LVPEI
So that all may see

L V Prasad Eye Institute

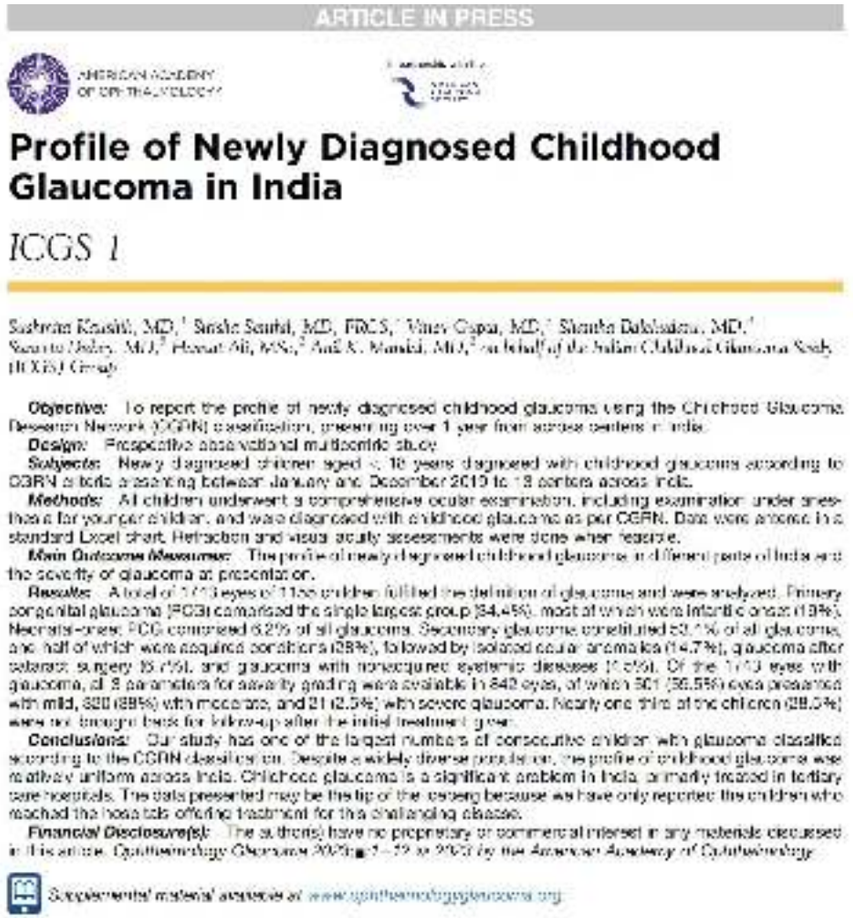
Challenges in the Management of Glaucoma associated with Syndromic/Systemic conditions

Sirisha Senthil, MS, FRCS (Edin)
Head, VST Center for Glaucoma Care
L V Prasad Eye Institute
Hyderabad

Outline

- Proportion of cases
- Common groups of conditions
- Phakomatosis
- Metabolic
- Ectopia Lentis
- Challenges in diagnosis, evaluation, management, complications

1743 eyes of 1155 children NEWLY DIAGNOSED GLAUCOMA



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Profile of Newly Diagnosed Childhood Glaucoma in India

ICGS 1

Subrata Kundu, MD,[1] Sasha Sushil, MD, FRCS,[2] Vinay Gupta, MD,[1] Shanta Balakrishna, MD,[1] Sourav Dubey, MD,[2] Hesnat Ali, MSc,[2] Anil K. Mandal, MD,[2] on behalf of the Indian Childhood Glaucoma Study (ICGS) Group

Objective: To report the profile of newly diagnosed childhood glaucoma using the Childhood Glaucoma Research Network (CGRN) classification, presenting over 1 year from across centers in India.

Design: Prospective observational multicentric study.

Subjects: Newly diagnosed children aged < 16 years diagnosed with childhood glaucoma according to CGRN criteria presenting between January and December 2019 to 13 centers across India.

Methods: All children underwent a comprehensive ocular examination, including examination under anesthesia for younger children, and were diagnosed with childhood glaucoma as per CGRN. Data were entered in a standard Excel sheet. Refraction and visual acuity assessments were done when feasible.

Main Outcome Measures: The profile of newly diagnosed childhood glaucoma in different parts of India and the severity of glaucoma at presentation.

Results: A total of 1743 eyes of 1155 children fulfilled the definition of glaucoma and were analyzed. Primary congenital glaucoma (PCG) comprised the single largest group (34.45%), most of whom were infantile onset (19%). Neonatal-onset PCG comprised 6.2% of all glaucoma. Secondary glaucoma constituted 52.1% of all glaucoma, one-half of which were acquired conditions (28%), followed by isolated ocular anomalies (14.7%), glaucoma after cataract surgery (6.6%), and glaucoma with nonacquired systemic diseases (3.6%). Of the 1743 eyes with glaucoma, all 3 parameters for severity grading were available in 842 eyes, of which 301 (35.5%) eyes presented with mild, 320 (38%) with moderate, and 221 (26.5%) with severe glaucoma. Nearly one-third of the children (28.3%) were not brought back for follow-up after the initial treatment given.

Conclusions: Our study has one of the largest numbers of consecutive children with glaucoma classified according to the CGRN classification. Despite a widely diverse population, the profile of childhood glaucoma was relatively uniform across India. Childhood glaucoma is a significant problem in India, primarily treated in tertiary care hospitals. The data presented may be the tip of the iceberg because we have only reported the children who reached the hospitals offering treatment for this challenging disease.

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Supplemental material available at www.ophthalmologyglaucoma.org

CG 35%

JOAG 12%

Ocular Anomalies-- **18.46%**----syndromic-- **3.78%**

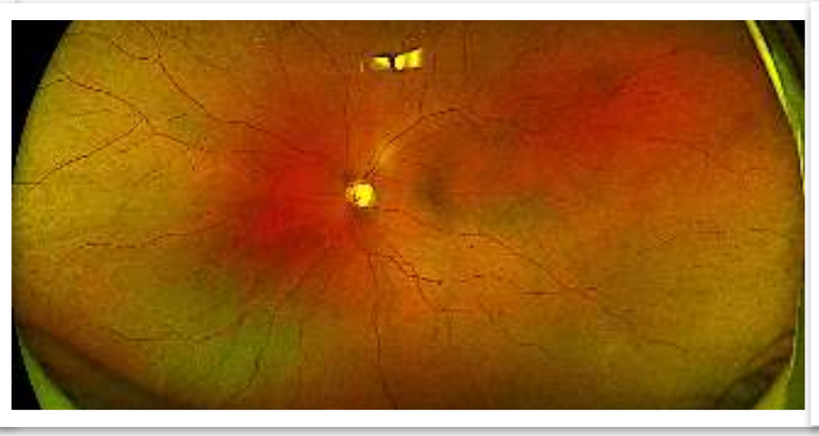
Acquired 28%

Post Cat 7%

Nonacquired glaucoma with systemic anomalies	66	3.78%
Sturge–Weber syndrome	41	2.35%
Downs syndrome	3	0.17%
Neurofibromatosis	5	0.29%
Phacomatosis pigmentovascularis	5	0.29%
MPS	4	0.23%
Hellerman Steriff Syndrome	2	0.11%
KTS	2	0.11%
Weill Marchesani syndrome	2	0.11%
Norrie's disease	1	0.06%
Prader Willi syndrome	1	0.06%

Phakomatosis

Sturge Weber Syndrome and Phakomatosis Pigmentovascularis (SWS+ODM)

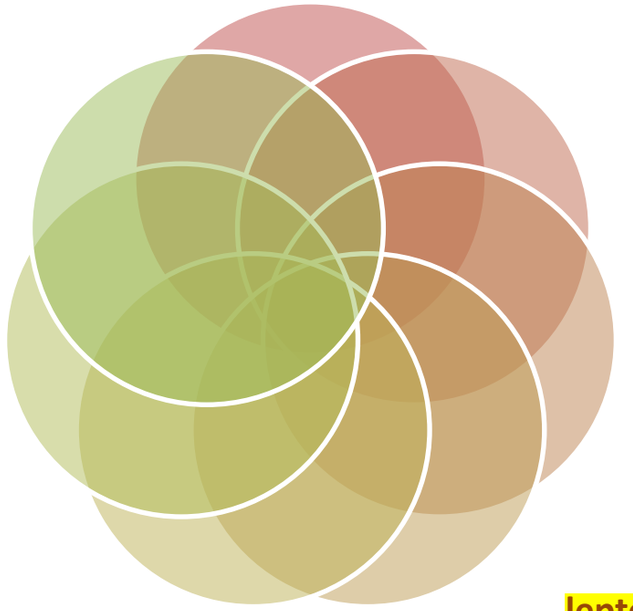



Sturge-Weber Syndrome(SWS)

