

WWW 12 Panellists



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1. In developing countries, is it better to do WES instead of gene panels?

AOK: it depends on what the phenotype is. In general, if the phenotype allow you do to specific testing, it is better to do that specific testing. However, if the phenotype has many possible genetic causes (e.g. non-specific retinal dystrophy), WES may be more appropriate. The major problem with WES is interpretation and the possibility of uncovering things you were not expecting to find.

KKN: If you have a strong clinical suspicion as to what the diagnosis is, then you are better going for a panel. Some panels, e.g. for inherited retinal diseases will include genes for familial vitreoretinopathy (FEVR) too, so it is worth checking which genes are covered in the specific panel. This avoids the issues that a Whole exome sequence (WES) can raise such as incidental findings that can be clinical significant. For just such an example please see To LK, Shah PR, Scanga HL, Franks AL, Cladis FP, Nischal KK. Personalized pediatric ophthalmology: a case report. *J AAPOS*. 2019;23(4):234-236. doi:10.1016/j.jaapos.2019.03.003. However, WES, can be worth doing if the clinical suspicion or diagnosis is not robust.

HS: The detection rate of targeted gene panels in ophthalmology is quite good and can be the best option when you have a solid phenotype. Targeted panels also limit the “surprise factor” of unanticipated findings or revealing abnormalities unrelated to the reason for testing (which is a significant risk in WES).

WES is an excellent tool to obtain a larger amount of genetic information about a patient or family in comparison to a phenotype-driven gene panel. However, WES comes with additional burdens including counselling and opt-in/opt-out options for incidental findings (e.g. *BRCA1* mutation, cardiomyopathies, etc.) and carrier status, trio sample collection, risk of identifying additional variants for which there is little to no information available, and the ability or need to revisit/reanalyse data in the future. All things considered, WES can be a good option for a patient who may only have one opportunity to pursue genetic testing, especially for those who are suspected to have a complex phenotype or more than one suspected genetic disorder.

ASK: **Irrespective of the country where you work**; you need to consider WES only if you are not able to make a clinical diagnosis or when the clinical features don't fit in to any specific diagnosis or when there is overlap of many findings that don't fit in to any known syndrome or genetic condition.

WES may reveal many unanticipated information (incidental findings that may pose special set of new challenges in counselling the parents). Obtaining too much information may not always help if the information is not reliable or dubious or may forewarn about some other problem for which the patient is still asymptomatic.

It all depends upon how sure you are about the phenotype. **Hence thorough documentation of the phenotype and extensive literature search may help you narrow down your clinical diagnosis and will give you what set of genes you could consider testing.**

Take cost also in to consideration.

To summarize, when you suspect a specific disorder associated with a small number of genes using a single gene or gene panel is better. However as explained above if it is genetically heterogeneous, you can consider a gene panel.

DBG: Sorry I don't understand; WES Gene panels are useful when the panel is adapted to the phenotype as anterior syndrome panel or retinal dystrophies panel

2. What metabolic work up would you do for bilateral cataracts?

AOK: For bilateral congenital cataract, I would do good physical examination, history, and follow-up. I would also examine the parents. If all normal, I would not pursue further. However, if the child has any co-morbidities then further workup is important. I prefer whole-exome sequencing with the parents' samples for confirmatory analysis.

KKN: This is a great question and one that can be answered by looking at three factors;

Age at onset – congenital cataracts with microcephaly or heart problems or other system problems: TORCH/VDRL - if these are negative then check Chromosomes.

Congenital cataracts in an ill child with failure to thrive – if jaundiced Galactosemia; if hypotonic with or without seizures hypocalcemia, hypoparathyroidism.

Developmental cataracts in Older children (toddlers and above) – CTX, hyperferritinemia, Galactokinase deficiency.

HS: TORCH, VDRL, serum ferritin (for hyperferritinemia-cataract syndrome), serum calcium and phosphorous (for hypoparathyroidism), red cell galactokinase, and either GALT enzyme tests or urine for reducing substances (for galactosemia).

ASK: If any one of the parents has congenital cataracts or developmental cataracts and if the parents are systemically normal and if the morphology of the cataract does not provide any suspicion or suggest a metabolic aetiology, I would do only those tests that are required for the anaesthetic work-up prior surgery.

