Retinoblastoma Look-Alikes
A Diagnostic Challenge

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EGYPTIAN OPHTHALMOLOGICAL SOCIETY

Appreciation

Saleh Almesfer, MD
Leader 1990

Azza Maktabi, MD

All staff who help in management of Retinoblastoma in KKESH

Introduction:

- Retinoblastoma is a rare cancer of the infant retina, comprises 4% of all pediatric cancers.
- **Most common intraocular malignancy in childhood,**
- **Global retinoblastoma incidence (1 in 16,000– 18,000 live births)**
- **Patient survival is >95% in high-income countries, but <30% globally.**

A TRUE SUCSEESFULL STORY

Grossniklaus HE. Retinoblastoma. Fifty years of progress. The LXXI Edward Jackson Memorial Lecture. Am J Ophthalmol. 2014 Nov;158(5):875-91. doi: 10.1016/j.ajo.2014.07.025. Epub 2014 Jul 24. PMID: 25065496; PMCID: PMC4250440.
Dimaras H, Corson TW, Cobrinik D, White A, Zhao J, Munier FL, Abramson DH, Shields CL, Chantada GL, Njuguna F, Gallie BL. Retinoblastoma. Nat Rev Dis Primers. 2015 Aug 27;1:15021. doi: 10.1038/nrdp.2015.21. PMID: 27189421; PMCID: PMC5744255.

RETINOBLASTOMA REGISTRY

Tertiary eye care Hospital Experience (KKESH)

Total number of patients: **1137**

(1983 - April 2025)

Patients

Total number of eyes: **1587**

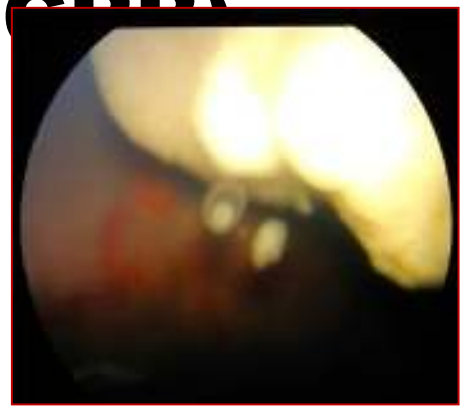
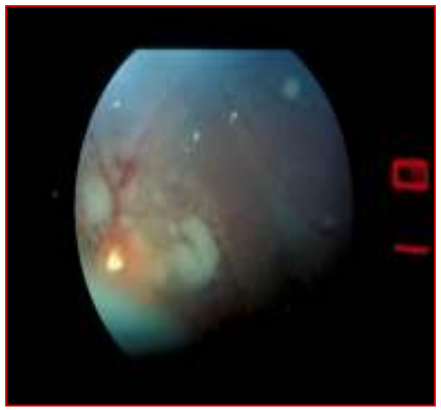
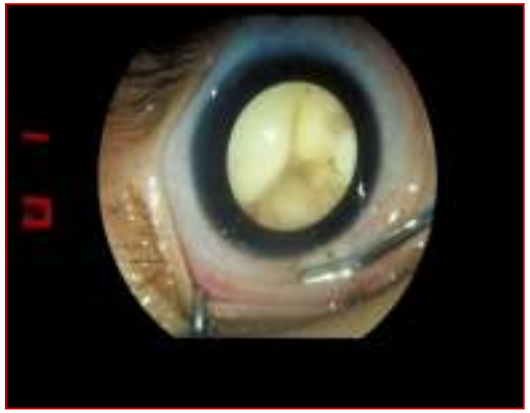
Eyes

Age at Diagnosios

	Mean	Median (month)
Unilateral	30.5	24
Bilateral	19.9	11
Family Hx	10.6	6

INTERNATIONAL CLASSIFICATION Of RETINOBLASTOMA (ICRB)



A	B	C	D	E
1-Small tumors (≥3mm) restricted sites 2- ≥2 DD from the Fovea 3- ≥1 DD from the OD 4-No seeding	1-Large tumors (>3mm) 2-Any locations 3-No seeding 4-RD>5 mm from the tumor base	1-Localized seeding to vitreous/SRF 2-RD >5mm to one quartan RD 3-No snowballs or masses	1-Massive diffuse seeding to vitreous/SRF 2-RD >5mm to total RD 3- Vitreous / SRF snowballs or masses	Unsalvageable No visual potential, Presence of one or more: CB, AS involvement, glaucoma, phthisis changes, Hyphema, cellulites like picture.
Very Low Risk	Low Risk	Moderate Risk	High Risk	Very High Risk
A+B: Tumors Confined to Retina		**C+D: Tumor invade adjacent tissues & spaces**		**Enucleation**

Shields CL, Mashayekhi A, Au AK, Czyz C, Leahey A, Meadows AT, et al. The International classification of retinoblastoma predicts chemoreduction success. Ophthalmology. 2006;113:2276–80. doi: 10.1016/j.ophtha.2006.06.018.

Intraocular tumors in children

- Diagnosing is often difficult
- Medical diagnosis of retinoblastoma
- For **non-functional eyes** with unilateral mass, **enucleation**
- Followed by histopathological examination is often the only way to reach a definitive diagnosis.

Azimi F, Mirshahi R, Naseripour M. Review: New horizons in retinoblastoma treatment: an updated review article. Mol Vis. 2022 Jul 11;28:130-146.
Khandekar RB, et al. Ocular malignant tumors. Review of the Tumor Registry at a tertiary eye hospital in central Saudi Arabia. Saudi Med J. 2014 Apr;35(4):377-84. PMID: 24749135.

If not retinoblastoma then it could be:

- Coats' disease
- Persistant fetal vasculature (PFV, PHPV)
- Endophthalmitis
- Astrocytomas
- Medulloepitheliomas
- Retinal dysplasia
- Glaucoma
- Periorbital cellulitis
- Toxocariasis
- Uveitis
- Intraocular lymphoma
- Juvenile Xanthogranuloma
- Ciliary Body Adenoma
- **Squint**
- others.

Suspect RB , and prove it is not before you diagnose it is any of those

Alghofaili RS, Almesfer SA. Bilateral Retinoblastoma Presenting in an in vitro Fertilization Infant with Retinopathy of Prematurity. Case Rep Ophthalmol. 2021 Apr 30;12(1):306-310. doi: 10.1159/000513181. PMID: 34054475; PMCID: PMC8138227.
AlQahtani GMS, Alkatan HM, AlMesfer S, Elkhamary S, Maktabi AMY. A case of retinoblastoma masquerading as endophthalmitis: Unusual presentation and clinicopathological correlation. Int J Surg Case Rep. 2024 Oct; PMC11424937.

Fine-needle aspiration biopsy (FNAB)

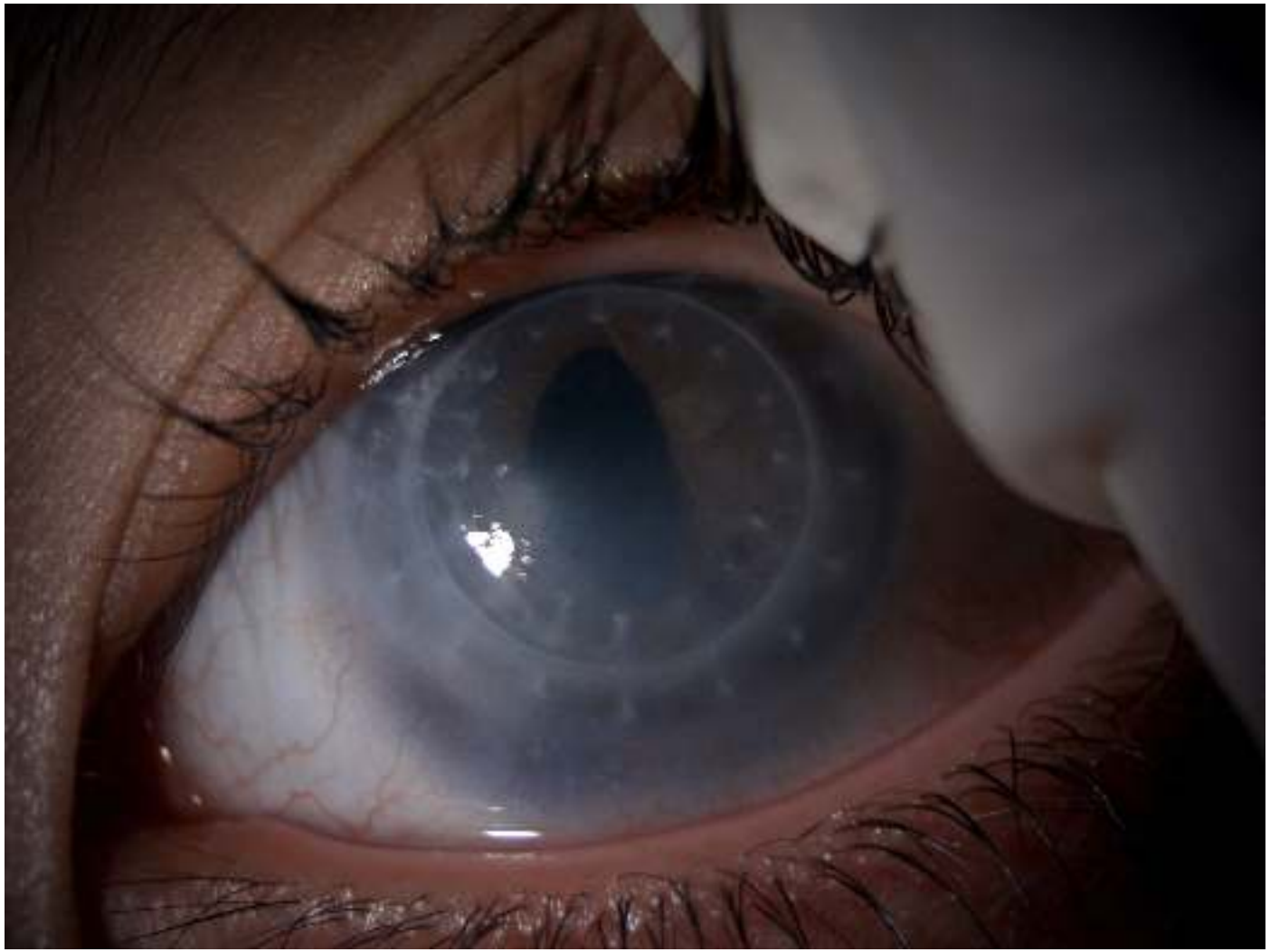
- Biopsy of retinoblastoma is not recommended, as it can induce seeding and extraocular spread along the needle tract.
- Case reports of tumor cell seeding into the biopsy tract.
- Can be done in selective cases in higher centers.

Dimaras H, Corson TW. Retinoblastoma, the visible CNS tumor: A review. J Neurosci Res. 2019 Jan;97(1):29-44. doi: 10.1002/jnr.24213. Epub 2018 Jan 3. PMID: 29314142; PMCID: PMC6034991.

Karcioglu ZA. Fine needle aspiration biopsy (FNAB) for retinoblastoma. Retina. 2002;22(6):707–710. doi: 10.1097/00006982-200212000-00004.