Sporadic congenital neurocutaneous disorder

Glaucoma is seen in 30-70% of patients

Somatic mosaic mutations in *GNAQ* gene

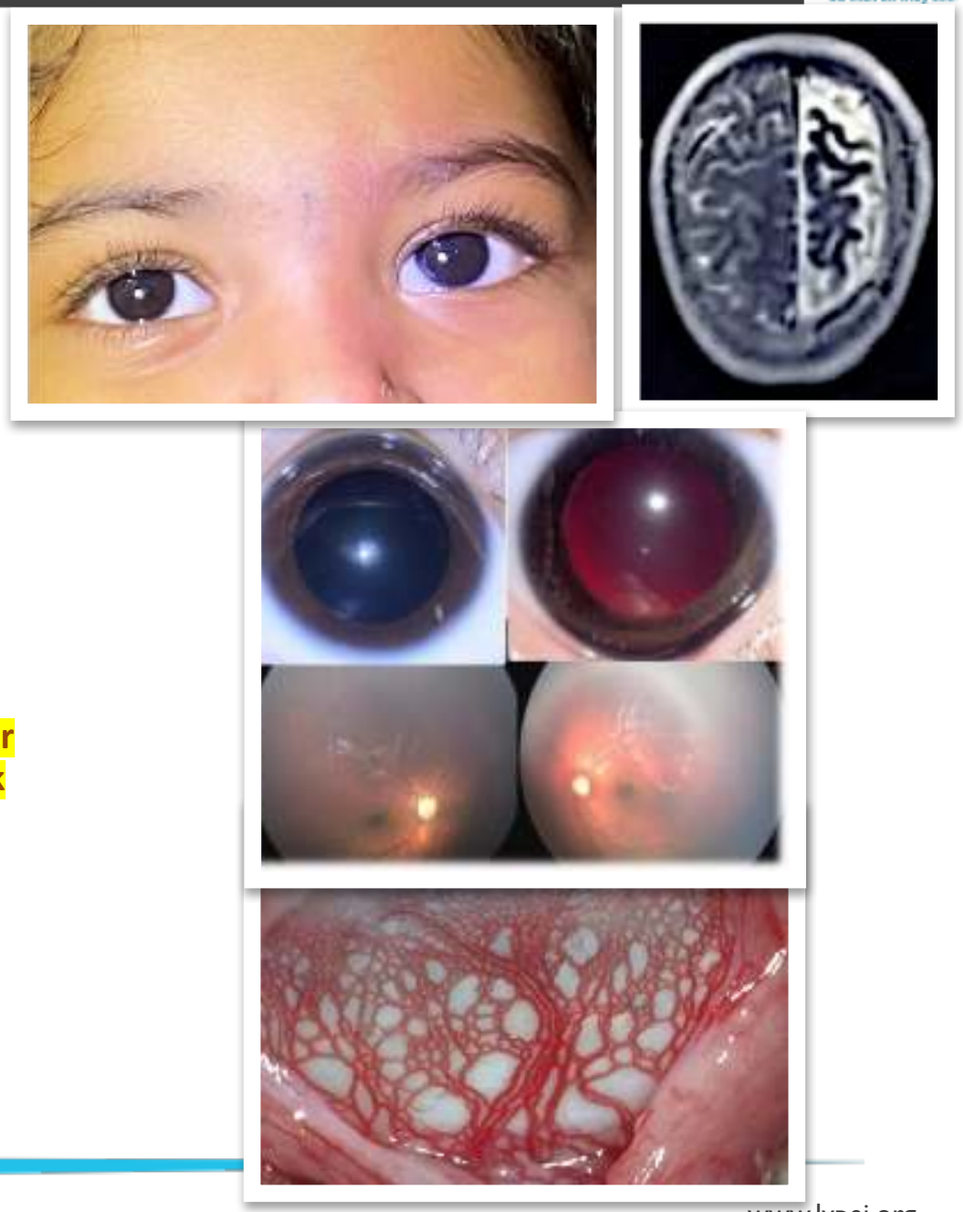


Encephalotrigeminal angiomatosis affecting the cephalic, facial and ocular venous microvasculature

Facial hemangioma or port wine birth mark

leptomeningeal hemangioma

Ocular hemangioma (episcleral and choroidal)



Thomas-Sohl KA, et al. 2004

Phacomatosis-Pigmento-Vascularis (PW birthmark+ ODM)

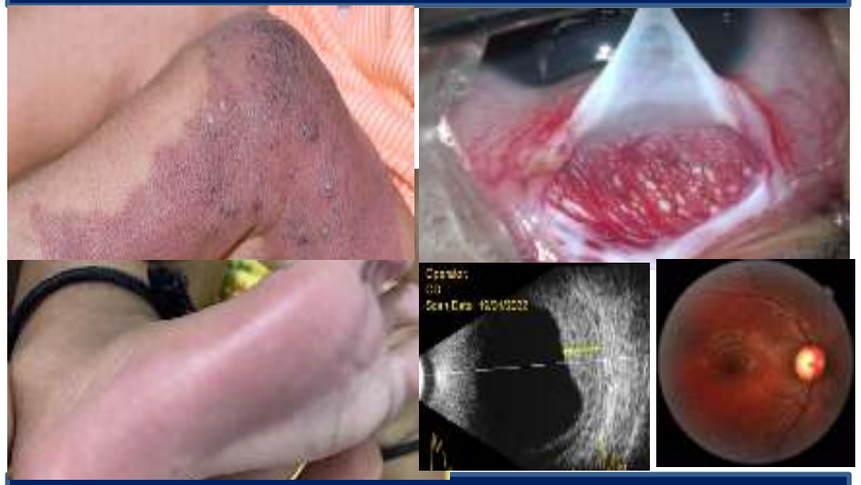
Congenital neurocutaneous multisystemic condition

Concurrent Pigmentary Nevi + Capillary Malformation

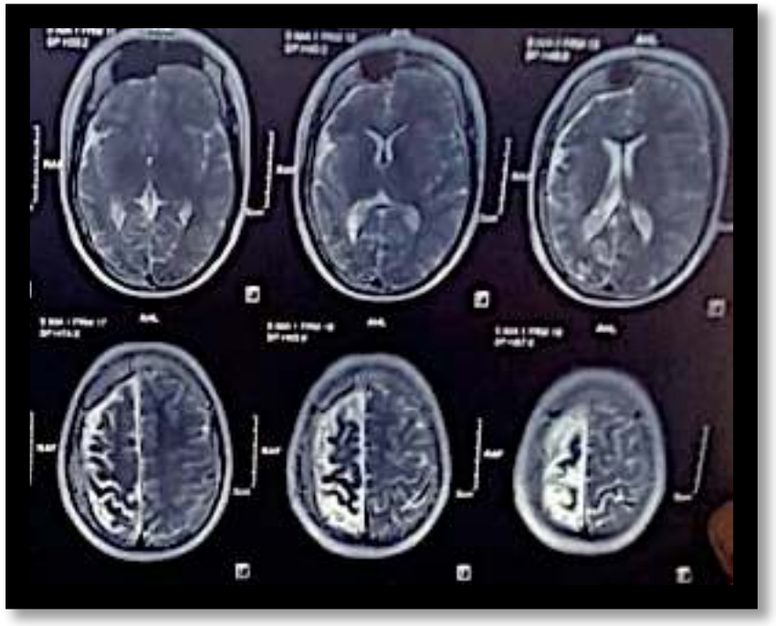
Early and late onset glaucoma >50%

Soft tissue/ limb hypertrophy

Pigmentary nevi



Vascular malformation



Leptomeningeal enhancement, enhanced choroid plexus, hemispheric brain atrophy

Seizures, intellectual disabilities, Hemiparesis

Facial soft tissue hypertrophy

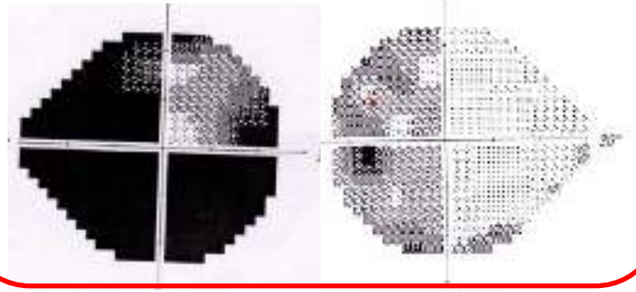
Bilateral Port wine stain with Pigmentary Nevus

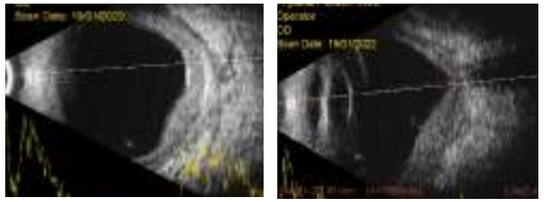
26 and 35 mmHg

0.9 CDR, bipolar notch

On Antiepileptics

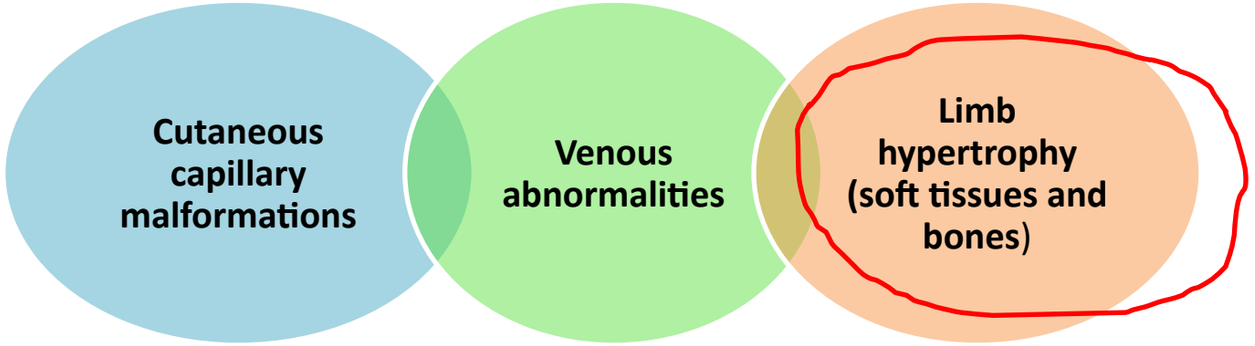
Left sided Hemiparesis

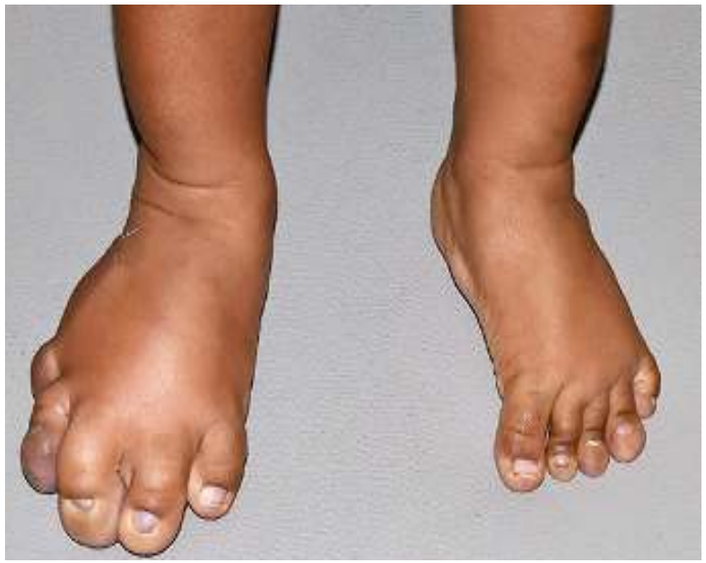


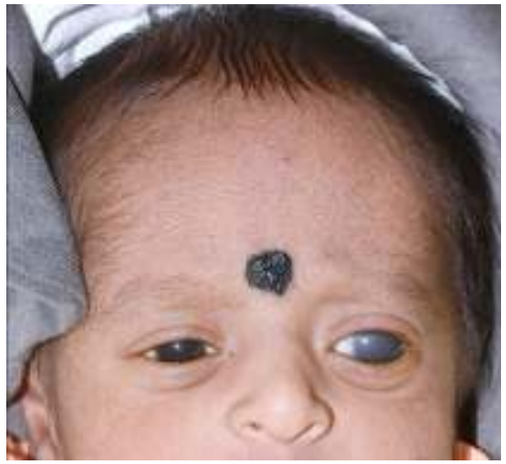


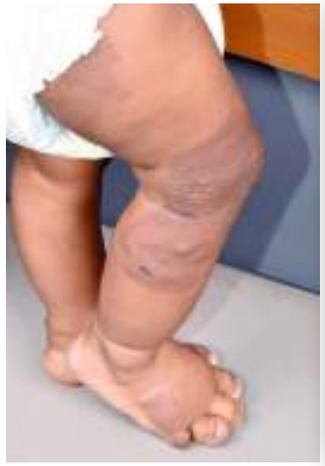
Diffuse choroidal hemangioma

Klippel Trenaunay Syndrome (KTS)









