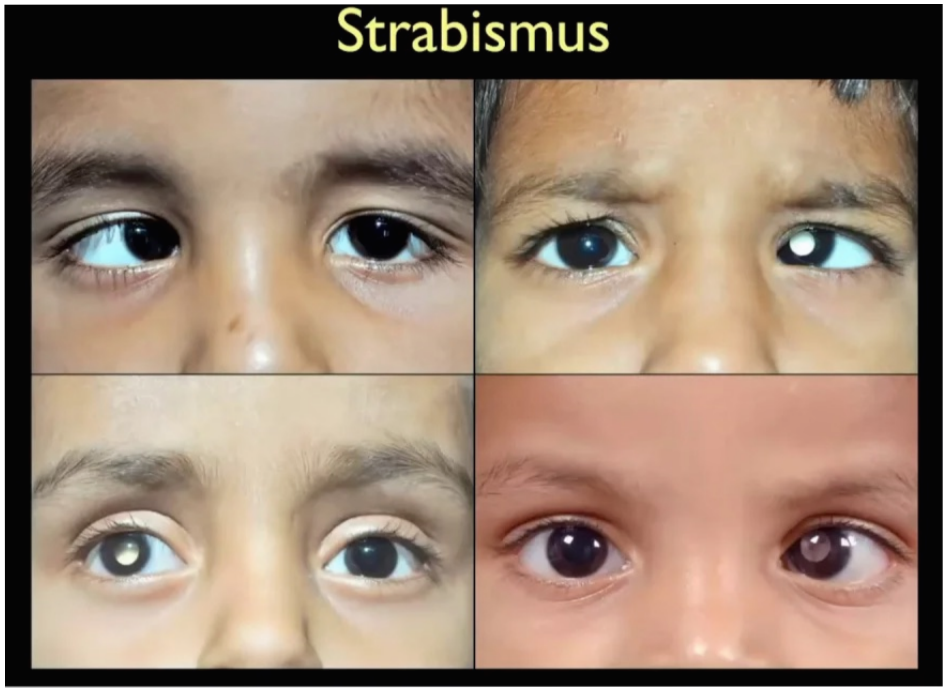
* M/c cause of Unilateral leukocoria = Retinoblastoma
Bilateral leukocoria = Cataract.

(ii) Strabismus (2nd m/c)

(iii) Neovascular glaucoma (3rd m/c)

(iv) Red painful eye

(v) Pseudohypopyon.