Patient B: Presented to KKESH for graft failure and glaucoma

Right Eye



Left Eye

Patient B:
Came with a report from Hospital X

Presenting Complaints :

4 years old boy presented on 2018 with history of right eye changes since age of 9 months.

Diagnosed as secondary glaucoma due to Uvieits.

Brief History:

-not known to have medical illness,
-ve family history no history of trauma, no preceding viral illness.
no other associated medical or neurological signs.
no mouth or genital ulcers no joints pain or swelings

Patient B: Report

Examination :

Right eye within normal.
left eye showed megalocornea + corneal edema +2.
corneal diameter 11 OD 12 OS
axial length 20.8 and 23.4 mm
OD: cupping: 0.1 od
OS: 0.3 clear vitreous on fundoscopy with limited view.

AC: fluffy like whitish plaques and inferior membrane with iridocorneal adhesion 180 degree inferiorly.
no KPs no AC cells or flare.no catract.

s/p AC wash +tap + injection of TPA 20 microgram OS

Patient B:
Invistigations outside KKESH

SLE antibodies ANA, ANCA
HLA B27 , RF,
TB quantiferone test
TORCH AB were negative.
AC tap sent for HSV & CMV PCR + TB culture +cytology to R/O malignancy or a typical cells
all were negative

all other uveitis investigation and chest Xray all were negative brain MRI was unremarkable

Patient B:

Diagnosis:

Uveitis of unknown origin with secondary glaucoma left eye

Management :

Humera (total 4 injection) and acyclovir injection

Patient B: Went to Europe

Patients managed by
S/P trabeclecctomy OS
S/P PKP OS

Patient B: Summary all outside KKESH

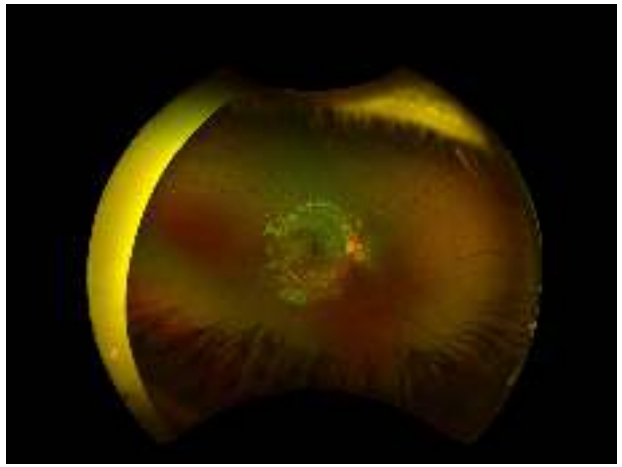
6 years old , Labelled as Uveitis of unknown origin and glaucoma and was following in **other hospitals**

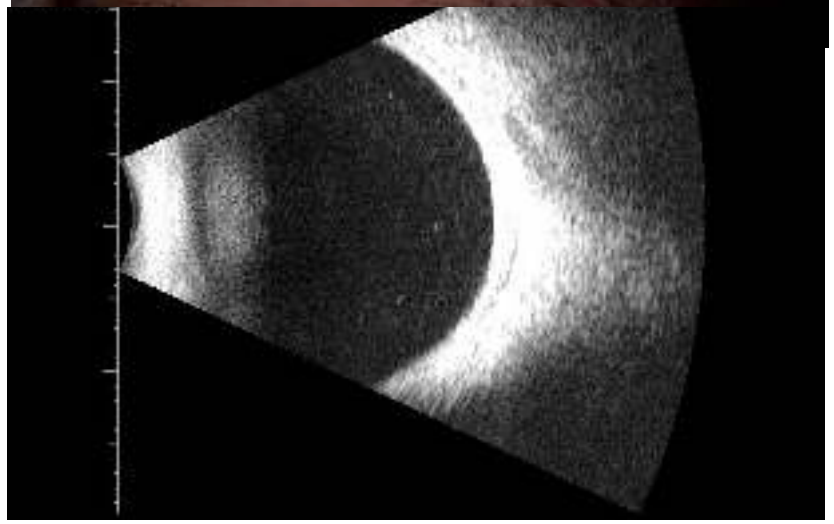
Uveitis Invitations : all negative
AC tap for: HSV , CMV + TB cytology + malignancy or atypical cells: all negative

Rx:
Oral and topical steroid, topical anti glaucoma drops,
Humera (total 4 injection) and Oral Acyclovir
S/p AC wash and tissue plasminogen activator (tPA) in AC
S/P trab OS
S/P PKP OS

Patient B: Presented to KKESH for graft failure and glaucoma

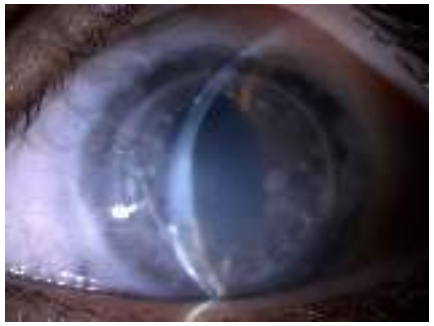
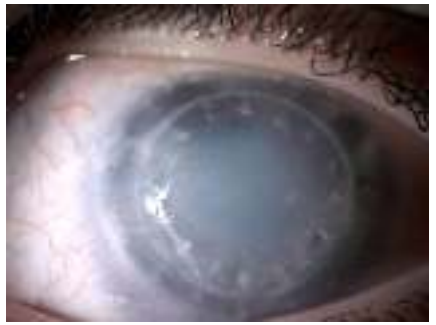
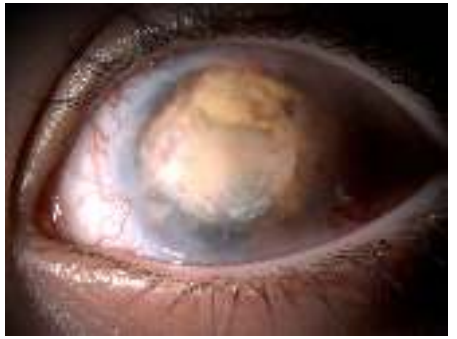
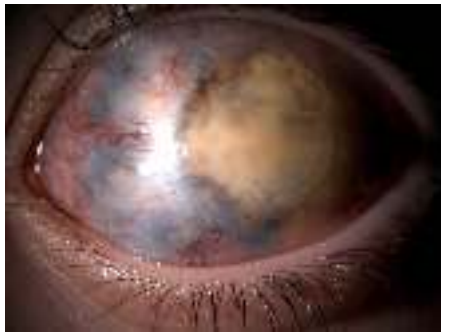
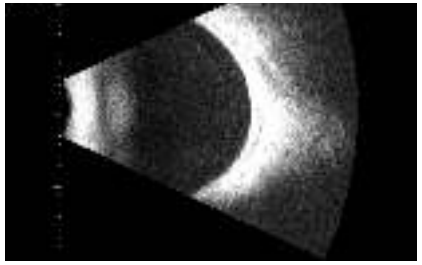
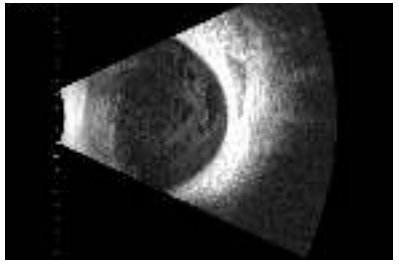
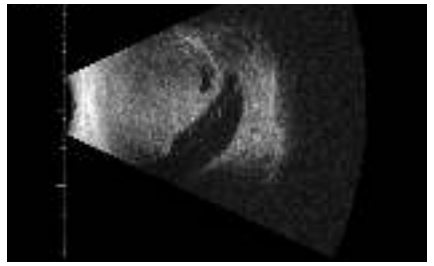
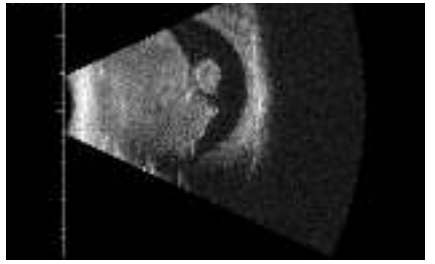
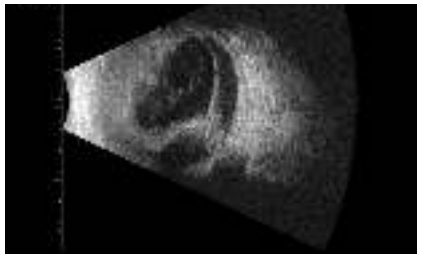
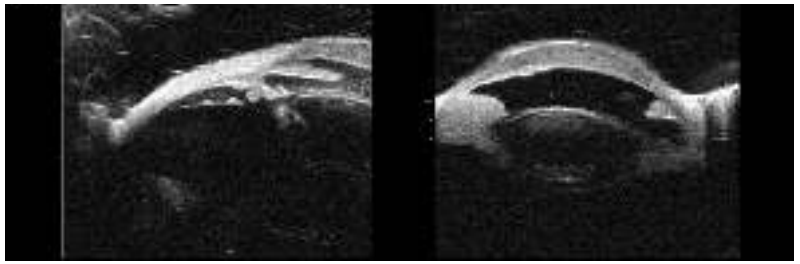
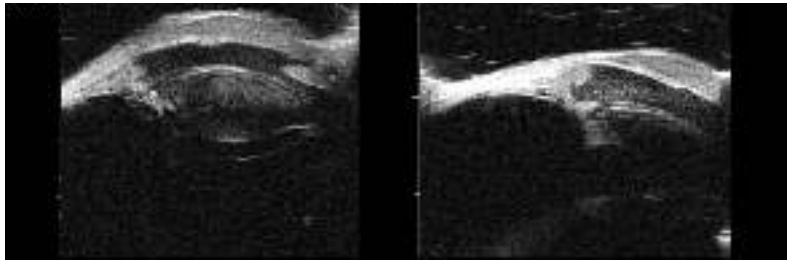
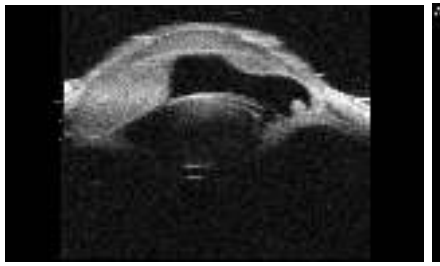
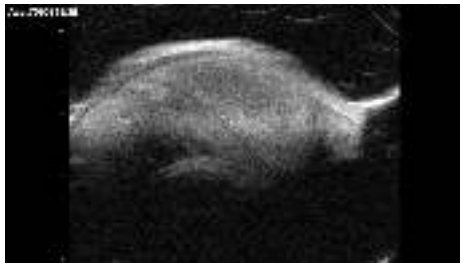
Right Eye





Left Eye

Patient B: on follow ups

What is Really Happening ?

Uveitis uncontrolled, IOP uncontrolled leading to all those changes

RB without a mass in the fundus initially

Presented to ER with open globe

Evisceration was done

RB cells found in histology with MRI showed orbit involvment.

Diffuse infiltrative Retinoblastoma

Table 1. Published cases of diffuse anterior retinoblastoma through 2012.