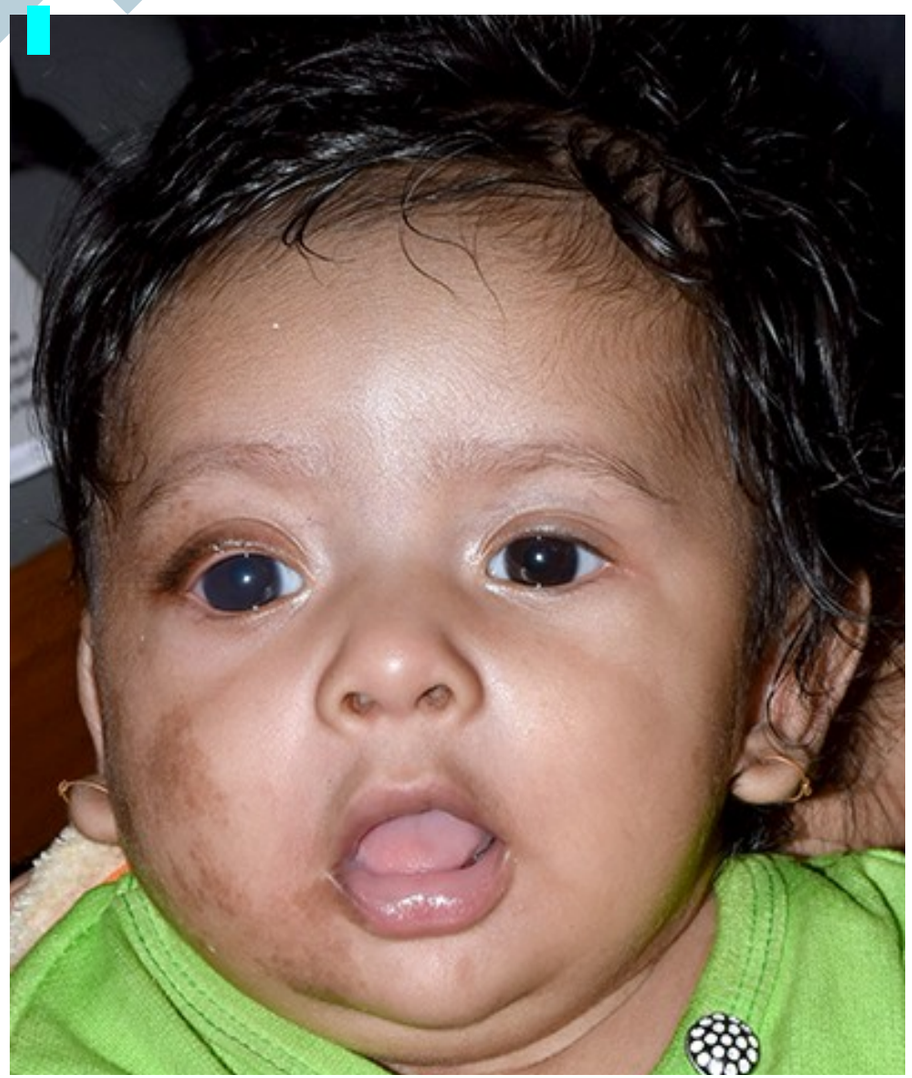
A rare presentation of pupillary block glaucoma and persistent tunica vasculosa lentis in Klippel–Trenaunay syndrome

Persistent tunica vasculosa lentis with pupillary block glaucoma

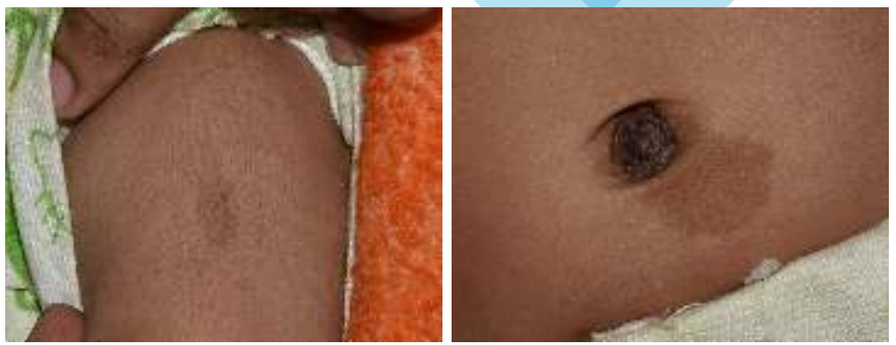
Harshitha Kadava, Sirisha Senthil IJO, 2024

Neurofibromatosis 1

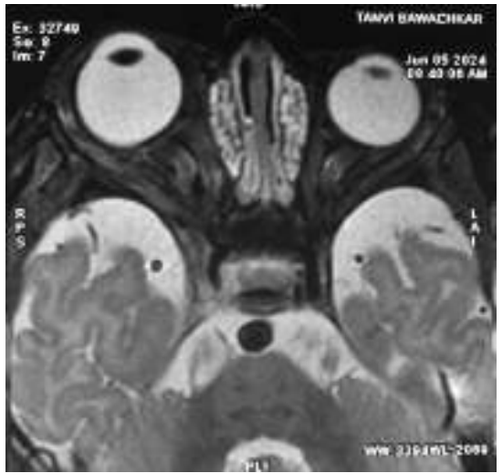
3-months-old
RE upper lid thickening
Lower half of face involved



Unilateral megalocornea



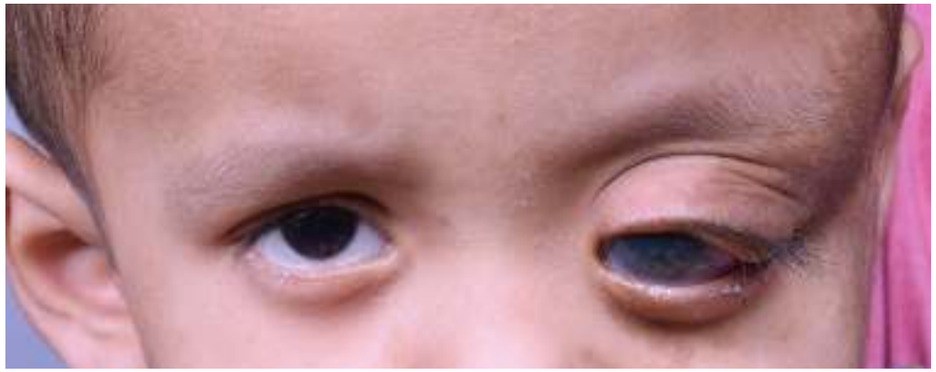
Multiple cafe-au-lait spots on the cheeks, limbs and trunk



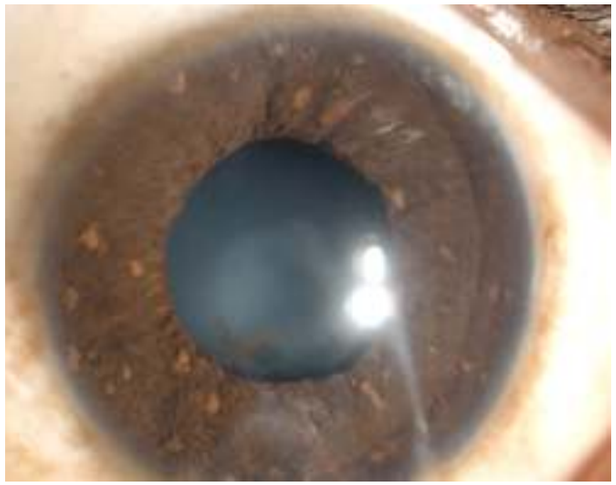
MRI – Mildly enlarged right globe with posterolateral contour bulge

mutation in the *N1* gene on Ch 17, glaucoma commonly occurs ipsilateral to lid plexiform neurofibromas

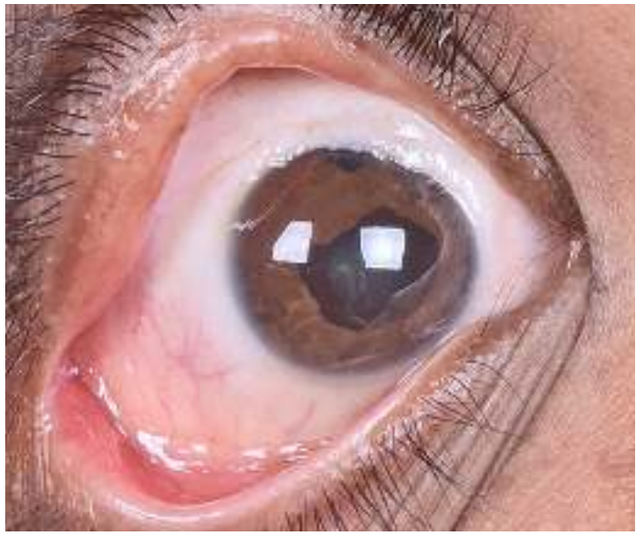
Can have Optic nerve Glioma and absent GWS



Plexiform Neurofibroma, Lisch nodule, ectropion uveae, unilateral glaucoma, Choroidal nodule



- 23% eyes develop Glaucoma
- Congenital or older children



Abdolrahimzadeh B, et al. 2016

Systemic evaluation and Anesthesia

Seizures, Anemia, Clotting disorders and thromboembolism/ Stroke

May lead to deep vein thrombosis and pulmonary embolism

Minor- ectasias within vascular system

Major- gastrointestinal tract and bladder

Anaesthesia management in a child with Klippel-Trenaunav Syndrome posted for examination of both eyes under general anaesthesia: A case report

Sirisha Senthil[1], Harshitha Kadava[2], Hari Shanker Charan[3], Raja Narsing Rao[3].
[1]Department of Cataract and Glaucoma, LVEPI, Hyderabad, [2]Department of Glaucoma, LVEPI, Hyderabad, [3]Department of Anaesthesia, LVEPI, Hyderabad