If I suspect a metabolic aetiology, I would consider the following basic tests:

Urinalysis for reducing agents and organic amino acids

Plasma galactokinase levels

Complete-blood count and Liver function tests and Blood routine.

DBG: First you have to eliminate galactosemia, then cholestanol must be tested as there is a treatment, MPS as well

3. Any considerations in causes of patient with bilateral congenital cataracts, sensorineural hearing loss, devpt. delay?

AOK: Yes! This definitely needs workup. There are many potential causes, including genetic (e.g., peroxisomal disease) and non-genetic (infection). If infection is not likely, I prefer whole-exome sequencing with the parents' samples for confirmatory analysis.

KKN: It is important to have a geneticist or a paediatrician evaluate such a child. These findings could be due to a TORCH infection but if it is due to a genetic condition then it is likely one that affects metabolising tissues; so things like peroxisomal diseases but this is the kind of situation where whole exome sequence can be helpful.

HS: There are many potential genetic diagnoses linking these symptoms together. An approach to genetic evaluation cases with multiple findings could include chromosomal tests (SNP microarray) and a large gene panel for nonsyndromic and syndromic forms of cataracts.

ASK: There are few conditions that can cause this combination.

Rubella is common in developing countries as a non-genetic cause of the above findings.

Alport syndrome, Alstrom syndrome, BOFS, Cockayne syndrome, Fabry disease, Incontinentia pigmenti, NF2, Refsum, Norrie, stickler and Marfan are some of the conditions. However most of these have other striking identifying features that help you in making the diagnosis. I would recommend you to read an excellent article by Dr. Anya Trumler to know about the systemic associations of cataracts

DBG: Must be evaluated with other clinical signs (as microcephaly, T21, trisomy13, rubella...) so a cytogenetic exploration and TORCH analyses must be performed first however it could be

- (a) Lowe syndrome+++
- (b) Some special clinical form of Stickler syndrome
- (c) Aymé-Gripp syndrome is classically defined as the triad of bilateral early cataracts, sensorineural hearing loss, and characteristic facial features in combination with neurodevelopmental abnormalities
- (d) Congenital macrothrombocytopenia, MYH9-related disease+++
- (e) Huppke-Brendel syndrome
- (f) rarely Uscher syndrome as congenital cataract is unusual at the opposite of hearing loss
- (g) Dominant WFS1 mutation (Wolfram syndrome)
- (h) Vici syndrome
- (i) mitochondrial disease with disulfide relay system anomalies

4. How does heterozygous *cyp1b1* in PCG occur?

AOK: Heterozygous CYP1B1 mutations do not cause disease in isolation.

KKN: as far as our knowledge base is concerned at present heterozygous mutations in CYP1B1 do not cause primary congenital glaucoma; it may be that as of now we have not worked out if PCG can be caused by interaction of mutations in two different genes -this is called digenic inheritance.

HS: An individual who is heterozygous for a *CYP1B1* mutation is typically viewed as a carrier and should not have primary congenital glaucoma. If a patient with primary congenital glaucoma is heterozygous for *CYP1B1*, this may indicate that the genetic diagnosis is correct but that the second mutation was unable to be detected by the testing method. Alternatively, the patient could have primary congenital glaucoma for another reason and this was an incidental finding. There is a role for heterozygous *CYP1B1* mutations in primary open angle glaucoma (POAG), where heterozygosity has been hypothesized as a risk factor for development of POAG.

ASK: PCG caused due to homozygous mutations or compound heterozygous mutations in *CYP1B1* and are inherited in an autosomal recessive manner. If only one mutation is found in a patient with a known autosomal recessive disorder, the following reasons need to be considered

Not able to sequence the other mutation if the gene itself was deleted. A deletion duplication analysis needs to be done to find out if the second allele was deleted. 90-95 % can be detected by sequencing and 5-10 % can identify a deletion of the entire gene which cannot be detected by sequencing.

Need to look if there is involvement of any other gene causing PCG. (FOXC1, BMP4, LTBP2 OR TEK)

Sometimes patients who harbour heterozygous mutations both in *CYP1B1* and *MYOC* have shown to develop severe POAG. *CYP1B1* may act as a modifier of *MYOC* expression and that these two genes may interact through a common pathway. The role of *MYOC* alone in causing PCG is not conclusive as most patients also had simultaneous mutations in *CYP1B1*. Wrong sample and wrong naming.