Article author (Year)	Eye	Age/ Sex	Presenting symptom	Eye exam		US imaging	Diagnosis	Treatment	Retinal involvement under microscopy	Immuno-histochemical stains	Follow-up
				Anterior segment	Posterior segment						
Garner et al. (1987)	OD	7yo/ F	Redness, Blurring of vision	"Severe anterior uveitis with large iris nodules and cells and opacities in the anterior vitreous"	–	–	Biopsy of iris, lens excision	Topical corticosteroids, oral prednisone 5 mg TID, sub-Tenon's injection of methylprednisolone, lens excision, enucleation, orbital radiotherapy, adjuvant chemotherapy	2 foci at extreme periphery of retina, minimal thickening, <1.5 mm in	+NSE, –S100, –GFAP	Recurrent orbital retinoblastoma 8 mos after enucleation; No sign of further recurrence at
					retina		fine needle aspiration biopsy	vincristine	identified		

Conclusions

Diffuse anterior retinoblastoma is an uncommon variant of diffuse infiltrating retinoblastoma that occurs unilaterally in children between the ages of 3 and 9 years. The majority of cases are nonhereditary, however there is one reported case in a child with a germline mutation of the *RB1* gene. Since the tumor can masquerade as a variety of conditions, diffuse anterior retinoblastoma should be considered in all cases of refractory uveitis in children. Fine needle aspiration biopsy should only be performed at highly specialized centers with experienced ophthalmologists and ophthalmic pathologists as a last resort to narrow the differential diagnosis due to the risk of tumor dissemination. Treatment involves enucleation of the involved orbit and in some cases may require external beam radiation or systemic chemotherapy.

Message:

Suspect and r/o RB even if you are not oncologist.

Investations are NOT ture all the time

Have the courage to change the diagnosis

Experts might be wrong sometimes. Challenge their diganosis if needed.

Patient W :

- A 6-year-old girl presented **elsewhere** with gradual decreased vision in the right eye for 5 weeks.
- **Clinical examination:**
  - **VAsc:** OD No light perception , OS 20/20
  - **Slit lamp and fundus examination:**

    OD retrolental floppy **mass** with retinal detachment and pre-retinal infiltration

    OS normal anterior and posterior segment examination.

- A clinical diagnosis of **endophthalmitis OD** was made
  - vitreous tap with intravitreal injection of Cefazolin and Vancomycin was performed.

- Follow up (2 weeks later): No change in vision.
  - Slit lamp examination: OD NVIs, and a complicated cataract.

- **Then patient was referred to KKESH**

Patient W :

Clinical examination:

- **Vasc:** OD light perception, OS 20/20
- **IOP:** OD 30 mmHg , OS 15 mmHg

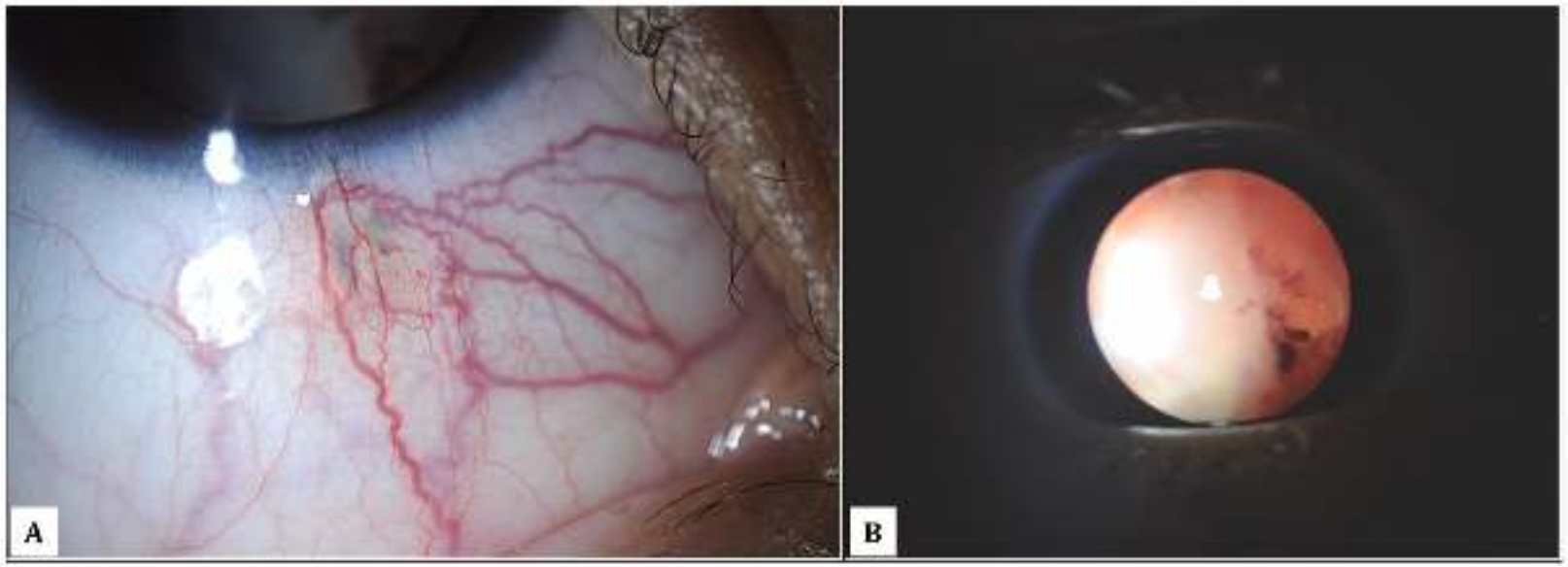


Fig. 3. A: Conjunctival injection inferiorly at the propable site of vitreous tap and intravitreal injection. B: An external photo exhibiting a white mass with hemorrhage seen behind the lens through a dilated pupil.

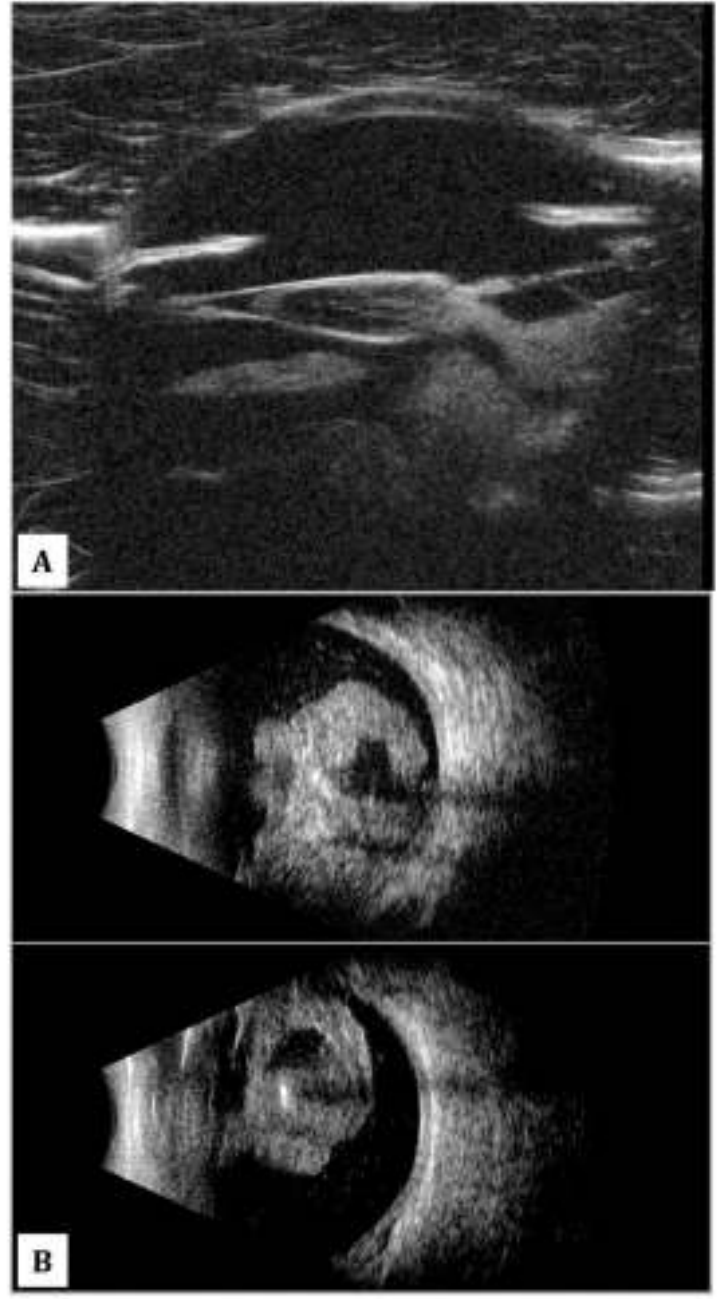
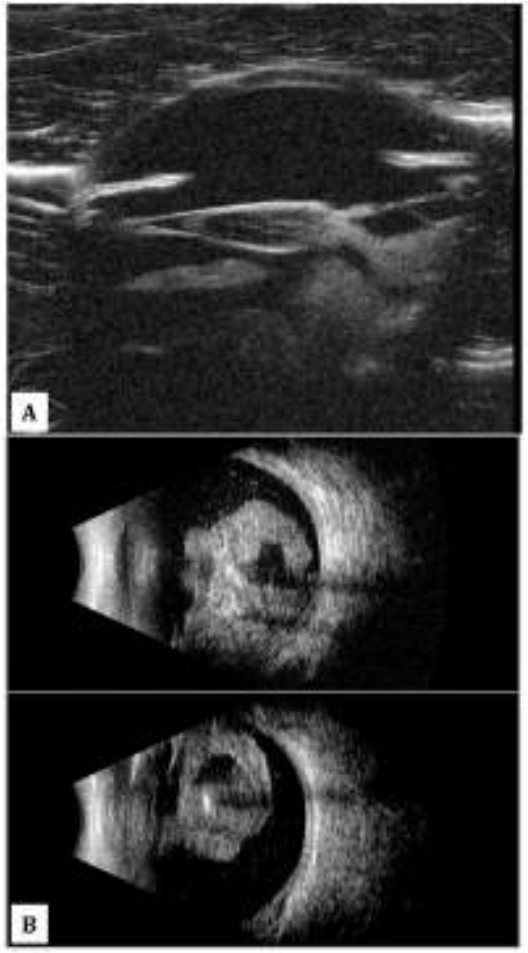


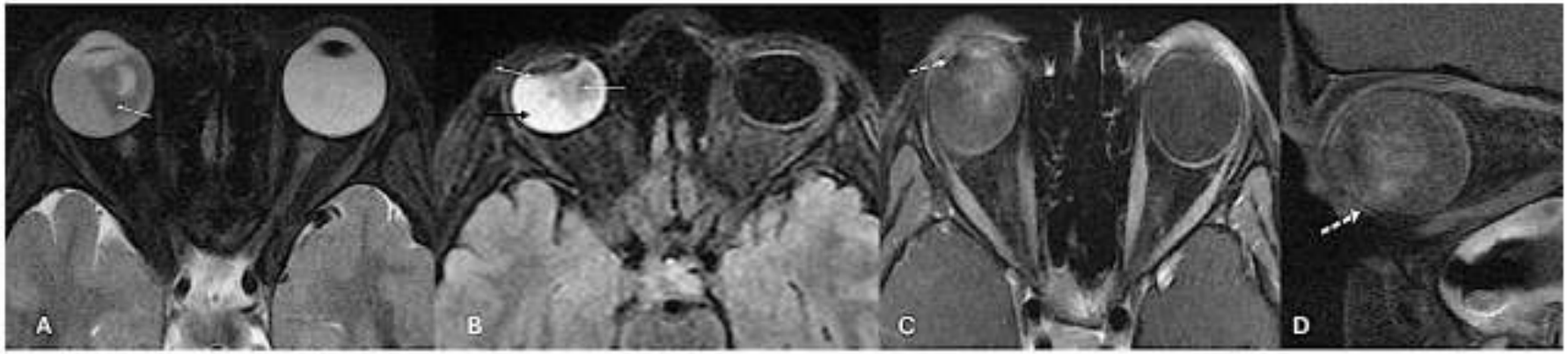
Fig. 1. A: Ultrasound biomicroscopy (UBM) of the right eye demonstrating posterior cavity mass and a ruptured lens. **B:** B-scan of the right eye demonstrating dense vitreous opacities with area of calcification and acoustic shadowing.