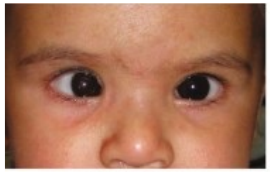


(vi) Loss of Vision

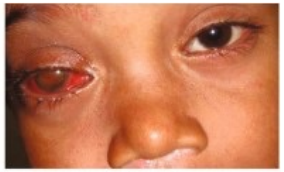
(vii) Heterochromia

(viii) Hyphema

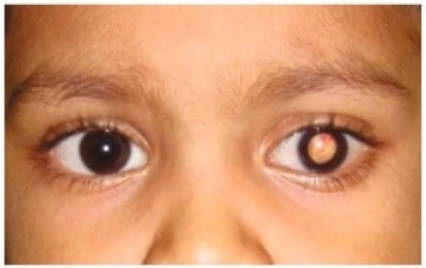
(ix) Uniocular mydriasis



Strabismus

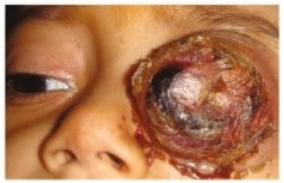


Red Eye



Leucocoria

Shrunken Eyeball

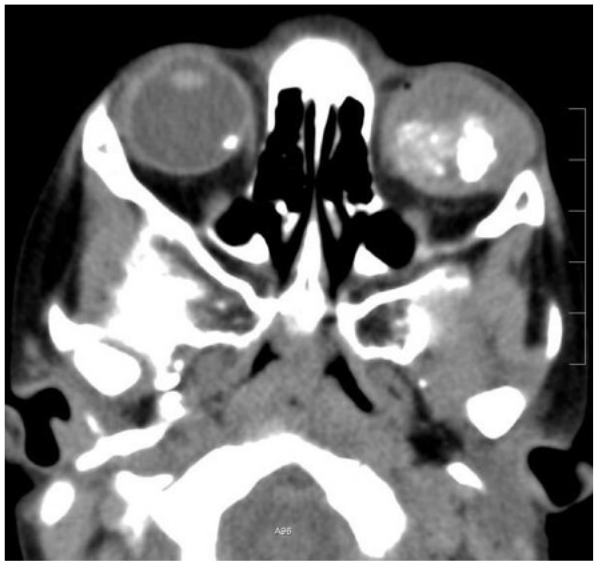


Orbital mass

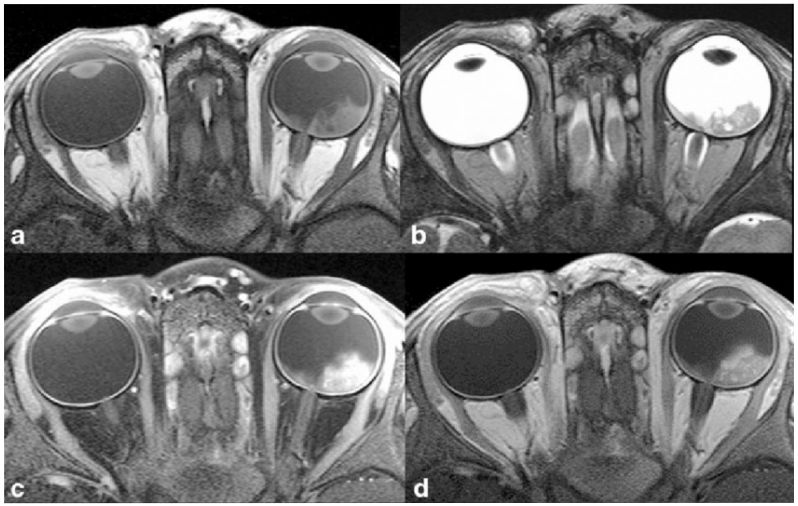
Diagnosis:

(i) In India (mainly) = X-Ray or CT scan.

(ii) CT: Intraocular calcification



(iii) MRI (Investigation of Choice)

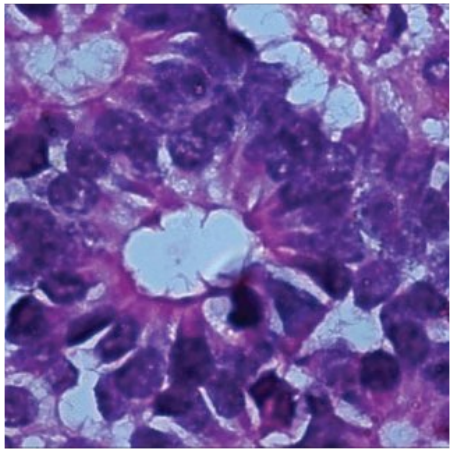


Histopathology Features:

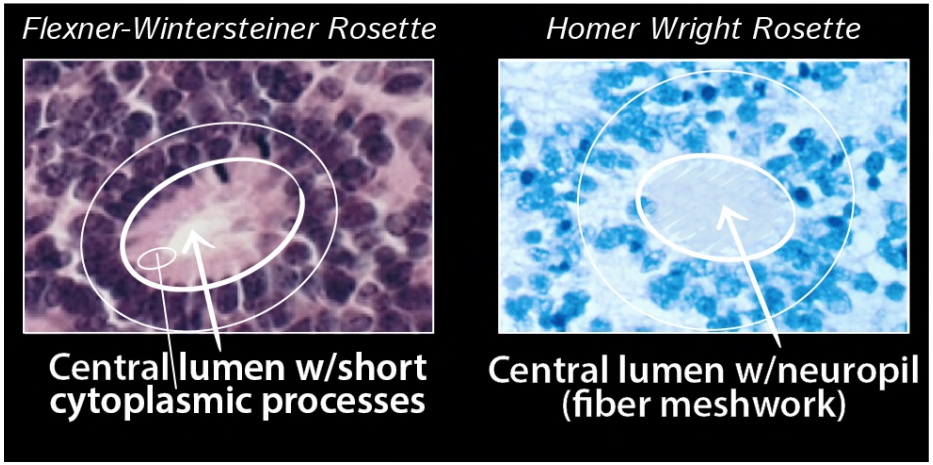
(i) Flexner-Wintersteiner rosettes (Hallmark)

(ii) Homer wright rosettes (Pseudo-rosettes)

(iii) Fleurettes.