DBG: Usually inherited in an autosomal recessive pattern, if it occurs as a PCG with heterozygous mutation, a deeper exploration may find another mutation on the second allele.

5. What was the first symptom that raised the possibility of the Alagille syndrome of the first case?

ASK: It was the history of cardiac anomaly in the child and the cardiac anomaly and the intra cranial bleeding in the younger child that suggested the possibility of Alagille syndrome. The visual complains of the patient did not suggest the possibility of Alagille. The presence of posterior embryotoxon and the RPE mottling along with the history prompted the diagnosis. Examining the records of the younger sibling helped to clinch the diagnosis.

6. Is it necessary to do genetic analysis in all cases of congenital glaucoma?

AOK: Diagnosis and management of an individual child with primary congenital glaucoma does NOT need genetic testing. However, if genetic counselling is desired and reasonable given the family structure, genetic testing is indicated. Also, if there are co-morbidities, genetic testing is useful to understand what the child may be at risk for.

KKN: no. The important thing is to make a clinical diagnosis, treat the patient to control the intraocular pressure.

HS: Genetic analysis in congenital glaucoma is an option, but not always necessary. As outlined by Dr. Khan, diagnosis and management of primary congenital glaucoma does not require a genetic test. However, genetic analysis in these cases can play an important role for families seeking genetic information for future family planning. It is important to consider that if there are extra-ocular abnormalities in addition to primary congenital glaucoma, there may be a genetic basis (related or unrelated) and genetic evaluation becomes more necessary. Alternatively, if the phenotype does not appear to fit PCG exactly, it may be useful to pursue genetic analysis to confirm a diagnosis.

It remains worthwhile to consider genetic testing in cases of developmental glaucoma as there are several syndromes featuring anterior segment dysgeneses and a constellation of extra-ocular features that are subject to screening or ongoing medical surveillance.

ASK: Genetic analysis is not required to make a diagnosis of PCG. It is a clinical diagnosis. Some of the reasons include:
If the diagnosis is in doubt

If the parents are planning another child when the first child is already having PCG, especially if the parents have had a consanguineous marriage or if the incidence of PCG is high in an ethnicity.

To identify the cause as in to differentiate between X linked Megalocornea and LTBP2 (AR inheritance) as the prognosis greatly differs between the 2 conditions and it also might help the family in taking better family planning decisions.

DBG: Of course not useful in practical life however interesting in PCG families. It appears only as a bonus in the idea for the future offspring of the child

7. It is a package of findings, cornea-pressure-myopia?

AOK: I think the question is 'if increased intraocular pressure causes both corneal enlargement and myopia'? The answer is yes.

KKN: so if I understand correctly, you are asking 'if the diagnosis of PCG is like a jigsaw puzzle where all the signs must fit'? So enlarged cornea, with raised IOP and subsequent myopia are all pieces of the jigsaw that help make the diagnosis.

HS: Unfortunately, I am unsure of the question being asked

DBG: In babies high IOP induces increased axial length

ASK: I do not understand the question fully. The diagnosis of PCG is based on corroborative findings. (Corneal diameter, IOP, Disc, Anterior segment findings like Haabs striae, axial length and refraction). There are charts that can help you compare the change in the axial length and judge whether the increase in axial length is because of growth or because of uncontrolled glaucoma.

8. Does the presence of PCG alone justify Genetic testing?

AOK: No. Genetic testing would be for genetic counselling, if desired, and if the family structure is suitable. Also, if there are co-morbidities, genetic testing is useful to understand what the child may be at risk for.

KKN: No; only if there is some confusion about the underlying diagnosis e.g. if a child has CHED but has been treated for Glaucoma, the genetic testing will confirm NO PCG and so the family is reassured. Otherwise there is no real indication for genetic testing when the diagnosis of PCG is made.

HS: Genetic analysis in congenital glaucoma is an option, but not always necessary. As outlined by Dr. Khan, diagnosis and management of primary congenital glaucoma does not require a genetic test. However, genetic analysis in these cases can play an important role for families seeking genetic information for future family planning.

ASK: Answer almost same as for question 6.

Genetic analysis is not required to make a diagnosis of PCG. It is a clinical diagnosis.

It is useful in the following situations and could be considered.