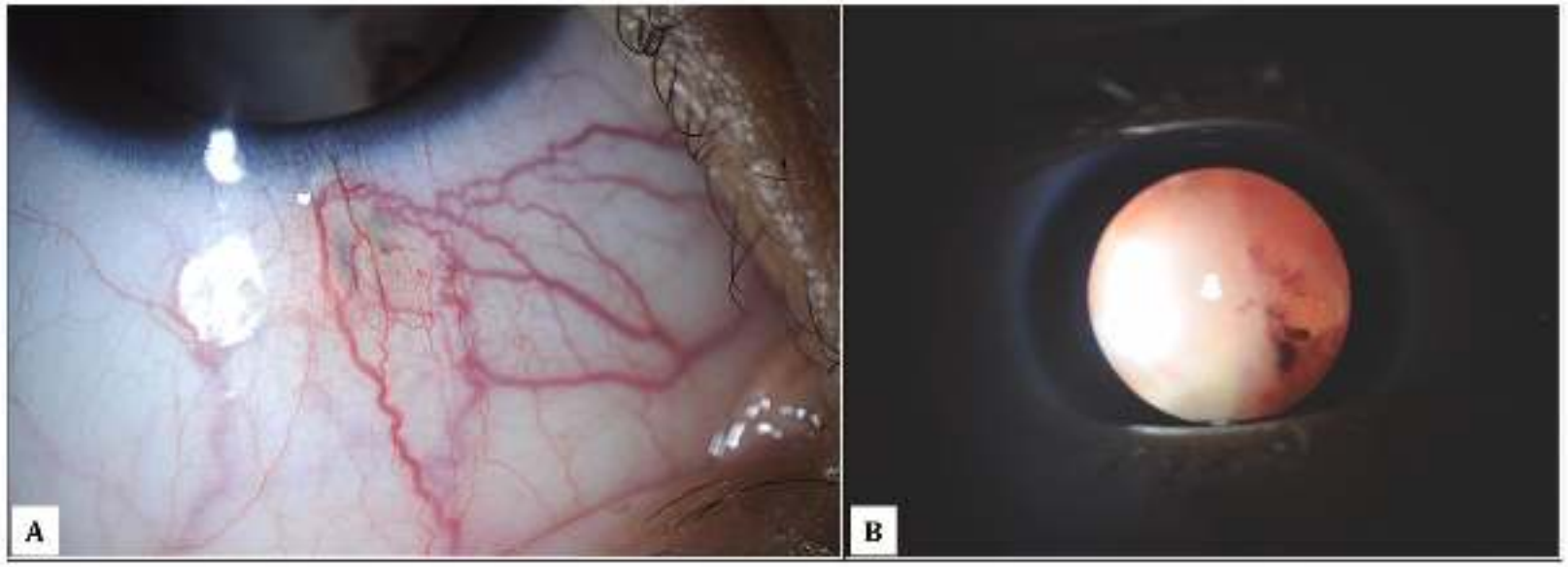
What's the most likely diagnosis?

- Partially treated Endophthalmitis , that needs PPV !
- RB !

Patient W :







Patient W :

Enucleation was done

Confirmed the diagnosis of Retinoblastoma

Histopathology:

Iris and anterior chamber angle invasion by undifferentiated retinoblastoma

Ruptured cataractous lens with leaking cortical substances

The posterior cavity showed vitreous tumor seeding, epiretinal fibrovascular membrane, and a superficial optic nerve invasion.

No choroidal invasion, and no definite extraocular extension.

Rx:

adjuvant systemic chemotherapy

The patient received 6 cycles of systemic chemotherapy.

Discussion

- Stafford et al: **41 (6.6 %) out of 618** retinoblastoma cases were misdiagnosed and mistreated as ocular inflammation. **Endophthalmitis** being the initial diagnosis **in 14 of them**.
- Kaliki et al: 14 patients were exposed to intraocular surgeries prior to being diagnosed with retinoblastoma[3]
  - The most frequent misdiagnosis was **endophthalmitis** in 4 cases
  - The most common surgery was PPV +/- lensectomy
  - **57% died** over 27 months mean period of follow-ups; due to advanced disease despite multimodal treatment.

- Meel et al: **endophthalmitis** was the most prevalent misdiagnosis in retinoblastoma patients aged more than 6 years

S. Kaliki, S. Taneja, V.A.R. Palkonda, Inadvertent intraocular surgery in children with unsuspected retinoblastoma: a study of 14 cases, Retina 39 (9) (2019)
S.G. Honavar, C.L. Shields, J.A. Shields, H. Demirci, T.J. Naduvilath, Intraocular surgery after treatment of retinoblastoma, Arch. Ophthalmol. 119 (11) (2001 Nov)
A.L. Blitzer, S.A. Schechet, H.A. Shah, et al., Retinoblastoma presenting as pseudohypopyon and preserved visual acuity, Am J Ophthalmol Case Rep. 23 (2021)
W.R. Stafford, M. Yanoff, B.L. Parnell, Retinoblastomas initially misdiagnosed as primary ocular inflammations, Arch. Ophthalmol. 82 (6) (1969) 771–773,
R. Meel, S. Kashyap, S. Bakhshi, M. Singh Bajaj, M. Wadhwani, Retinoblastoma in children older than 6 years of age, Ocul Oncol Pathol. 6 (6) (2020) 395–404,.

Message:

10 % of retinoblastoma cases are older than 5 years.

Anterior segment or vitreous seeding can leading to the misdiagnosis of endophthalmitis.

Intraocular interventions **must be avoided** in these cases. Till you confirm the diagnosis

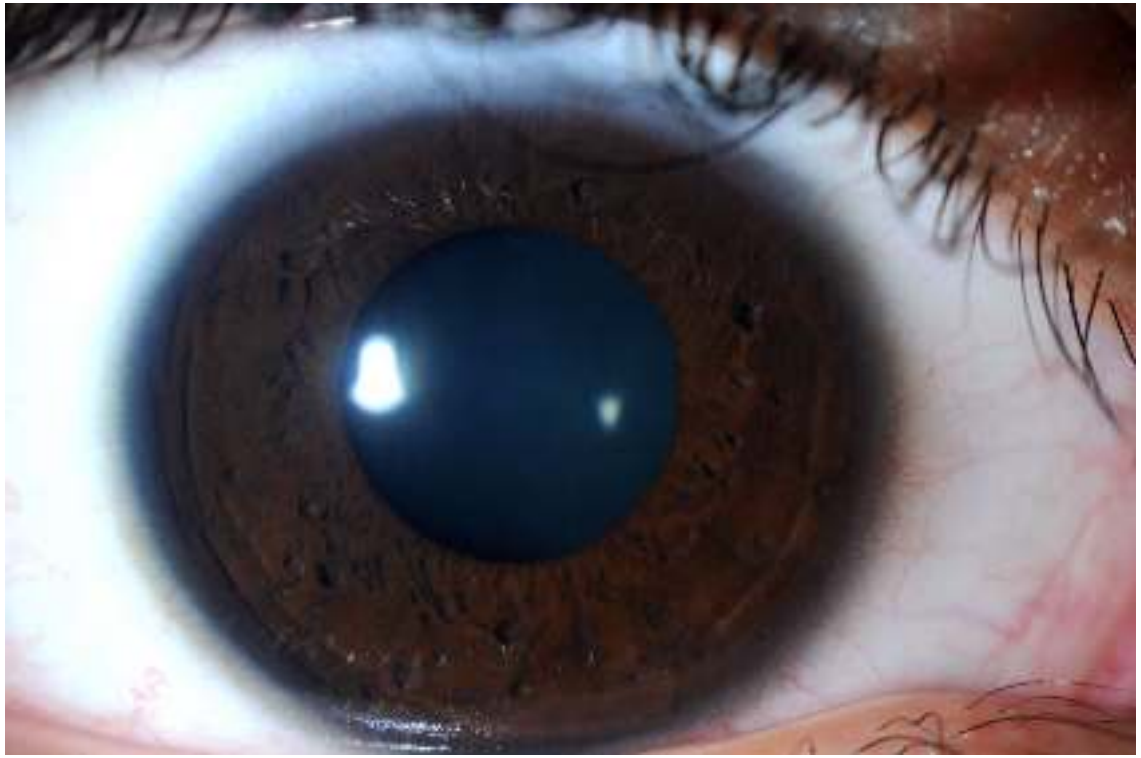
David H. Abramson, Christopher M. Frank, Mark Susman, Mary P. Whalen, Ira J. Dunkel, Norman W. Boyd, Presenting signs of retinoblastoma, J. Pediatr. 132 (3) (1998)
T.W. Pendergrass, S. Davis, Incidence of retinoblastoma in the United States, Arch. Ophthalmol. 98 (1980) 1204–1210.