- **Difficult intubation**

✓ **Facial anomalies**

✓ **Upper airway angiomas**

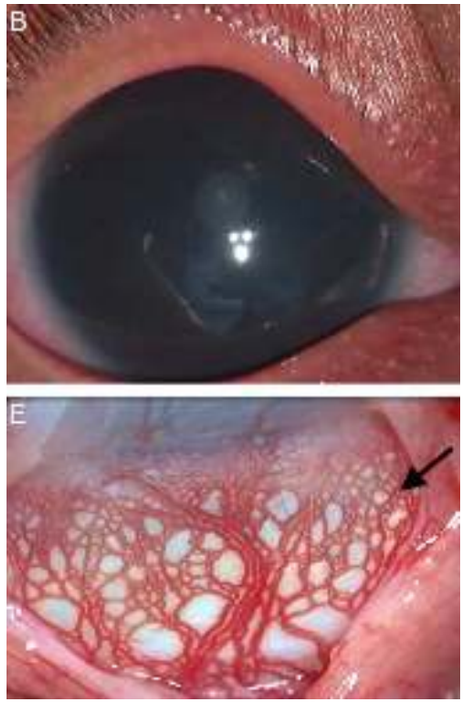
✓ **Soft tissue hypertrophy in the airway**

- Loss of autoregulation predisposes to hemorrhage

Treatment Outcomes of Primary Combined Trabeculotomy With Trabeculectomy in Early Onset Glaucoma With Sturge-Weber Syndrome

JOG, 2024

Sirisha Senthil, MS, Shravya Sri Durgam, BOpt,† Hasnat Ali, MBA,† Kolipaka Gowri Pratinya, DNB,* Rashmi Krishnamurthy, DNB,* and Anil K. Mandal, MD**



Post CTT for SWS in early onset glaucoma

1 of the 49 eyes had complication

Ophthalmol Glaucoma. Jan-Feb 2022;5(1):101-109. doi: 10.1016/j.ogla.2021.06.003. Epub 2021 Jun 27.

Outcomes of Management of Glaucoma in Phacomatosis Pigmentovascularis Over the Last Three Decades: A Single-Center Experience

Anil K Mandal [1], Krishnapriya Kodavati [2], Vijaya K Gothwal [3]

- 55 eyes of 38 patients (21 unilateral and 17 bilateral) with glaucoma in PPV
- 4/10 eyes Trab MMC had RD poor outcome post retinal surgery

Outcomes and lessons learned from two decades' experience with glaucoma drainage device implantation for refractory Sturge Weber–associated childhood glaucoma

Tanya S. Glaser, MD, Landon C. Meekins, MD, and Sharon F. Freedman, MD

GDD in 22 eyes

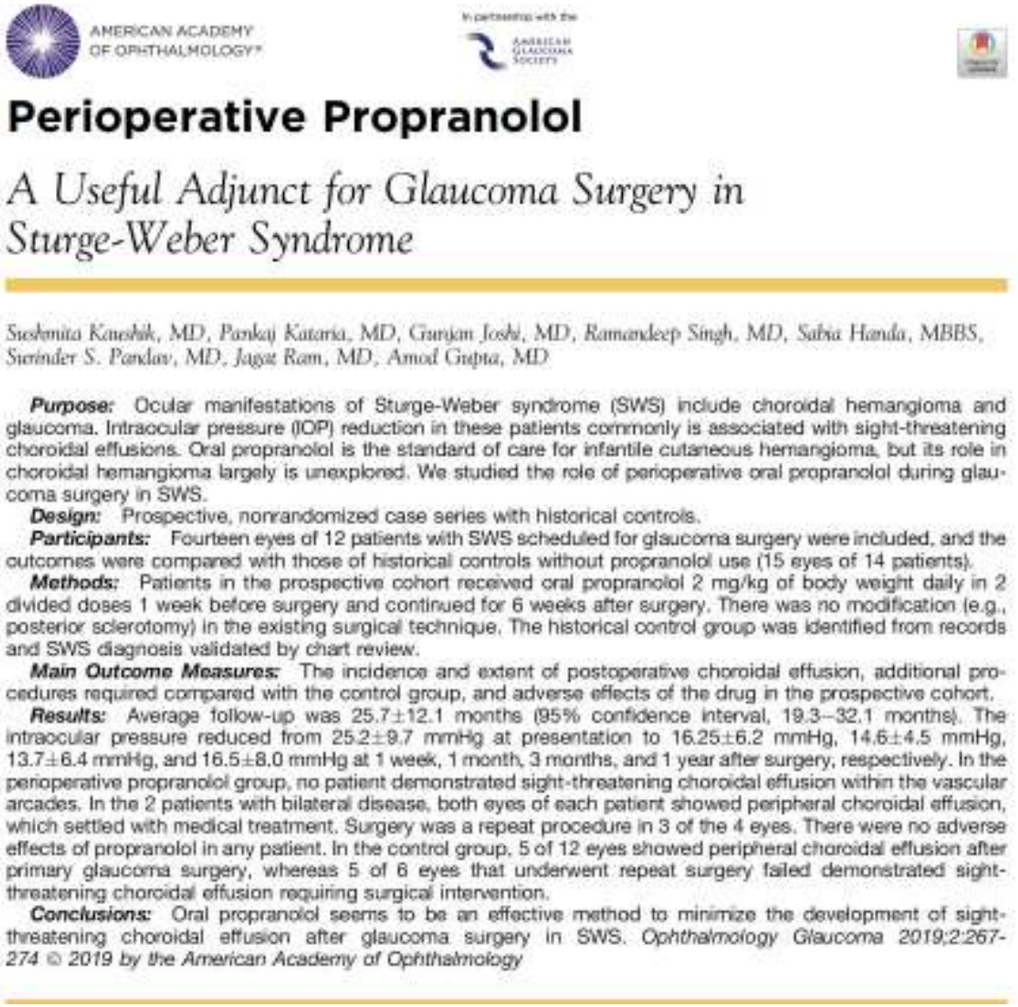
22 eyes, Repeat intervention in 2/3rds

Young age, mean 4.5 years

Success 75% at 3 years

50% eyes had complications

What is the role of oral propranolol??



AMERICAN ACADEMY OF OPHTHALMOLOGY

Perioperative Propranolol

A Useful Adjunct for Glaucoma Surgery in Sturge-Weber Syndrome

Sushmita Kaushik, MD, Pankaj Kataria, MD, Gunjan Joshi, MD, Ramandeep Singh, MD, Sabia Handa, MBBS, Surinder S. Pandav, MD, Jagat Ram, MD, Amod Gupta, MD

Purpose: Ocular manifestations of Sturge-Weber syndrome (SWS) include choroidal hemangioma and glaucoma. Intraocular pressure (IOP) reduction in these patients commonly is associated with sight-threatening choroidal effusions. Oral propranolol is the standard of care for infantile cutaneous hemangioma, but its role in choroidal hemangioma largely is unexplored. We studied the role of perioperative oral propranolol during glaucoma surgery in SWS.

Design: Prospective, nonrandomized case series with historical controls.

Participants: Fourteen eyes of 12 patients with SWS scheduled for glaucoma surgery were included, and the outcomes were compared with those of historical controls without propranolol use (15 eyes of 14 patients).

Methods: Patients in the prospective cohort received oral propranolol 2 mg/kg of body weight daily in 2 divided doses 1 week before surgery and continued for 6 weeks after surgery. There was no modification (e.g., posterior sclerotomy) in the existing surgical technique. The historical control group was identified from records and SWS diagnosis validated by chart review.

Main Outcome Measures: The incidence and extent of postoperative choroidal effusion, additional procedures required compared with the control group, and adverse effects of the drug in the prospective cohort.

Results: Average follow-up was 25.7±12.1 months (95% confidence interval, 19.3–32.1 months). The intraocular pressure reduced from 25.2±9.7 mmHg at presentation to 16.25±6.2 mmHg, 14.6±4.5 mmHg, 13.7±6.4 mmHg, and 16.5±8.0 mmHg at 1 week, 1 month, 3 months, and 1 year after surgery, respectively. In the perioperative propranolol group, no patient demonstrated sight-threatening choroidal effusion within the vascular arcades. In the 2 patients with bilateral disease, both eyes of each patient showed peripheral choroidal effusion, which settled with medical treatment. Surgery was a repeat procedure in 3 of the 4 eyes. There were no adverse effects of propranolol in any patient. In the control group, 5 of 12 eyes showed peripheral choroidal effusion after primary glaucoma surgery, whereas 5 of 6 eyes that underwent repeat surgery failed demonstrated sight-threatening choroidal effusion requiring surgical intervention.

Conclusions: Oral propranolol seems to be an effective method to minimize the development of sight-threatening choroidal effusion after glaucoma surgery in SWS. *Ophthalmology Glaucoma 2019;2:267-274*

- Showed the benefit of Oral Propronolol in the prophylaxis and management of postop CD in SWS
- Bilateral cases, repeat intervention had higher risk of CD

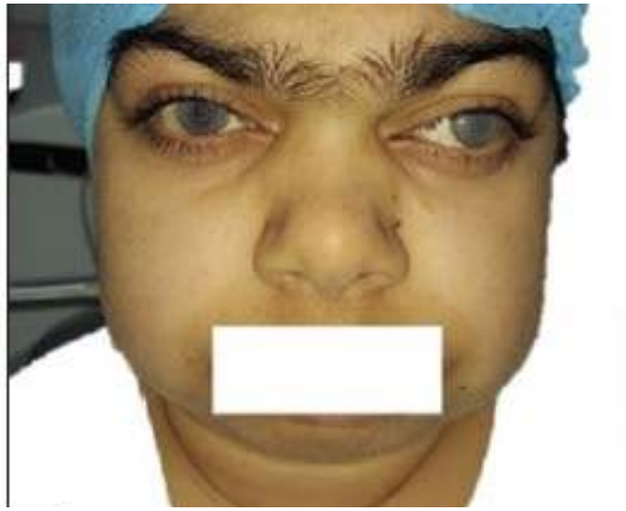
Beware of risk of CVA and get clearance for use