- a. If the diagnosis is in doubt
- b. If the parents are planning another child when the first child is already having PCG especially if the parents have had a consanguineous marriage or if the incidence of PCG is high in an ethnicity.
- c. To identify the cause as in to differentiate between X linked Megalocornea and LTBP2 (AR inheritance) as the prognosis greatly differs between the 2 conditions and it also might help the family in taking better family planning decisions.
- d. Along with genuine indications for testing, if the parents are also interested and can afford for the testing.
- e. Carrier testing for other members at risk may be considered. The proband need to be tested first.

DBG: Of course not useful in practical life however interesting in PCG families. It appears only as a bonus in the idea for the future offspring of the child

9. What is the youngest age of a patient that you've inserted an Ahmed valve?

AOK: 9 months' old

KKN: 12 months

ASK: I have not done Pediatric glaucoma surgeries in the recent past.

DBG: I prefer the smallest Van Baerveldt valve

10. Should we send for a specific gene or send for all the genes involved in the spectrum of Cong. Glaucoma?

AOK: It depends on where you live and whether or not there is a good panel available. If it is primary congenital glaucoma and a good panel is not available, CYP1B1 analysis is often sufficient.

KKN: There are gene panels that can cover the majority of genes known to cause PCG

HS: If you are practicing in an area of the world where primary congenital glaucoma is largely due to mutations in *CYP1B1*, there is likely to be a high diagnostic yield from a single test and it would be prudent to do. If you are practicing in an area of the world with diversity in your patient population, the diagnostic yield may increase by panel-based testing. The advancement in genetic technology has made it quite affordable to pursue a panel of genes all related to the congenital glaucoma phenotype. Pursuing a panel-based test is also more justified in the setting of anterior segment dysgenesis, where there are numerous involved genes with overlapping phenotypes and a panel would provide the highest chance of genetic diagnosis.

ASK: CYP1B1 is the commonest gene to be involved in PCG. It is very common in some ethnicities and less common in others. However, it is still the most common gene to be involved across most ethnicities as a cause of PCG.

You also need to talk regarding the panel that your genetic testing facility offers. You need to also consider the cost and turnaround time.

There are not that many genes implicated in PCG, so if the cost of the panel testing is not high, you can consider panel testing as it will provide results for all the genes tested in the panel simultaneous time. Since PCG can be caused by genes including FOXC1, a panel testing may reduce avoid any late surprises.

If you are considering individual genes, then you have to wait for the outcome of results of each gene tested and eventually take a longer time if the initial testing is not contributory. This becomes crucial especially If there is less time (if the mother is already pregnant with her second child) and wants to take a decision regarding the current pregnancy, a panel testing for the first affected child will be important to get results faster instead of sequential individual gene testing.

DBG: Gene oriented AS panel is better

11. Posterior embryotoxon is a very common finding. Does it require further evaluation?

AOK: Only a good exam and history, review of systems, and regular visits for IOP checks. If parents are available a slit-lamp exam is suggested. A very young child with this finding should be assessed for potential hearing loss as this is actionable.

KKN: in the absence of any other ocular signs such as corectopia, iris hypoplasia, 360 degree Posterior embryotoxon, I would not investigate further

HS: Defer to the ophthalmologists regarding clinical evaluation recommendations. Genetic evaluation should not be pursued on the presence of posterior embryotoxon alone.

ASK: Isolated posterior embryotoxon in a patient with otherwise normal findings (with no systemic concerns both in the child and in the family) along with normal ocular findings in the parents needs just periodic follow-up at 6 months-1 year for IOP and fundus evaluation. Gonioscopy can be considered if the embryotoxon is very prominent and if the child is able to cooperate for the procedure.

DBG: Just IOP regular evaluation

12. Is it easy to measure Plasmatic cholestanol?

AOK: This lab test requires a specialized lab.

KKN: you need a lab that can run the test. I don't know how easy or difficult that is across the globe in the various regions.

HS: Plasma cholestanol testing may be offered by a laboratory that tests for biochemical abnormalities. While the test may be a rare request, it is run on the same systems (GC-MS) as other biochemical tests and is likely to be available. Typically, patients with cerebrotendinous xanthomatosis (CTX) have cholestanol levels 5 to 10 times the normal value.

ASK: I do not have any personal experience in doing this test.

DBG: Only some specific lab can make the dosage of cholestanol

13. Which specific amino acid in urine do you order for Lowe syndrome?

AOK: I would not ask for a specific urine amino acid if this diagnosis is suspected; I would prefer genetic testing and request a simple urinalysis. I would defer more specialized metabolic testing to a pediatric metabolic specialist.