Patient D:

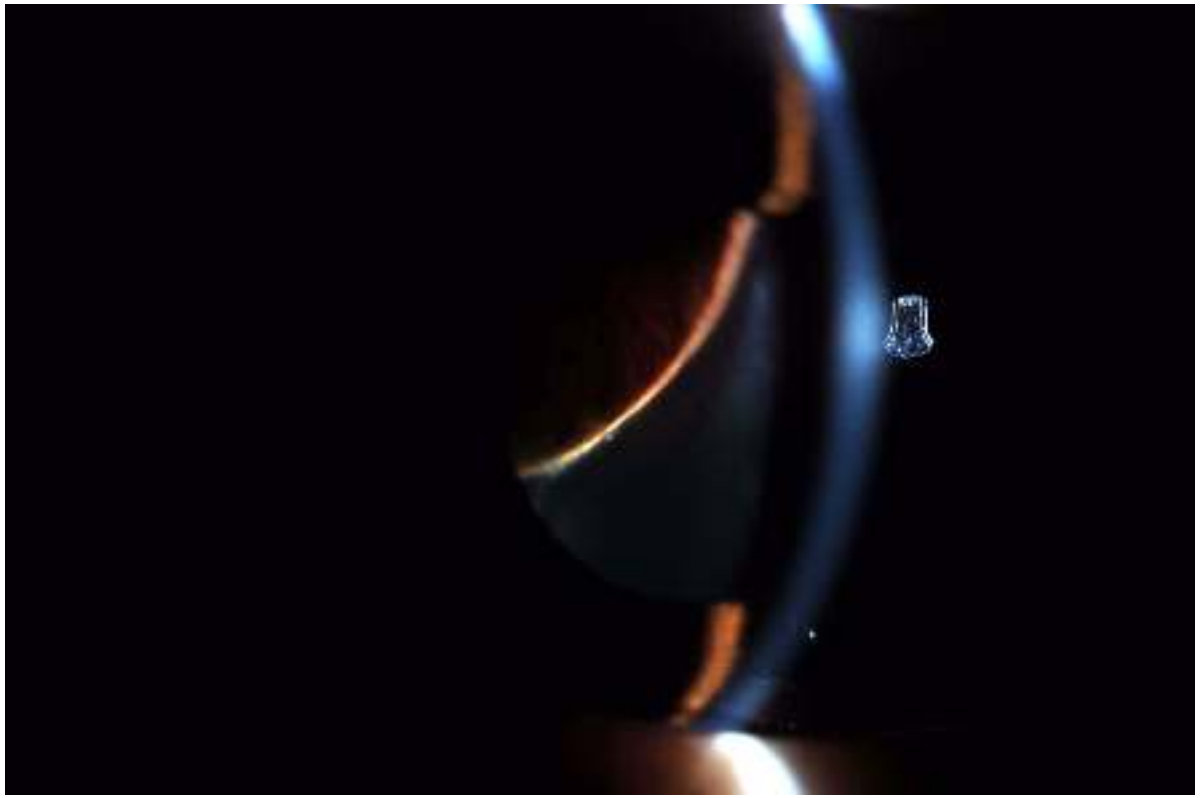
21yrs male c/o gradual decrease of vision OS for one month.

hx of redness before 1/12 , no hx of trauma

VA: 20/20 and LP



Right Eye



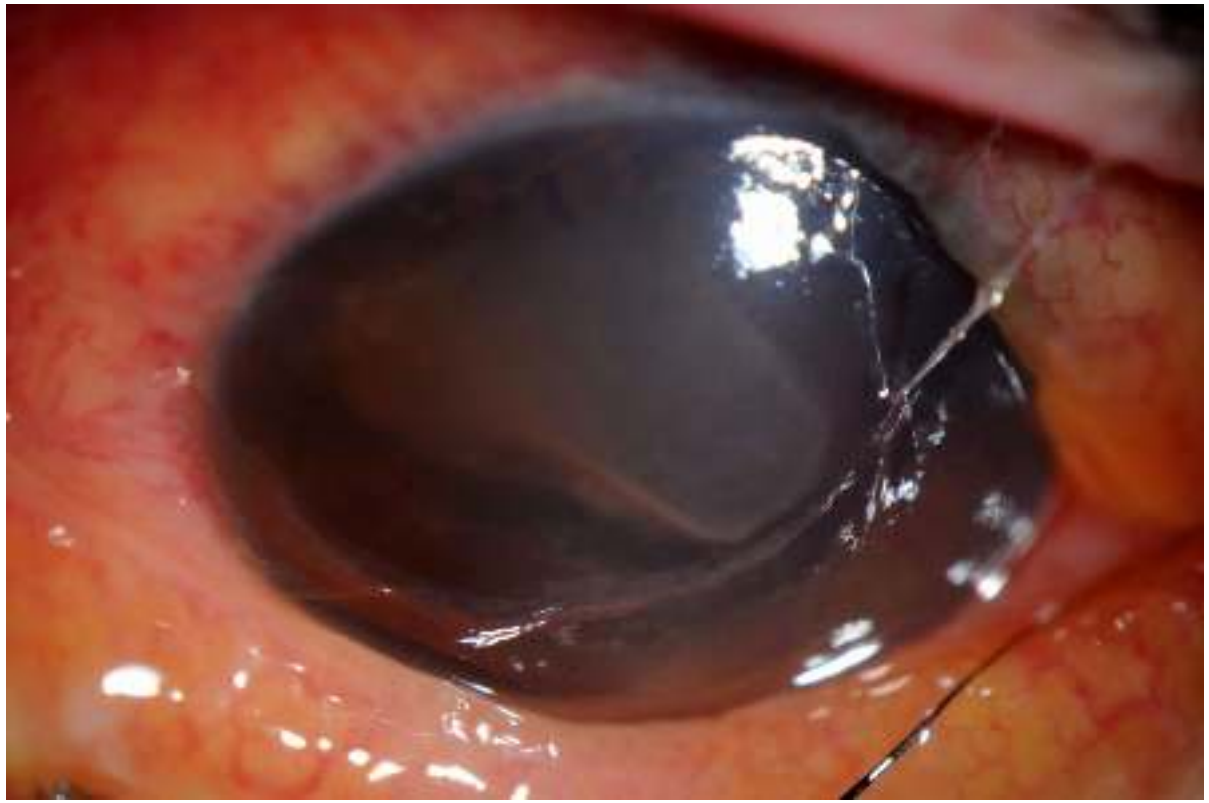
Left Eye

Patient D:

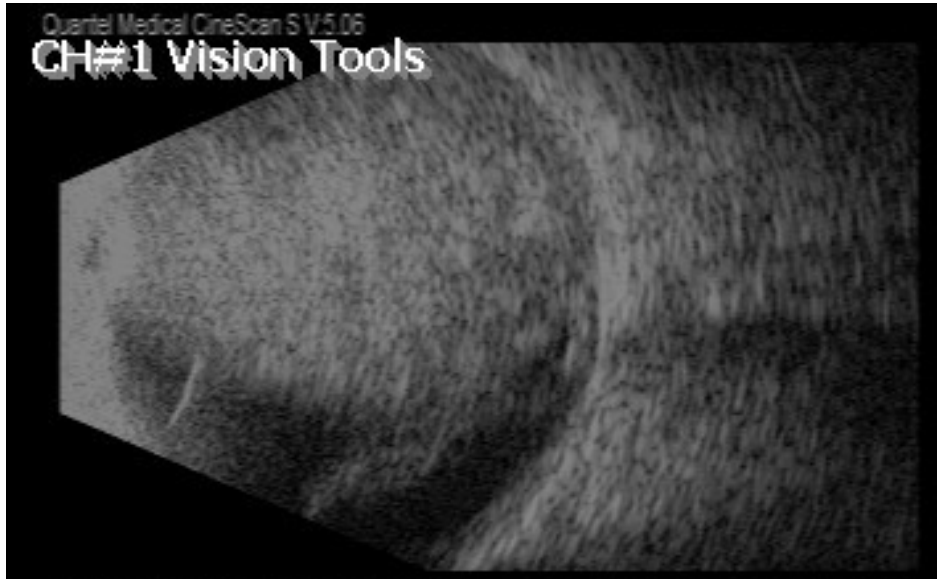
Two days later
IOP: 15 and 60
VA: 20/20 and NLP

Right Eye

Left Eye



Patient D: Two days later



OS:

1. Very large, solid choroidal mass extending from the superior, superior nasally and

superior temporally quadrant

2. It measures 17.3 mm in elevation (no change)

3. Medium low reflective, regular internal structure with strong angle kappa

4. No significant blood flow detected by color Doppler

5. Sclera is markedly thickened today with T-sign posteriorly

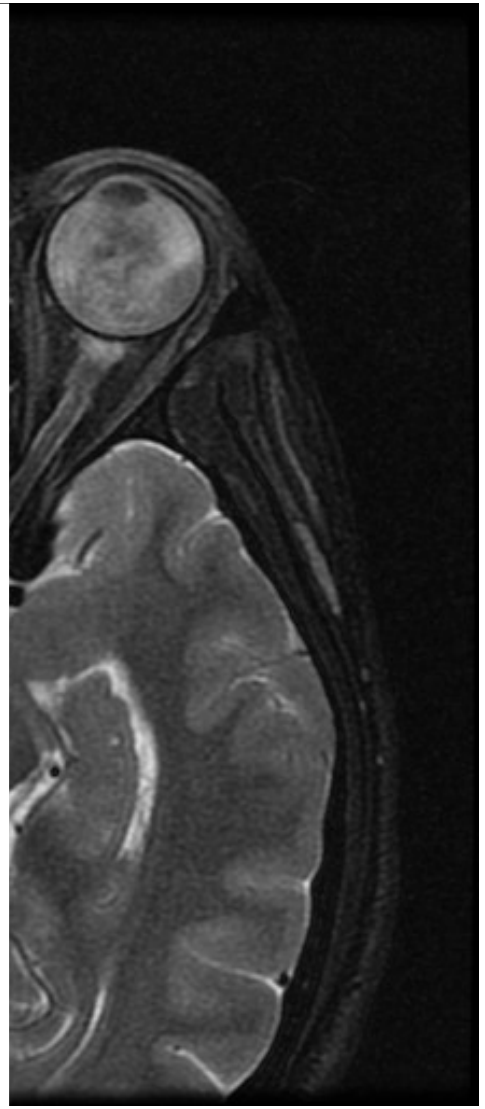
6. Suspicion of very tiny area of tumor/sclera communication (early extension to sclera) at

(12) Oclock equator

7. No other pathology

Patient D: Two days later

- Left globe is the seat **of total retinal detachment** with evidence of subretinal exudate of high signal intensity on T1-weighted image and intermediate to low on t2wi with bright signal on flair.
- Heterogeneous signal intensity mass originating from the left choroid and protruding within the vitreous 1.3x 1.4 cm with subsequent significant anterior displacement of the deformed slightly alternated signal intensity left lens with marked narrow anterior chamber possible to the degree of anterior angle closure glaucoma .
- The mass and the vitreous showed marked restricted pattern on diffusion weighted image suggestive to be tumor with vitreous seeding or severe inflammation with possible hemorrhagic content.
- The possibility of **malignant melanoma cannot** totally ruled-out, although absence of enhancing mass lesion is not typical pattern of the appearance.
- However other extensive infiltrative process like severe infection possibility should be put into consideration. For discussion with the referring physician.



What will you do?

FNA

Systemic Antibiotic

Systemic Steroid

Enucleation

Enucleation was done

Confirmed the diagnosis of Retinoblastoma

Histopathology: Orbital extension

Rx:
Chemotherapy x 6 cycle

EBR OS 4400CGY

Message:

Masquerading retinoblastoma can present in old age

Enculation still needed to confirm the diagnosis in presence of intra-ocular mass

Patient A:

3 years boy, refered to r/o RB by wise ophthalmologist.