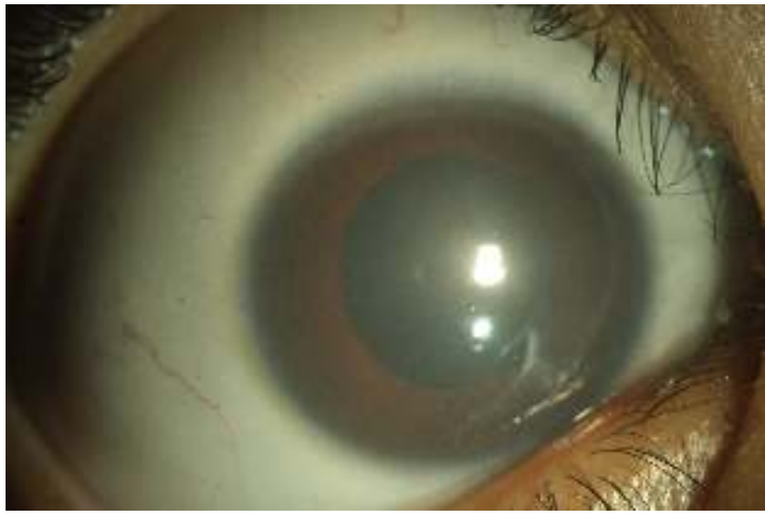
Follow up closely

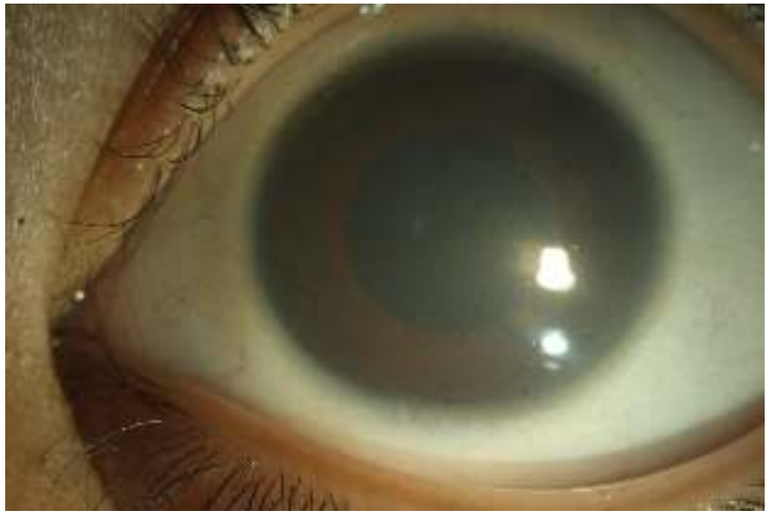
Metabolic

Mucopolysaccharidosis

Inherited metabolic disorders with abnormal deposition of dermatan sulfate in types I and VI and keratan sulfate in type IV MPS







Vision loss can be due to corneal clouding, **glaucoma (28%),** retinopathy, and optic neuropathy
intellectual disability, neurological, cardiac, hearing and musculoskeletal problems

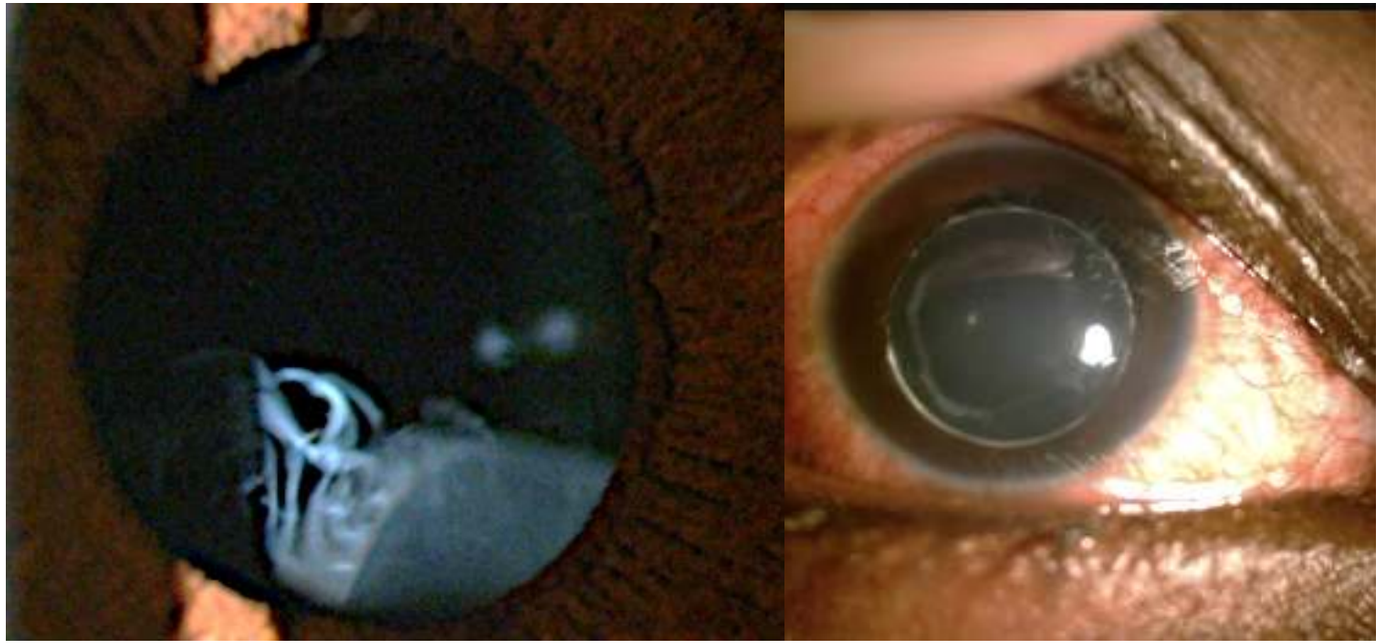
Objectively measuring anterior segment alterations in the eyes of mucopolysaccharidoses: Its utility in early diagnosis of glaucoma

Achanta, Divya Sree Ramya[1,2]; Mohamed, Ashik[1,3]; Chaurasia, Sunita[1,2,4]; Senthil, Sirisha[5]; Mandal, Anil Kumar[5]; Takkar, Brijesh[1,6,7]; Mishra, Dilip Kumar[8]; Edward, Deepak Paul[9]; Ramappa, Muralidhar[1,2,4]

IJO, 2022

Shorter AL, High Hyperopia, Flatter K

12-year-old, Male
Pain, vomiting, decrease in vision
Consanguineous parents, developmental delay



Gene & Transcript	Variant	Zygosity	Location	Disorder	Inheritance	ACMG Classification
CBS NM_000071.3	c.572C>T p.Thr191Met	Homozygous	Exon 7	Homocystinuria, B6-responsive and nonresponsive types / Thrombosis, hyperhomocysteinemic [OMIM ID: 236200]	Autosomal Recessive	Likely pathogenic PM2, PM5, PP2, PP3, PP5
FOXC1 NM_001453.3	c.740_756delinsCG p.Gly247_Ala251del	Heterozygous	Exon 1	Anterior segment dysgenesis 3, multiple subtypes [OMIM ID: 601631] /	Autosomal Dominant	Uncertain Significance PM2, PM4

CLINICAL PATHOLOGY REPORT

MRNo.	VC-TDK-N760603	UHID	1150589	Name	Mast. Shivalingam Kodimala	Sex	M	Age	12

SERUM HOMOCYSTINE

Homocystine (Enzymatic recycling)	47.9	4-12 mmol/L

Physician / Pathologist: Dr Nikitha Chelamela

Deficient Cystine causes increased fragility of the zonules, they break and curl up against the lens

Title: GAPO syndrome: A novel mutation in ANTXR1 gene

Author: Dr Manikanta Damagatla[1]

Co-authors: Dr Anshuman verma[2], Mr Venkatesh Pochaboina[3], Dr Manju Bhate[3], Dr Sirisha Senthil[1]

ANTXR1 gene mutation: extracellular-matrix homeostasis

Growth retardation, Alopecia, Pseudoanodontia (failure of teeth eruption) and Progressive optic atrophy

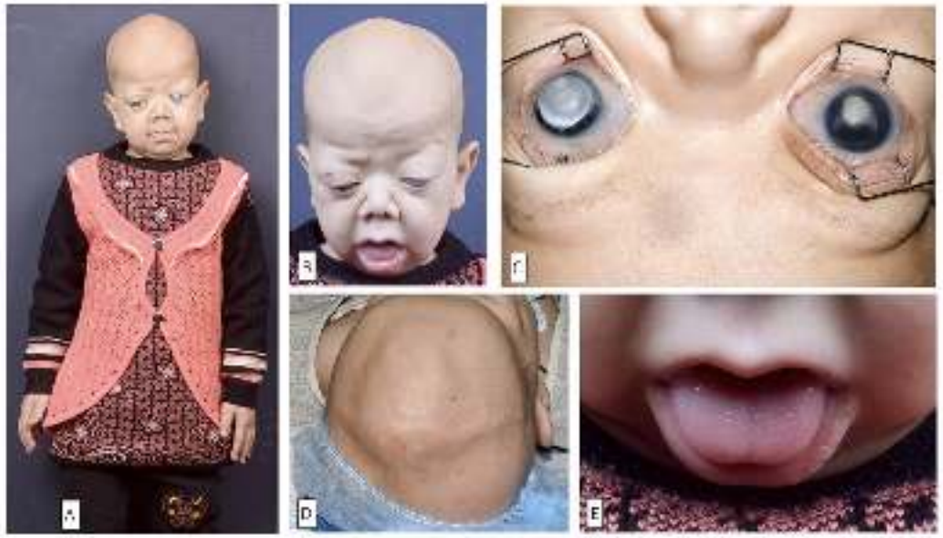


Fig 1. A. Phenotypic features of case 1. B. Facial features of GAPO syndrome. C. Ocular features showing Buphtalmos in both eyes, Central corneal opacities with Haab's striae in right eye, total luecomatous opacity of failed corneal graft in left eye. D. Frontal bossing. E. Protruding tongue

- Anodontia
- Wide open mouth
- Depressed nasal bridge
- Everted lower lip vermilion
- Early balding and Alopecia universals
- Hyperextensible skin
- Long philtrum
- Fluffy face
- Moderate height
- Eyebrow hypertelorism
- Spaced and thin eyebrows/eyelashes