KKN: It is not a single amino acid but aminoaciduria that helps with the diagnosis; however genetic testing can make the diagnosis more robustly

HS: Lowe Syndrome cannot be diagnosed by a single analysis in urine; however, aminoaciduria occurs due to the associated renal disease. While there are enzyme assays to diagnose Lowe Syndrome in skin fibroblasts, that would be an invasive method for diagnosing the condition. Genetic testing for Lowe Syndrome is very sensitive and detects at least 95% of cases in affected males. However, urinalysis does have a role in Lowe Syndrome as these children have renal tubular disease (Fanconi type) and proteinuria, albuminuria, and aminoaciduria may be present quite early on.

ASK: They have generalised aminoaciduria including organic aciduria. Aminoaciduria is assessed by using ion exchange chromatography. Urinalysis needs to include urinary electrolyte levels (including urine phosphorous and calcium levels), blood urea and serum creatinine. Urine is also checked for low molecular weight proteinuria (LMWP) and albuminuria.

DBG: In Lowe syndrome we observe generalized aminoaciduria

14. So if the systemic findings come later, then how do we predict cerebrotendinous xanthomatosis?

AOK: These children often have infantile intractable diarrhea. This question (if there was intractable diarrhea) should be asked of any child with juvenile cataract. Juvenile acquired cataract in general should trigger suspicion for metabolic disease in the differential diagnosis. Any evidence for developmental delay in a child with juvenile cataract increases the concern for underlying metabolic disease. If a child is otherwise normal, developmental should be continually followed and any suspicion for the diagnosis should trigger work-up.

KKN: any child with bilateral cataracts that has had or is having diarrhoea should be evaluated for CTX

HS: Ophthalmically, the cataract may evolve over time indicating that there is a metabolic component. An important medical history question for infants is infantile onset diarrhea (can be chronic or intractable). If cerebrotendinous xanthomatosis is suspected, a laboratory evaluation for elevated plasma cholesterol can be performed.

ASK: Personally, I have not seen a patient with Cerebrotendinous xanthomatosis and so I do not have any personal experience. So whatever I suggest would be only information that I know from what literature and textbooks describe. Literature describes infantile onset diarrhoea as the main initial presentation.

DBG: If the cataract appears progressively

15. How do you manage linear sebaceous nevus? Optical iridectomy?

AOK: It depends on the phenotype. Optical iridectomy is a potential treatment.

KKN: I have done corneal transplants in the past for 2 cases. The operation was technically very demanding and since if I have been able to, I prefer to do abroad iridectomy inferiorly

HS: Defer to the ophthalmologists regarding ophthalmic recommendations. If you suspect Linear Sebaceous Nevus Syndrome, it is important to evaluate the child for extra-ocular features including congenital cardiac and congenital renal malformations, neurology evaluation with neuroimaging, dermatology for monitoring of the skin lesion appearance, and oncology evaluation for the increased risk of neoplasia.

ASK: There is no direct management of the linear sebaceous nevus, which is a cutaneous manifestation of the syndrome. They usually have epibulbar complex choristomas and may have fundus lesions slightly mimicking flat choroidal osteoma. This appearance is basically because of intra scleral cartilage.

These children often have dense amblyopia. Optical iridectomy though may be considered in selected patients, if there is a possibility of allowing a clearer visual axis. However, because of the other coexistent abnormalities, there may be limited benefit in a very limited number of patients.

I have personally not done an Optical iridectomy in such patients though I felt it would have improved in one of my patients. However, the parents were not keen as I had explained to them that the amount of improvement may be only slight, not predictable and may not be very significant.

DBG: Cyclosporine to limit neovascularisation and corneal graft

16. Could the panel teach us how to discuss genetic tests, when positive?

AOK: This is a large complicated topic that cannot be answered in a few sentences. A genetic counsellor is very helpful in this situation.

KKN: this is a VERY DIFFICULT question to answer. I use genetic counsellors to do this.

HS: Unfortunately, that is out of the scope of this presentation. It is important to ensure that patients are receiving a detailed discussion of the results of any tests. The results of genetic testing can be straightforward or complicated and have a psychosocial overlay (both from individuals and within families) and it may be necessary to refer patients to genetics providers for these discussions, if available.