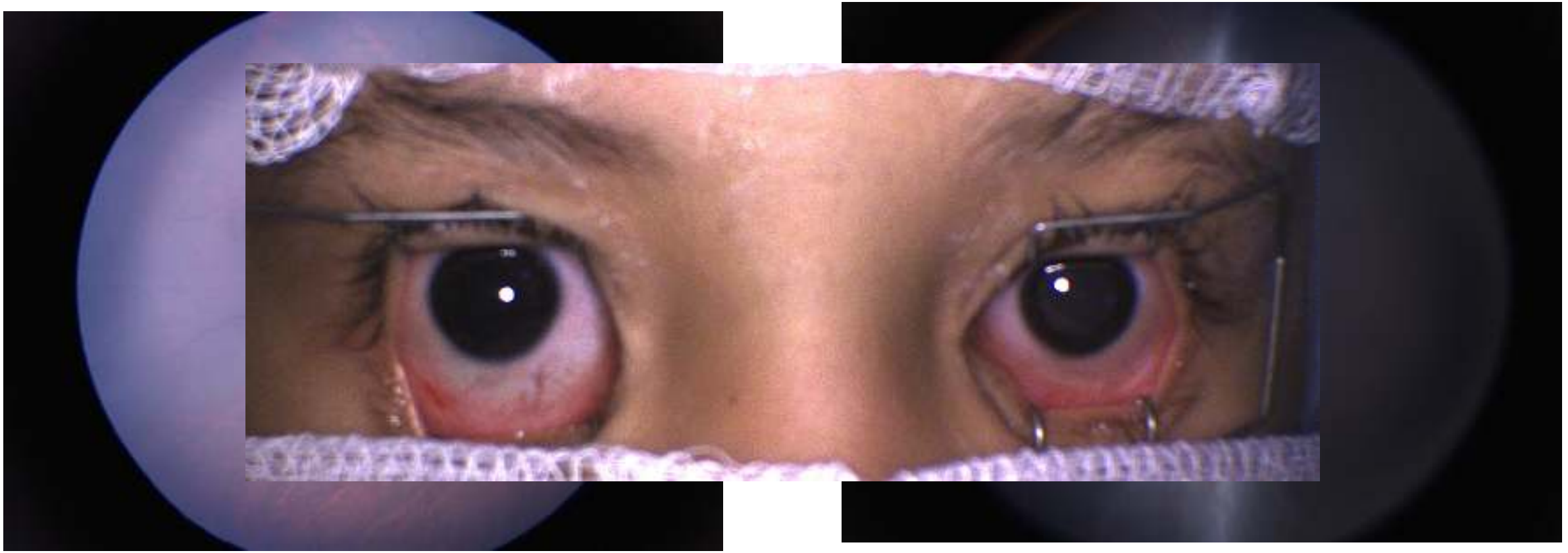
Mother noticed poor vision since the age of 1 year.

The left eye smaller since birth.

Exam:

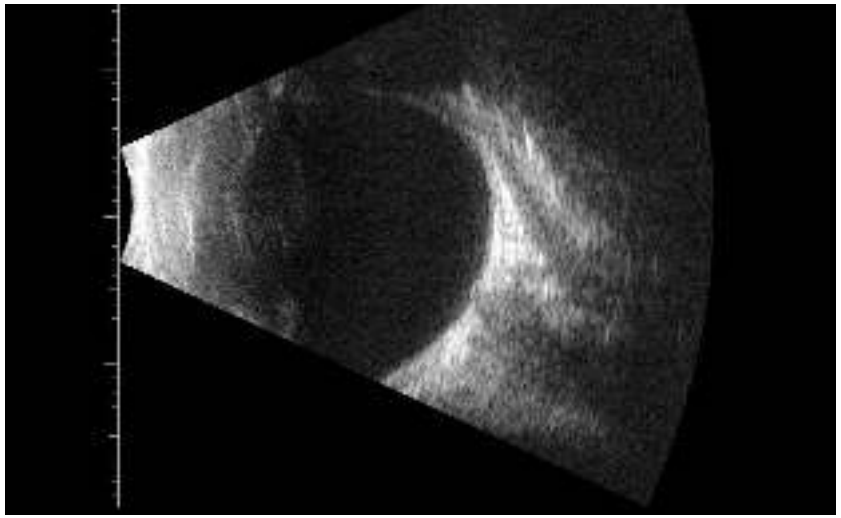
IOP 10/8

Axial length: 21.57 mm / 20.20 mm

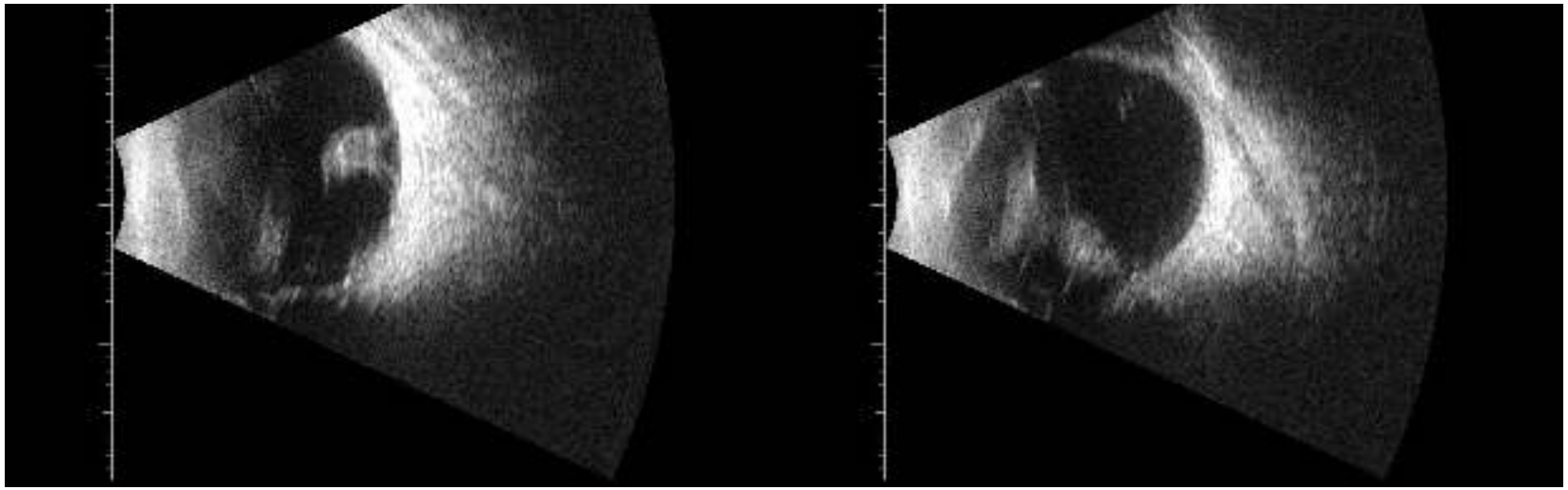


Right Eye

Left Eye



Right Eye : wnl



Left Eye : lesion superio-temporal with calcification

Findings:

Left intraocular mass with endophytic growth is shown along the nasal side.

It is extending laterally to the the optic nerve disk with inhomogeneous T2 and slightly hyperintense T-signal and has heterogeneous postcontrast enhancement associated retinal detachment and evidence of intense enhancement is shown at the optic disc indicated of intralaminar invasion and enhancement along the retinal leaflets is also seen.

The mass measures about 8.5 x 6.5 mm.

The choroid/sclera appear intact and no evidence of pathological enhancement could be seen in the rest of left orbital structures and no radiological sign of increase intraocular pressure.

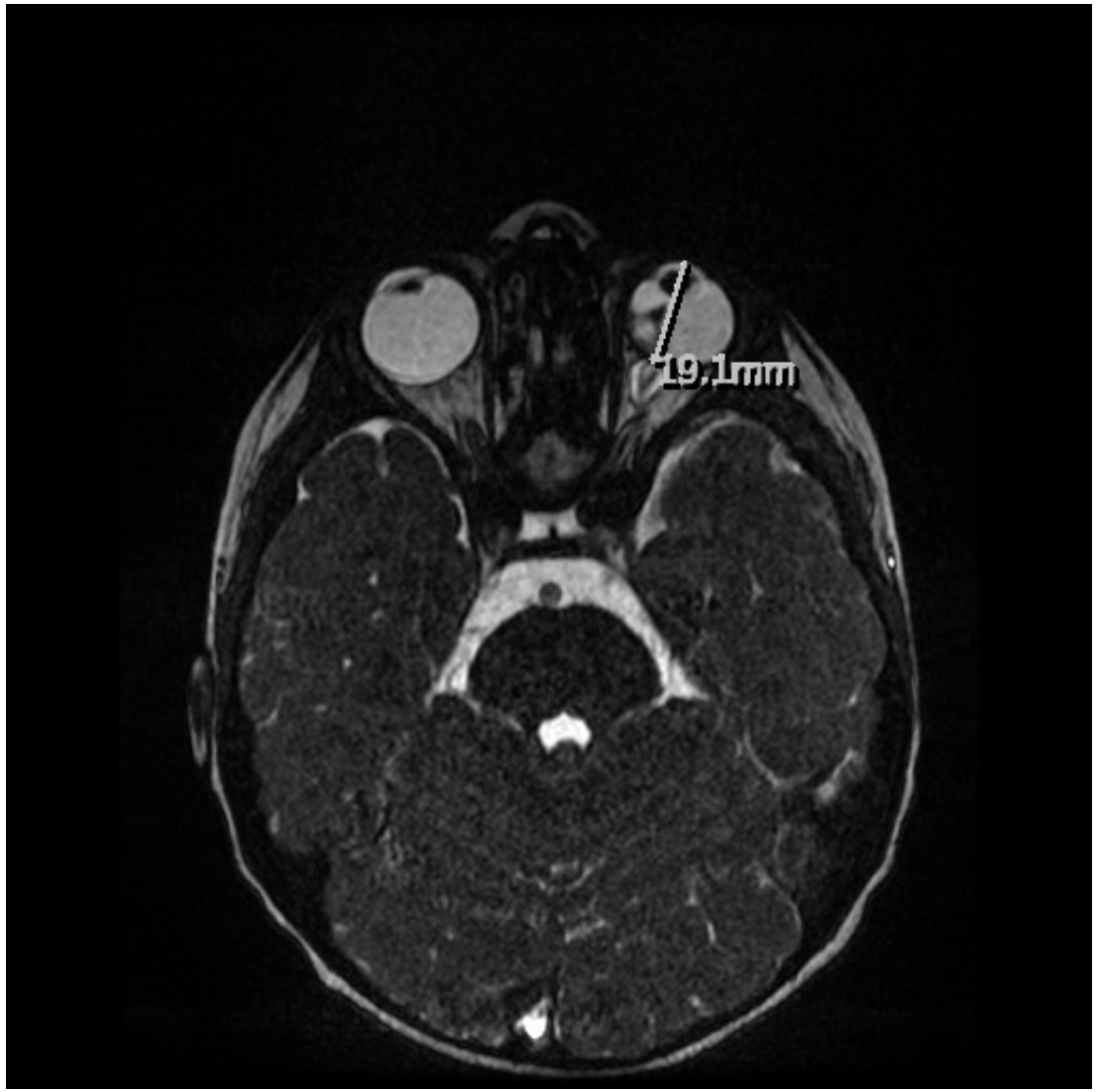
Normal sell and pineal gland regions with no evidence of gross abnormality.