(Flexner Wintersteiner) rosette



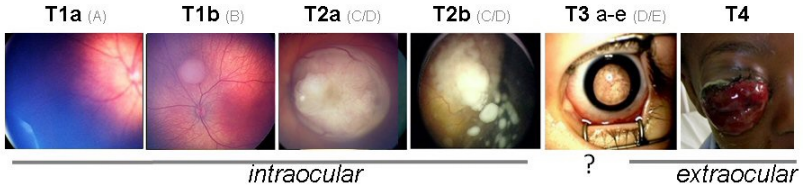
Staging:

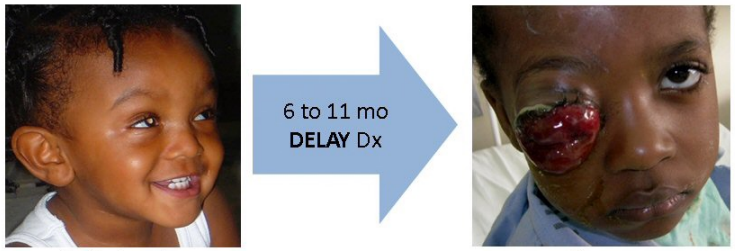
RB-Group	Sub group	Reference	Features
A	Very low risk	Small tumor	• ≤ 3mm in size and • > 1.5mm from the disc • >3mm from the foveola
B	Low risk	Eyes with no vitreous or subretinal seeding and discrete retinal tumor of any size or location	• Tumors not in group A • No vitreous or subretinal seeding SRF >5 mm from the base of the tumor
C	Moderate Risk	Eyes with only focal vitreous or subretinal seeding and discrete retinal tumors of any size and location	• Seeding local, fine and limited • Treatable with a radioactive plaque • Tumors discrete and of any size and location, • Up to one quadrant of SRF
D	High Risk	Eyes with diffuse vitreous or subretinal seeding and/ or massive, non-discrete endophytic or exophytic disease. Eyes with more extensive seeding than Group C	• Massive and/or diffuse intraocular disseminated disease • More than one quadrant of retinal detachment • Fine greasy vitreous seeding or avascular masses • Subretinal seeding, plaque-like
E	Very high risk	Eyes that have been destroyed anatomically or functionally by the tumor. Eyes with one or more than the following	• Irreversible neovascular glaucoma • Massive intraocular hemorrhage • Aseptic orbital cellulitis • Tumor anterior to anterior vitreous face • Tumor touching the lens • Diffuse infiltrating retinoblastoma • Phthisis or prephthisis

(*SRF= Subretinal fluid)

TNM Staging System for Retinoblastoma

(Comparison with International Intraocular Rb Classification)





North America
Unilateral Dx mean **27** mo
Bilateral Dx mean **15** mo

Kenya
Unilateral Dx mean **36** mo
Bilateral Dx mean **26** mo

Nyamori JM, et al. Br J Ophthalmol. 2012;96:141-3.

Treatment:

(i) Treatment of choice = Enucleation (whole eye with optic nerve) ← in advanced form

(ii) Focal = Cryotherapy (Transscleral cryotherapy
freezes tumor with ice ball)

(iii) Laser photocoagulation (Argon green laser)
↓
Coagulates blood vessels feeding tumor.

(iv) Transpupillary Thermo Therapy (TTT)
(Hyperthermia by infrared radiation) (Temp = 40 to 600°c)

(v) Chemotherapy → Carboplatin
Etoposide
Vincristine

(vi) Radiotherapy (Iodine-125, Cobalt-60, Ruthenium-160)

Causes of Death:

(i) Metastasis to Optic Nerve (within one year)

(ii) Intracranial tumors associated with Rb

(iii) Trilateral Retinoblastoma

(iv) Secondary Tumor = Osteosarcoma of Femur.