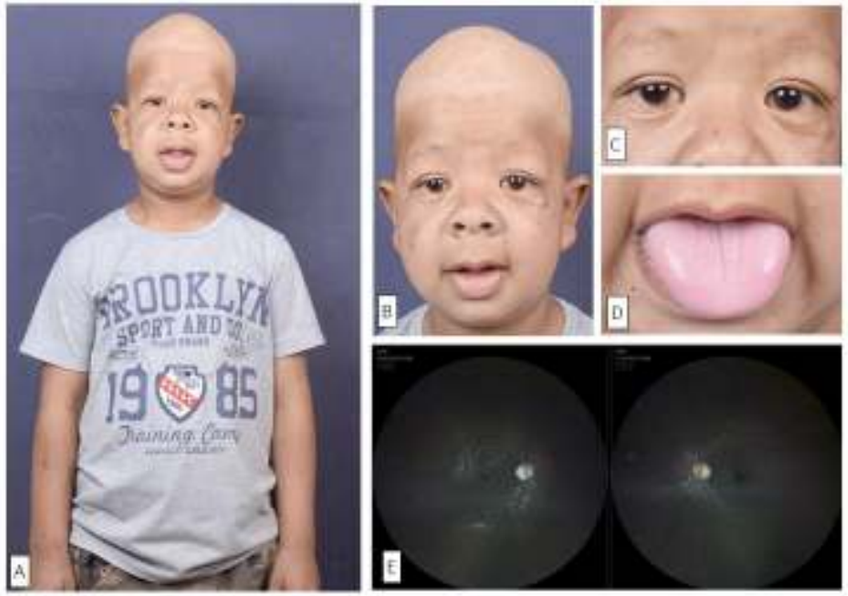


Fig 2. (A) Phenotypic features of case 2; (B) Facial features of GAPO syndrome; (C) Ocular features showing Flat nasal bridge, telecanthus, Buphtalmos in both eyes; (D) Protruding tongue. (E) Fundus image showing near total glaucomatous cupping in Right eye and early disc damage in left eye

The GAPO syndrome (OMIM ID: 230740) is a rare AR disorder from 1947 till date a total 35 cases have been reported

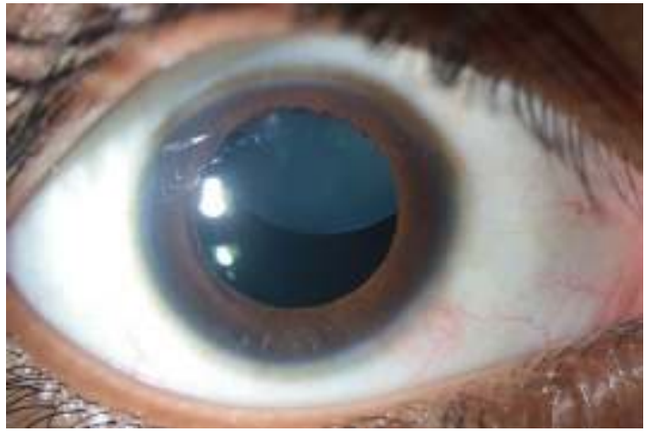
Gene & Transcript	Variant	Zygosity	Location	Disorder	Inheritance	ACMG Classification
ANTXR1 NM_032208.3	c.151_152+2delAAGT p.Lys51fs	Homozygous	Exon 1	GAPO syndrome [OMIM ID: 230740]	Autosomal Recessive	Likely Pathogenic PM2 & PVS1_Strong

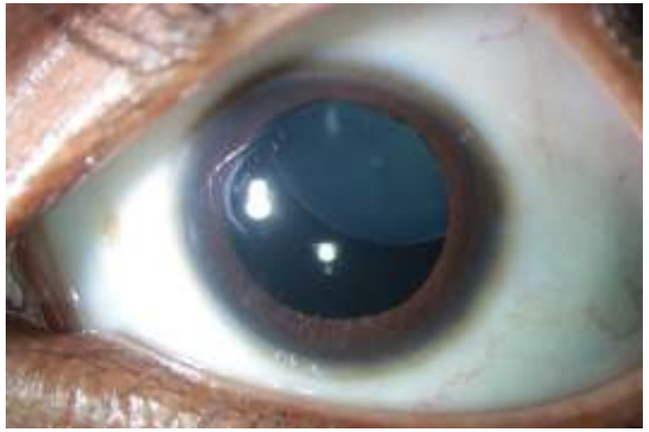
Identify metabolic problem
good phenotyping, systemic evaluation and genetic testing

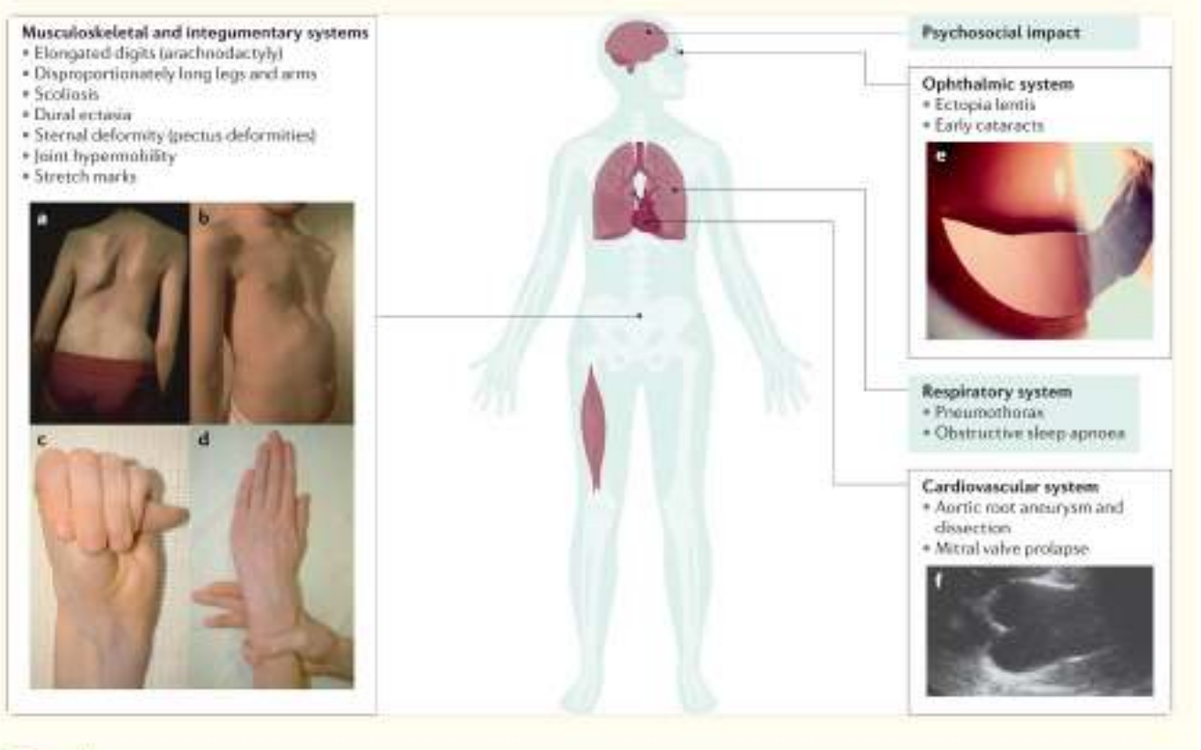
Anesthesia---Metabolic problem, Hydration, Cardiac, Hypercoagulation

Ectopia Lentis

- 17-year-old female, Marfanoid habitus
- BCVA: RE CFCF LE 20/250
- IOP: RE 23 LE 24 mmHg
- Gonio BE Open angles
- Fundus: RE CDR 0.8 LE CDR 0.7 Bipolar excavation



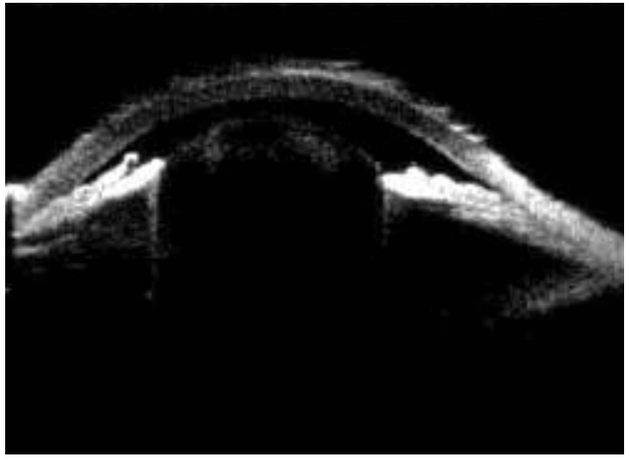


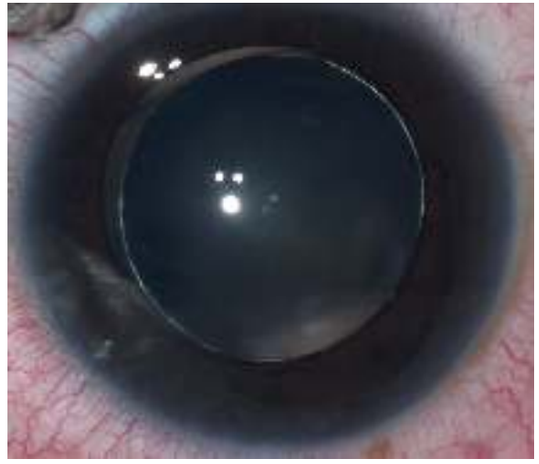


Cardiovascular System :

- Dissecting aneurysm of ascending aorta
- Mitral valve prolapse

Elastic fibers are found throughout the body, but are particularly abundant in the aorta, ligaments and the ciliary zonules of the eye; consequently, these areas are among the worst affected





Mutations in FBN1 gene---defective fibrillin-1

Present in microfibrils ---provide force-bearing structural support in connective tissue

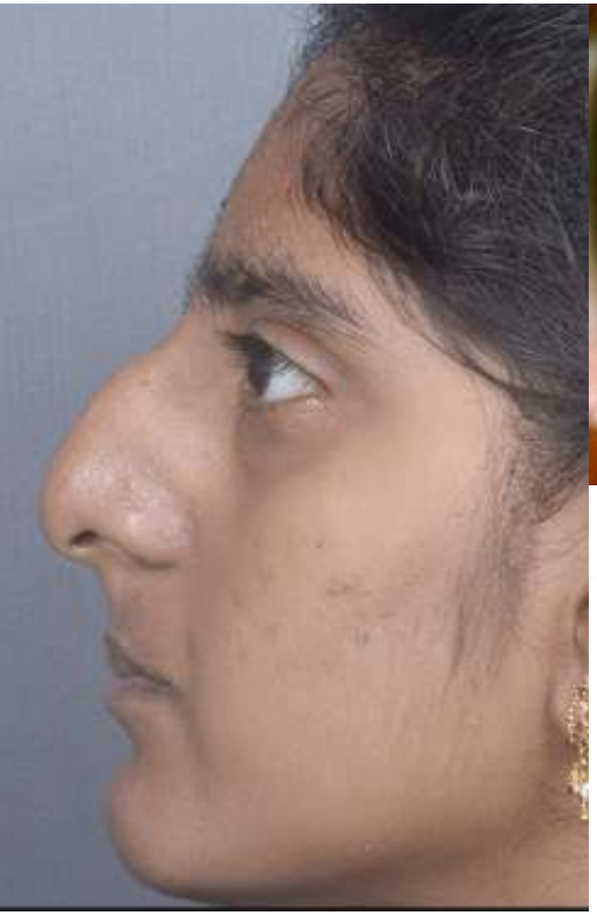
Gene & Transcript	Variant	Zygosity	Location	Disorder	Inheritance	ACMG Classification
FBN1 NM_000138.5	c.3874C>G p.Leu1292Val	Homozygous	Exon 32	Weill-Marchesani syndrome 2, dominant [OMIM ID: 608328]	Autosomal Dominant	Uncertain significance PM2, PM1 & PP2
				Marfan syndrome [OMIM ID: 154700]		