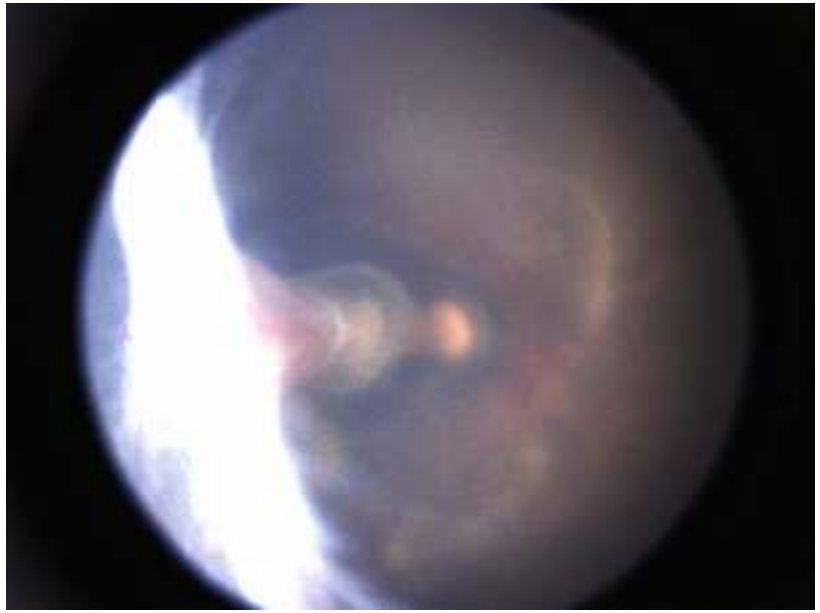
Right orbital cavity is unremarkable.

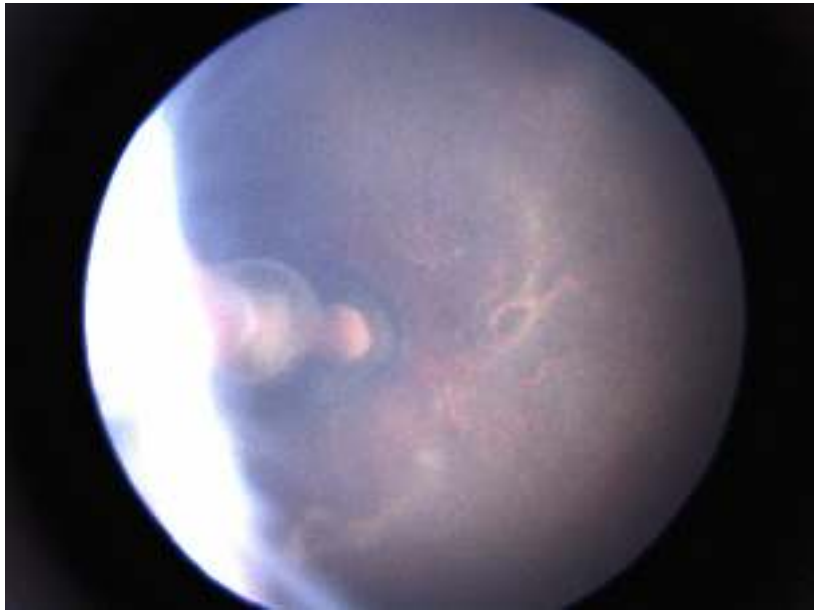
Conclusion:

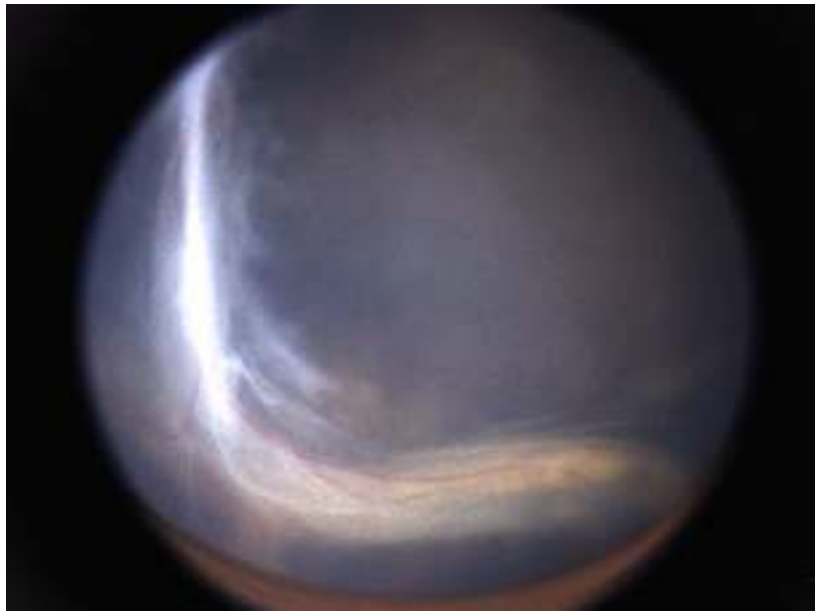
Left intraocular mass consistent with retinoblastoma, associated with retinal detachment and **intralaminar optic nerve invasion.**

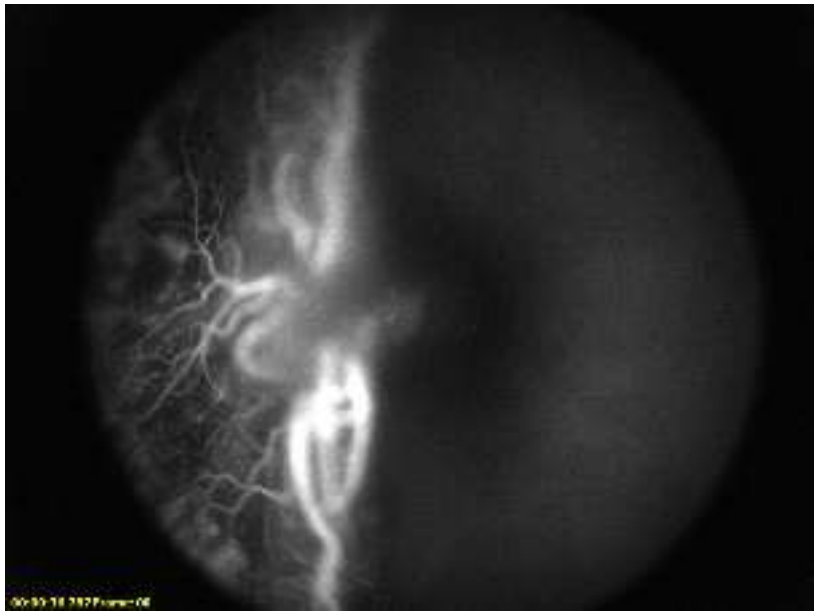
Normal pineal region and brain parenchyma.