ASK: I am answering this question assuming that the person who asked this question is either a general ophthalmologist or a Pediatric ophthalmologist / Retina specialist with interest in Ocular genetics but not having any formal training or experience in counselling for Ocular genetic disorders.

Generally, we do not call genetic test results as positive or negative. A So called “positive” result may have a negative impact on the family or a “negative” test result may leave the family clueless on how to proceed further and may not have added anything new to the clinical diagnosis. For this reason, we refer the results as either “**contributory**” or “**non-contributory**”. Sometimes unanticipated new incidental findings not related to the present condition may be discovered.

It is imperative to have a counselling session prior genetic testing (**Pre-test counselling**) is considered and ordered in which all the possibilities and expectations are addressed including no added benefit from the testing. These aspects need to be clearly understood by the adult patients and parents to avoid any disappointment following test results. Addressing all the issues in pre-test counselling will help the parents and patients to have a genuine expectation regarding the test results.

Next step is proper **interpretation of the genetic test results**. This requires knowledge and experience and comes for everyone with time with formal training. Sometimes it may be difficult even for the experienced.

Disclosing test results is the third step. (**Post-test Counselling**) It is a complex process and is not easy to communicate as an answer in a paragraph. Unless you have received a formal training in genetics or if you have a well experienced genetic counsellor working with you and you have sufficient time in your practice, you should preferably not do the counselling.

To say in simple words, you should not order a genetic test, if you cannot either interpret or counsel the patient either by yourself or if you do not have a genetic counsellor who can do it for you. It may actually cause more harm to the patient than benefit.

One should not forget the possibility of medico-legal litigations if a wrong / improper counselling or guidance is provided apart from the harm that it may have caused the family.

It would be better to refer the patient to an ocular geneticist or to your paediatrician friend with genetics sub-speciality. You can learn from your genetic specialist and over a period of time or you can have a well-trained genetic counsellor with you. If you do provide care to a lot of ocular genetic patients in your practice, I would recommend that you need to consider seriously doing an Ocular Genetic fellowship! You will truly find the difference what you can achieve and what you can bring in the life of your patients and their families!

DBG: Phenotype must be compare to genotype and you can drive a multidisciplinary staff with the geneticists

17. Does metabolic related cataract not present at birth?

AOK: Typically, metabolic cataract is juvenile rather than congenital as the abnormal metabolites accumulate.

KKN: usually develop after birth. The important exception is galactosemia. Other rare ones may also but the child is always unwell with failure to thrive.

HS: Defer to ophthalmologists. However, it is to be noted that visually insignificant opacities can progress and evolve in infancy and early childhood, indicating the metabolic basis of the cataract.

ASK: Some metabolic cataracts present at birth or early infancy. Galactosemia and Lowe syndrome can present with early cataract. I think this question is related to the later cataract presentation in **Cerebrotendinous xanthomatosis**. I do not have any personal experience in patients with this condition.

DBG: Usually metabolic related cataract appears usually progressively

18. What is the significance of adult patients with Xmas tree like cataracts?

AOK: It is not necessarily the sign of a systemic disease when age-related. Juvenile Xmas cataract is associated with myotonic dystrophy.

KKN: it is not always associated with a systemic disease when seen in adults. But when seen in children it may be due to myotonic dystrophy

HS: Christmas tree cataracts are associated with Myotonic Dystrophy, which in its mildest forms is associated with the cataract and an inability to release a hand grip while in its more severe forms is associated with muscle weakness, cardiac arrhythmia, respiratory disorders, intellectual disability, and other health issues. Myotonic Dystrophy is a triplet repeat disorder, where the genetic abnormality is a repetitive sequence and the number of repeats is associated with disease severity and onset (more repeats is associated with more severe disease and earlier onset). These repeats have the potential to expand between generations, leading to more issues in future generations. Therefore, it would be prudent to consider Myotonic Dystrophy in cases of Christmas Tree Cataracts, even in adults.

ASK: Christmas tree cataract consists of highly refractive multicolour "needles" crisscrossing the lens fibres of the deep cortex. The diffraction phenomenon causes this multi-coloured appearance and is mainly due to cysteine. It may be found in adult patients without causing significant visual concerns. It may be a part of myotonic dystrophy and can be diagnosed base on the other findings of myotonic dystrophy.

DBG: Myotony as Steinert disease