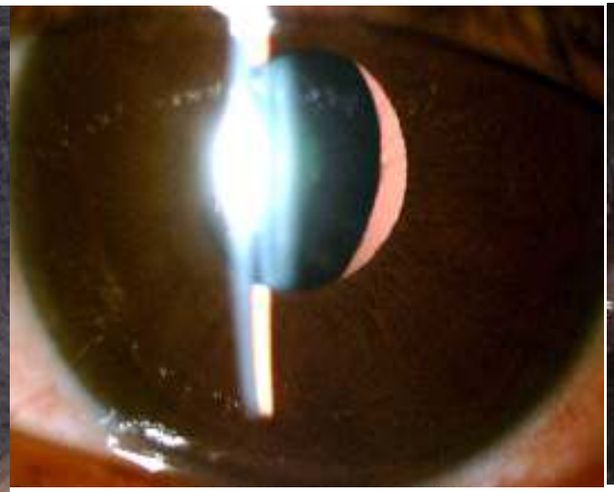
Joint stiffness, Cardiovascular defects (patent ductus arteriosus, pulmonary stenosis, thoracic aortic aneurysm, cervical artery dissection

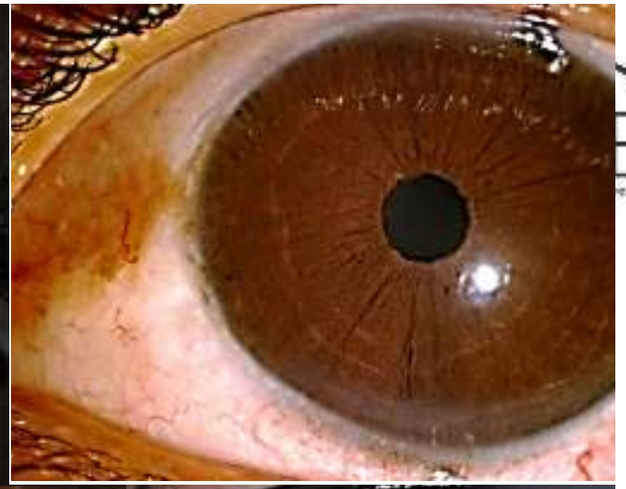
ASPH associated Ectopia lentis

- ASPH gene: a candidate gene for Traboulsi syndrome
- ASPH gene is located on chromosome number 8 (chr8q12.3)
- Autosomal Recessive inheritance
- Calcium homeostasis, Hydroxylation
- Lebanese, Saudi Arabia, Indian

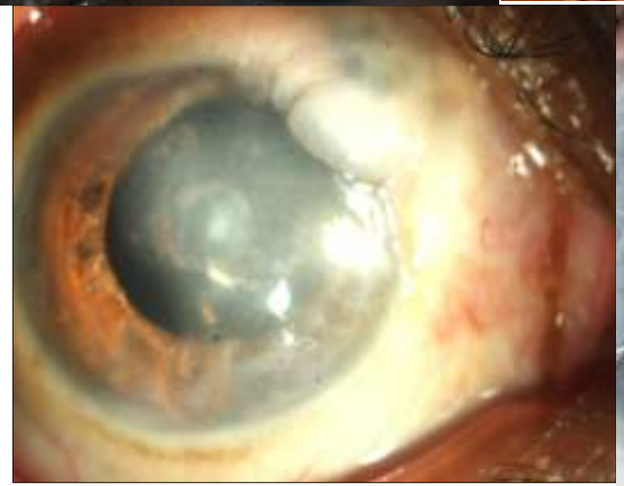
Shawaf 1995, Patel N, Khan AO et al. 2014, Senthil S 2020, Chandran P 2019,







- ✓ **F**acial **D**ysmorphism
  - Large beaked nose
  - High nasal bridge
  - Deviated nasal ridge
  - Malar flattening
  - Antimongoloid slanting of palpebral fissures,
  - Retracted chin
  - Cardiac problem

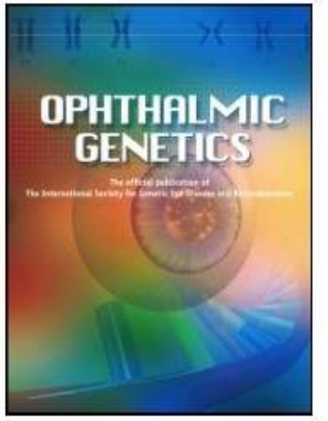


- ✓ **L**ens Dislocation
- ✓ **A**nterior segment abnormalities
- ✓ Spontaneous filtering **B**lebs

A novel mutation in the aspartate beta-hydroxylase (*ASPH*) gene is associated with a rare form of Traboulsi syndrome

Sirisha Senthil , Sarmeela Sharma , Sushma Vishwakarma & Inderjeet Kaur

Distinct Novel variant associated with cardiac problem



Clinical Features	Shawaf et al.						Haddad et al.				Mansour et al.	Patel et al.	Abarca et al.	Chandran et al.	Cheng at al.	This study		
Patients	1	2	3	4	5	6	1	2	3	4	1	1	1	1	1	1	2	3
Sex	F	F	F	M	M	F	F	F	F	F	F	F	M	M	M	M	F	M
Age	15>74						28>44				16	19	13	35	35	24	22	24
GENETIC VARIANTS							c.2424C > T				c.1941_1945 delinsGGG	c.171G > A	c.1943_1947 GGACT	c.2131delA	c.1853 T > A	c.1853 T > A	c.2425 G > A	
EFFECT OF VARIATION/MUTATION							Changes conserved AA residue				Affects ASPH oxygenase domain	u	u	Affects ASPH oxygenase domain	Nonsense-mediated decay of the ASPH transcript	Nonsense-mediated decay of the ASPH transcript	Changes conserved AA residue	
	Beaked Nose	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Mouth	Malocclusion/crowded teeth	-	+	+	-	+	+	+	+	-	+	ns	+	-	ns	ns	+	-	+
	High palate	-	-	-	-	-	-	ns	ns	ns	ns	ns	ns	-	ns	ns	+	-	+
Others	Long slender fingres	ns	ns	ns	ns	ns	ns	+	+	+	+	ns	ns	ns	ns	-	-	-	-
	Cardiovascular anomaly	ns	-	-	-	-	-	ns	-	ns	ns	-	-	-	-	-	+	+	-

Diagnosis is challenging

Ectopia lentis is diverse

Associated systemic problems

Deep phenotype and arrive at proper diagnosis

Evaluate siblings and parents

Challenges: Anesthesia, Systemic problems

Anesthesia

Micrognathia
large tongue
short neck
difficult intubation
central apnoea

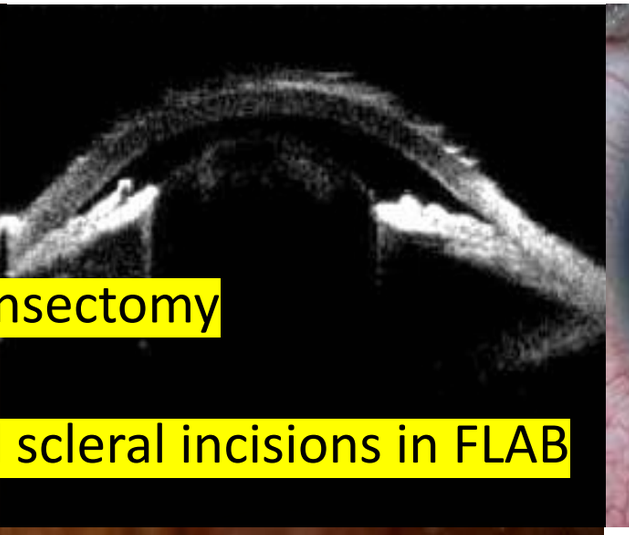
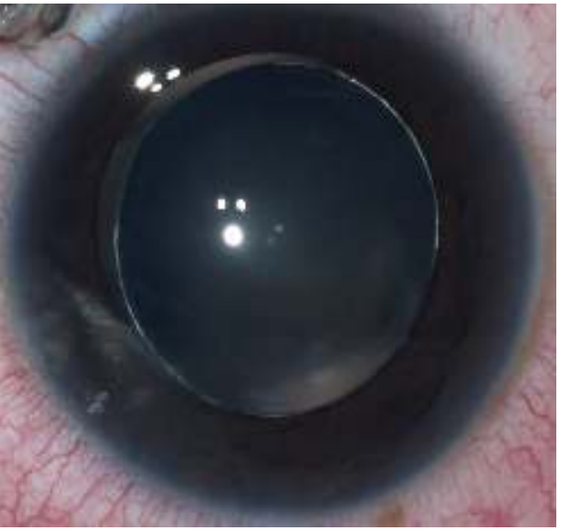
Cardiac/
renal/CNS
involvement

Coagulation
profile
abnormal

Homocystenemia
Metabolic problems
Endocrine disorders
(Hydration, sleep
apnoea)