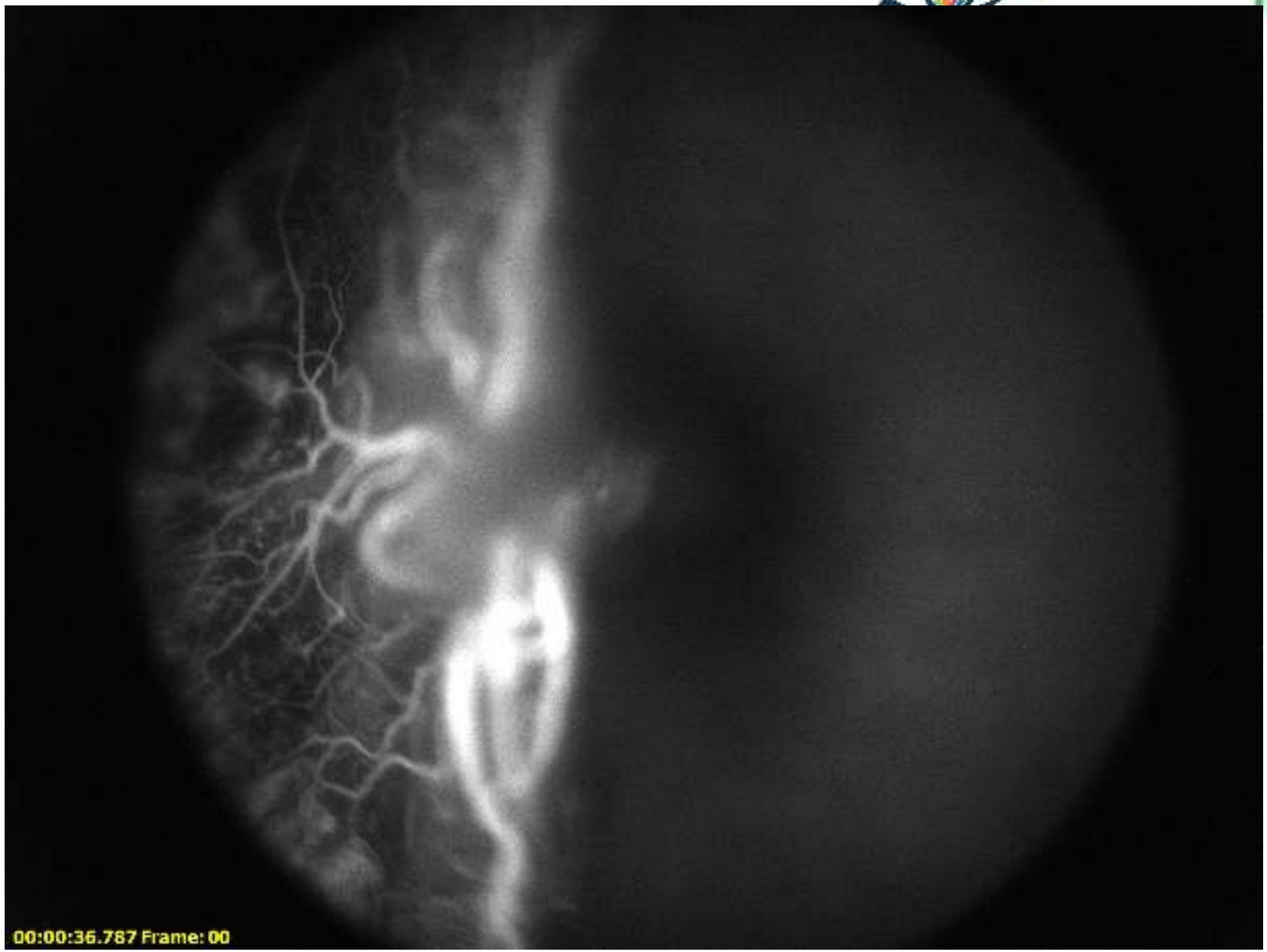








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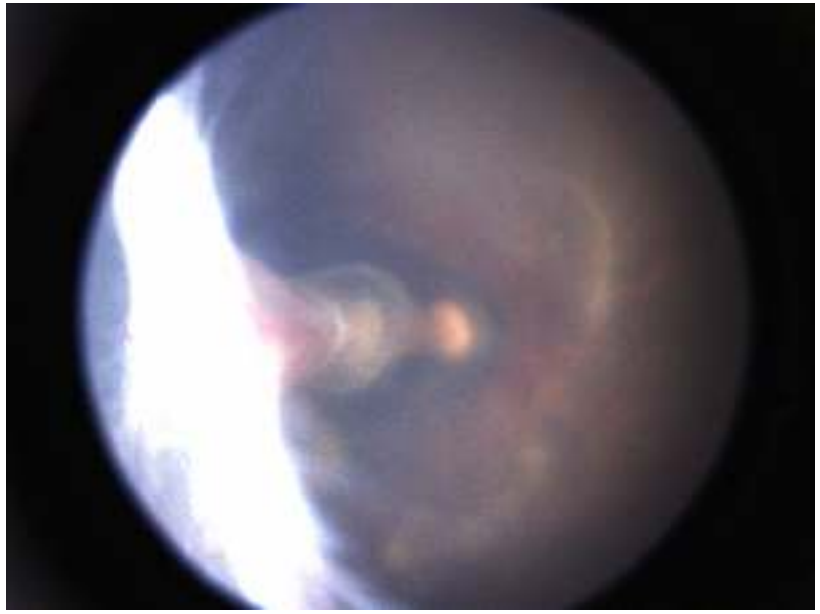
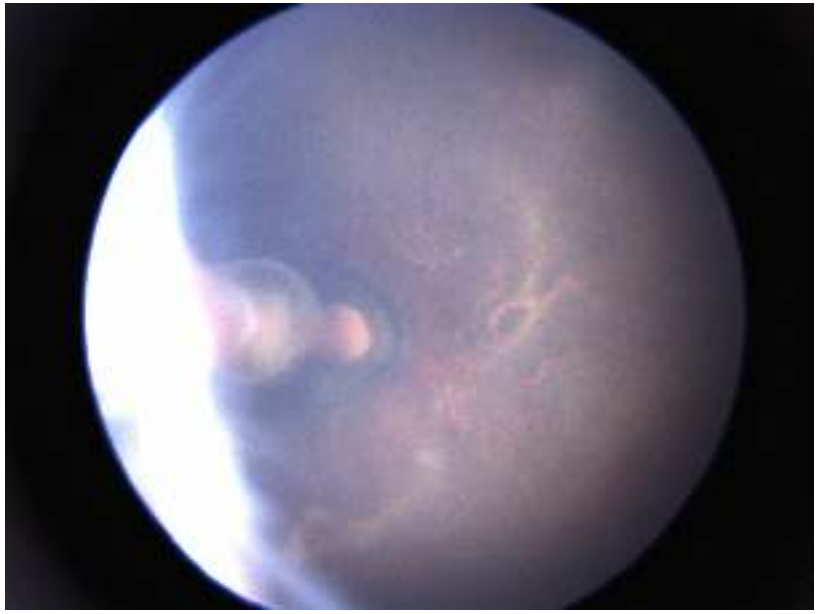
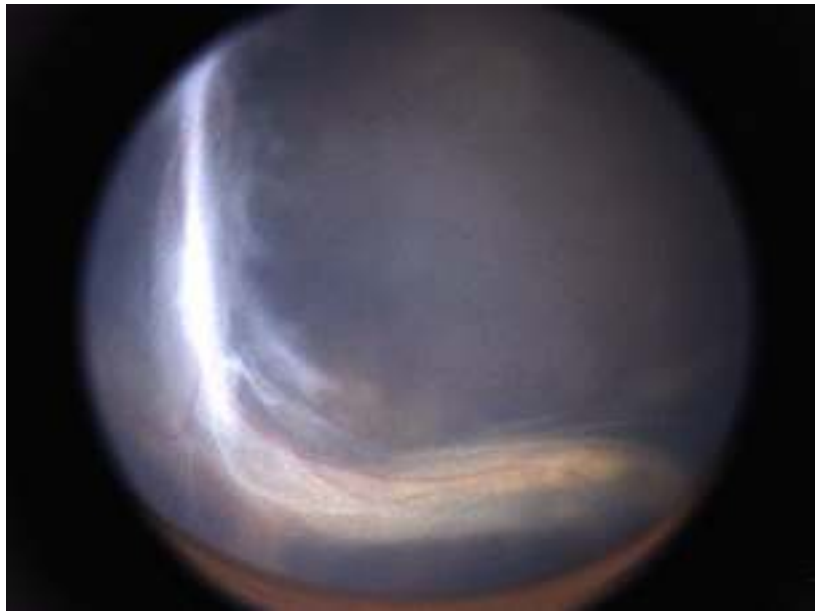
What is the diagnosis ?

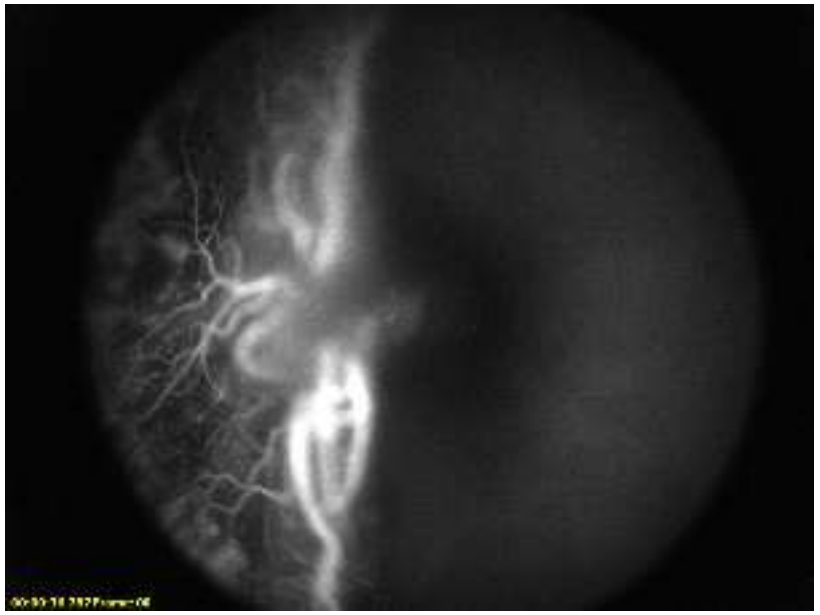
Persistent fetal vasculature (PFV) Vs. Retinoblastoma (RB)

Will you Observe, IAC, Enulcation,?









Dx:

PFV

Calcification of the globe

Retinal

- Drusen
- Retinoblastoma
- Retinocytoma
- Tuberous sclerosis
- astrocytic hamartomas
- Epiretinal membranes
- Retrolental fibroplasia (ROP or PHPV)
- Coats disease
- Asteroid hyalosis

Retinochoroidal

- Chorioretinitis
- Toxoplasmosis
- choroidal osteoma
- choroidal angioma: occasionally calcify
- choroidal nevus

Abnormal calcium and phosphate metabolism

- hyperparathyroidism
- pseudohypoparathyroidism
- renal tubular acidosis
- sarcoidosis 6

phthisis bulbi: shrunken ca lcified "lump" remaining

Others……

Gaillard F, Walizai T, Yap J, et al. Calcification of the globe (differential). Reference article, Radiopaedia.org (Accessed on 28 Apr 2025) https://doi.org/10.53347/rID-1043

Kachewar SG, Kulkarni DS. An Imaging Review of Intra-ocular Calcifications. J Clin Diagn Res. 2014 Jan;8(1):203-5. doi: 10.7860/JCDR/2014/4475.3904. Epub 2014 Jan 12. PMID: 24596775; PMCID: PMC3939552.

Message:

Wise referal when RB is suspected

Clinical exam was more valuable in this case

Calcification DOES NOT equal RB

MRI and B-scan help but can't diagnose

We see the same

Interpretation is different

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Saudi Group of Pediatric Ophthalmology & Strabismus

الجمعية السعودية لطب العيون
Saudi Ophthalmology Society

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King Khaled Eye Specialist Hospital

Thank You

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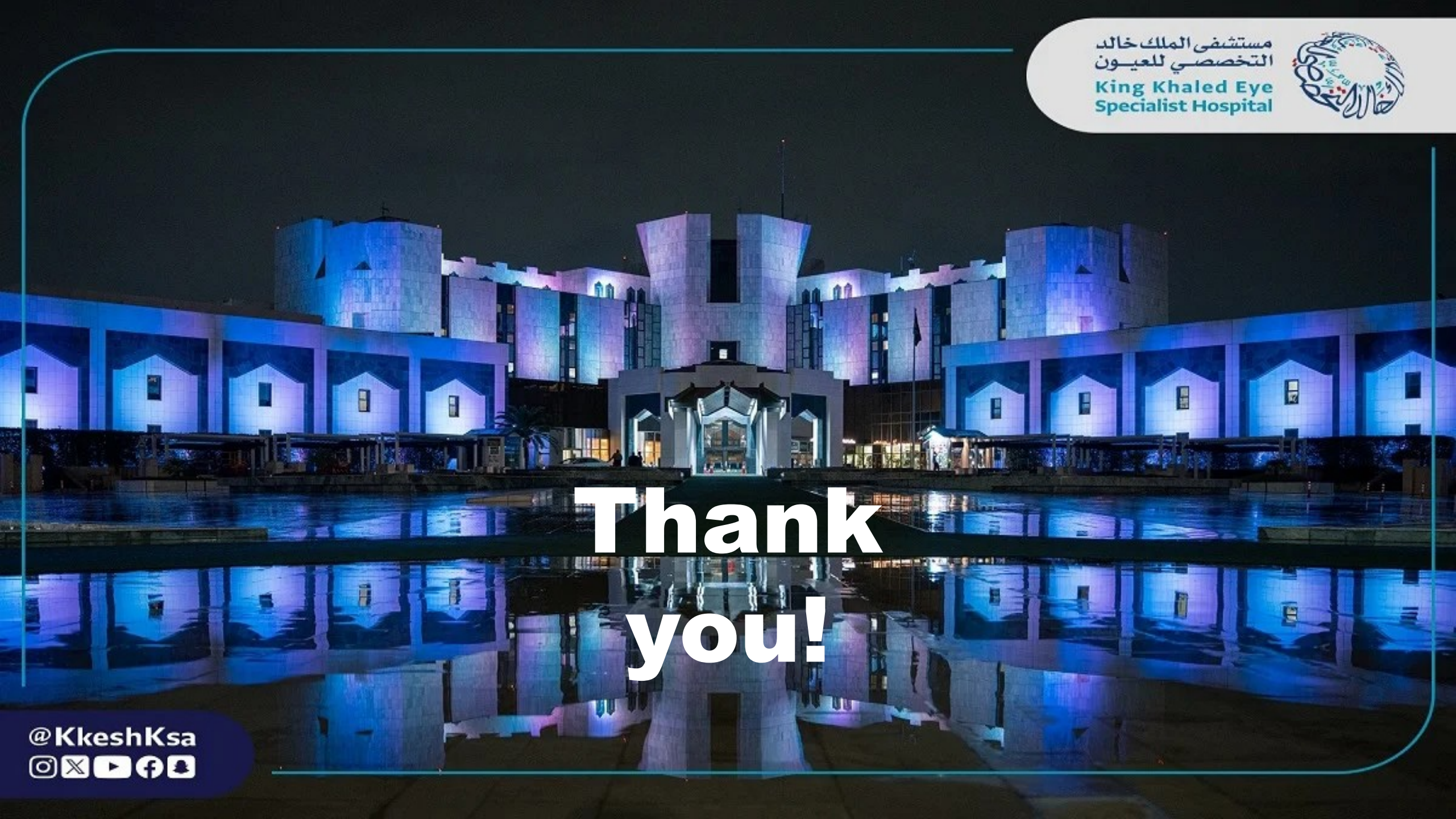
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Specialist Hospital
Thank
you!
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