Neuromuscular
disorder
Anemia
Seizures

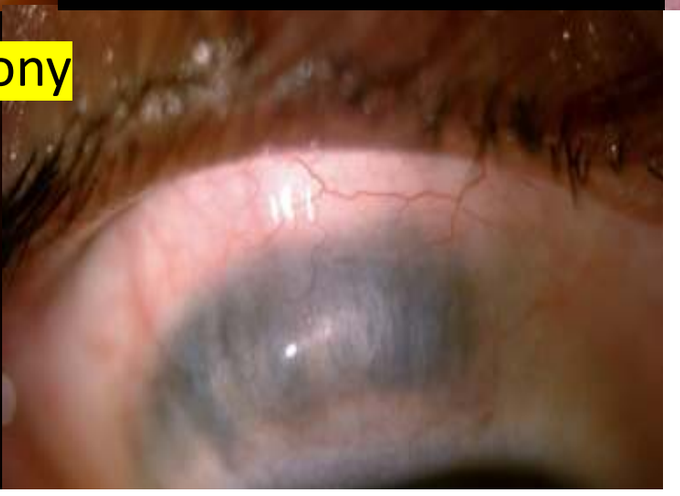


ECTOPIS LENTIS– will need lensectomy

Lensectomy is needed– avoid scleral incisions in FLAB



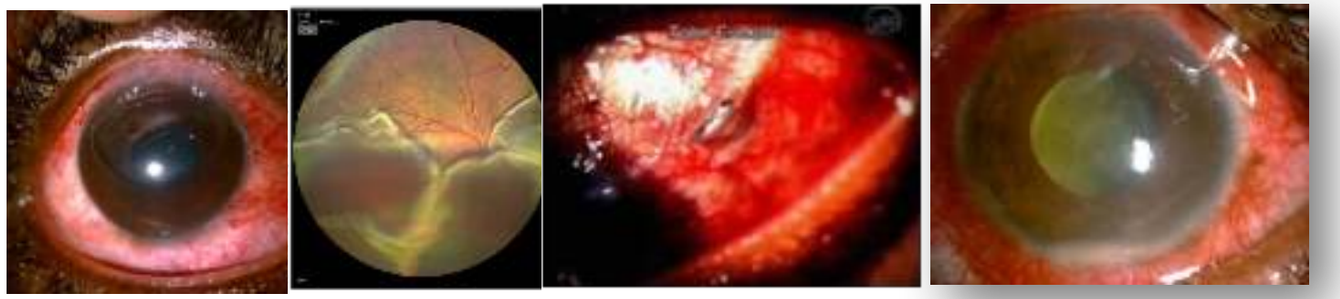


SCLERAL REPAIR for Hypotony

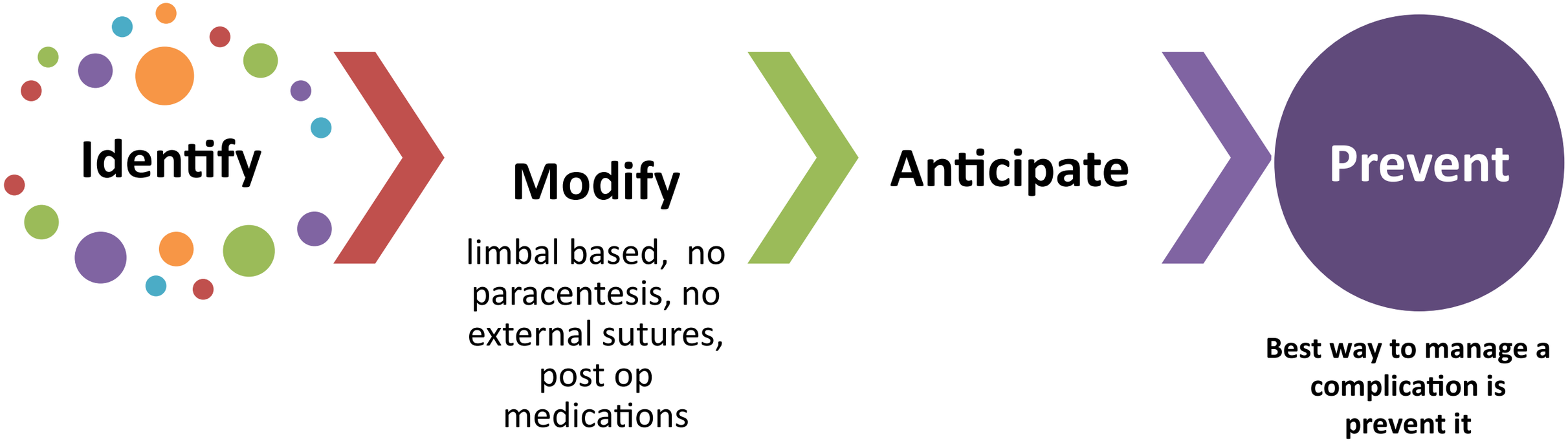
Glaucoma is refractory: Often they are associated with difficult and refractory Glaucoma, early diagnosis is the key and life long follow up

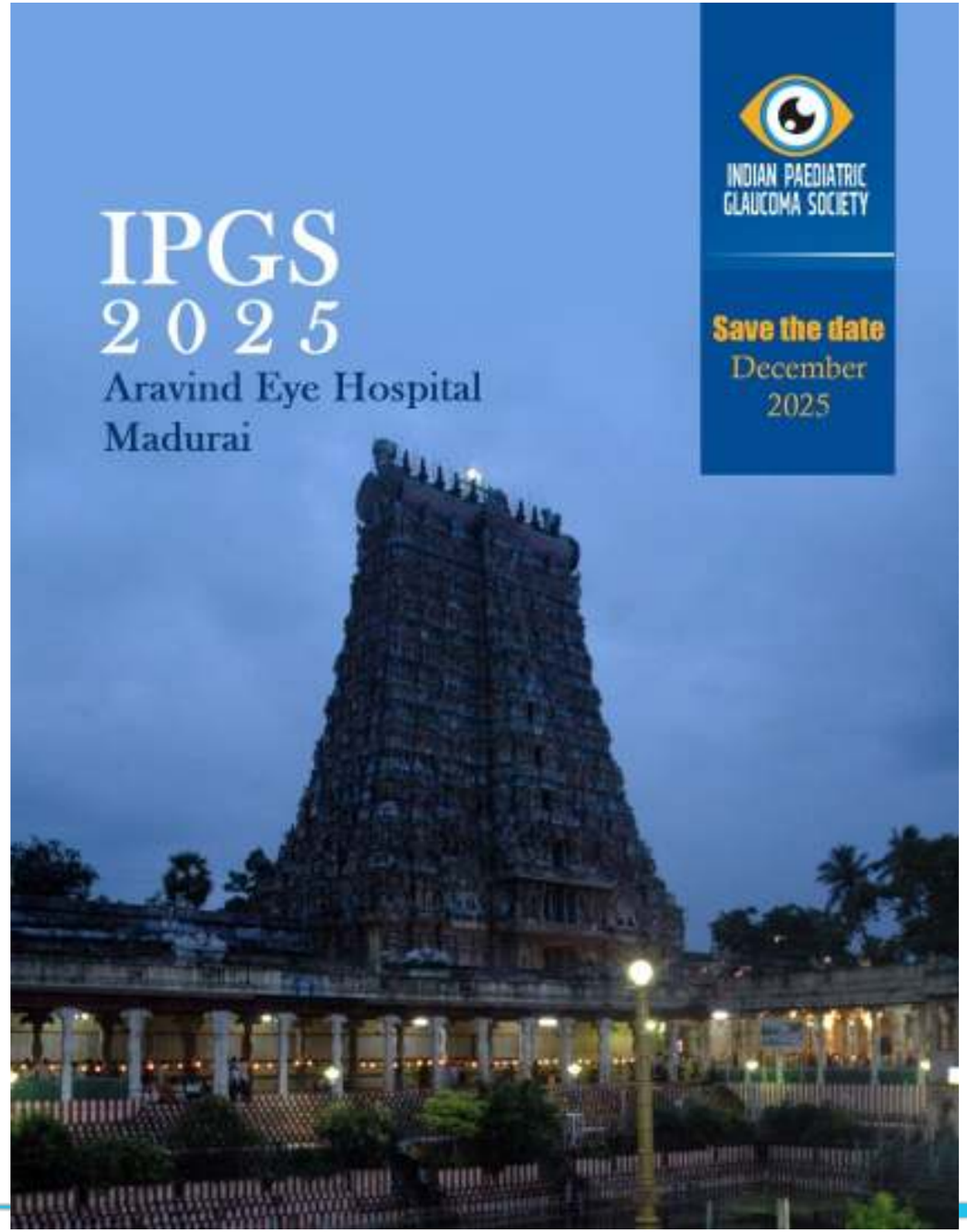
- **Surgery is complex**
- **Altered anterior segment anatomy**
- **Greater risk for failure**
- **More complications**
  Enlarged eye, stretched sclera, low scleral rigidity, they react adversely to hypotony
- **Difficult postoperative course**
- **Long term postop management**

Trab+ Trab	Gonotomy	GDD	TSCPC
• Prevent infection, limbal based, no MMC,	• Extent, Suture removal	• Tube related and plate related, conjunctival and corneal complications and hypotony	• Careful TSCPC • Location • Extent • Post op medications



Summary……


Identify
Modify
limbal based, no paracentesis, no external sutures, post op medications
Anticipate
Prevent
Best way to manage a complication is prevent it

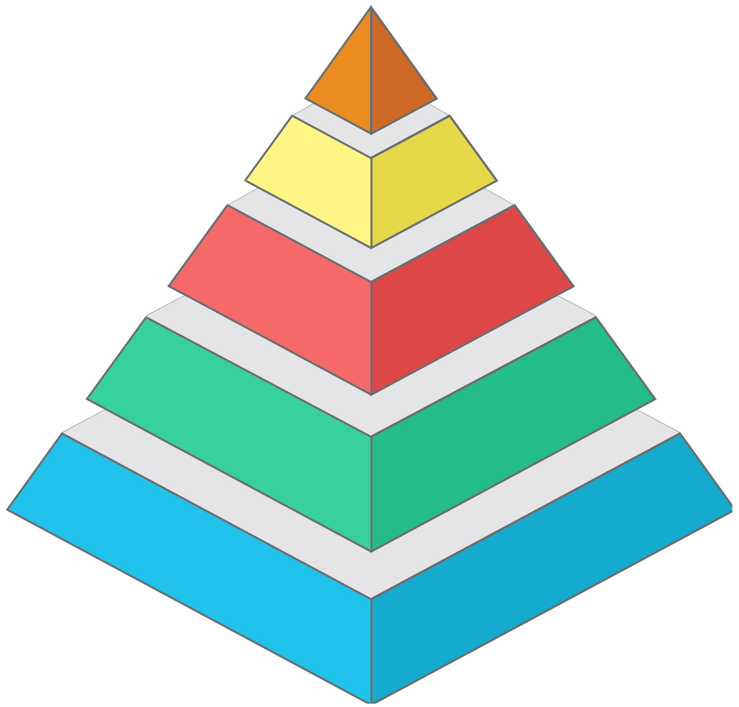


Welcome to INDIA

December 2025!

LVPEI
So that all may see

L V Prasad Eye Institute



Thank You