Answers to Audience Questions - WSPOS Worldwide Webinar 14:
Aniridia

WWW 14 Panellists


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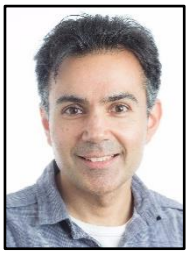
Neil Lagali

Dominique Brémond-Gignac *(DBG),* David Walton *(DW)*, Neil Lagali *(NL)*, Ken K. Nischal *(KKN* Hannah Scanga (*HS*)

1. **Can foveal hypoplasia be picked up pre-operatively?**

DBG: OCT is not feasible as cataract is present. Nystagmus can be an indirect sign however some cataracts without foveal hypoplasia can be observed.

DW: yes, no foveal landmarks

KKN: In children and patients with nystagmus trying to pick up foveal hypoplasia by OCT is not easy. If there is a view of the fundus, then looking for the loss of normal vascular pattern around the fovea is an option. If the media, either cornea or lens are opaque then there is no way to assess the fovea. You cannot do it with ultrasound

HS: Yes – an absent or dull foveal reflex can be an indicator of foveal hypoplasia. If the child is able to cooperate without sedation, an OCT can confirm foveal hypoplasia.

2. **When do we operate for cataract when it's associated with Aniridia?**

DBG: It is a subtle balance with a remained clear cornea and the density of the cataract as the surgery will increase ARK (as the latest is the best).

DW: when visually significant

KKN: The progression of a cataract in aniridia is often easier to help decide when to operate. When a child presents to you for the first time it can be difficult to try and know whether the amount of vision that they have is due to foveal hypoplasia which as we discussed in the previous question can be difficult to assess if the cataract is dense enough or because the lens is cloudy. It's then difficult to know how much the lens is contributing to the decrease in vision. If your view of the fundus is hazy such that you cannot see the details of the blood vessels clearly then it's likely the child would benefit from cataract operation. I would recommend that cataract surgery in children with aniridia be done by somebody who is experienced in doing cataract surgery in children. The reason is that if these children have to be left aphakic because of a problem during the surgery then they are in really big trouble because they cannot use contact lenses and they're going to have to use aphakic correction in spectacles. It is possible to do a scleral fixated lens but I do not recommend these in children and only consider them once the patient is 21 years or older. Obviously if the cataract is completely white that it needs to be removed. Remember in these particular types of cataracts the chances of a split occurring in the lens capsule and going all the way around the equator is higher so you must have a strategy to try and cope with that and prevent that.

3. **Do you think a child with partial aniridia and the mother with a more extensive aniridia should be tested for PAX6 mutation?**

   DBG: If possible all patients should be tested as the mutation may not be exactly the same or could be other mutation than PAX6. The interest is also for the gene therapy

   DW: not essential

   NL: Yes, definitely. In addition to confirming PAX6 mutation, it is important to know where the mutation is in both mother and child, to determine if mosaicism exists and also to assess likelihood of progression.

   KKN: I think that the short answer is yes they should be tested for PAX6 mutation. I think that the other signs of aniridia when it is PAX6 related should also be looked for and these include nystagmus, corneal pannus, posterior or anterior sub capsular cataract, or posterior and /or anterior polar cataract together with foveal hypoplasia. if you have these signs then there is definitely going to be a PAX6 related issue.

   HS: Yes – While *PAX6*-related aniridia has a high penetrance, it has variable expressivity. The variability can be intra- or inter-familial and it is worth investigating even when the phenotype does not appear to "run true" in a family.

4. **Any difference in complications seen in partial & total aniridia?**

   DBG: Complicated question as we are working on it and also depends of the mutation

   DW: milder with partial

   NL: We have generally seen milder keratopathy and better vision in partial aniridia.

   KKN: This is a good question because I do not think that there is necessarily and difference in the complications except that the keratopathy I think is less severe in the partial aniridia. What I don't know and what I haven't seen published is whether the glaucoma is any different.

5. **Have you seen patient with bilateral ptosis with aniridia?**

   DBG: Of course, as it is noted in my presentation ptosis is part of the disease. It may be absent or partial at birth and increase with age

   DW: very common

   NL: Have seen many with bilateral ptosis.

   KKN: When I think back over my career I think that I have seen some but not the majority so yes I have seen bilateral ptosis but in older children and I don't know if that's because of inflammation Because I have not seen them when they are newborns with ptosis.

   HS: While rare, congenital ptosis has been associated with *PAX6*-related aniridia in the literature.

6. **How do you fix the IOL in a patient with aniridia and subluxated cataract?**

   DBG: Usually myopia is associated and the IOL may be not needed. The unique solution is scleral fixation however it will increase significantly ARK

   DW: scleral fixation

KKN: As in the question above I do not recommend sclerally fixating an IOL in a child.

7. **Do you actually get glare issues in these cases?**

   DBG: With the nystagmus glare is secondary

   DW: rarely

   KKN: I think the question is about whether you get glare in children who have aniridia with cataract but I think it may also be 'do you get glare in children who've had cataract operation and now have an IOL.' For the first part the amount of glare that they get I think is difficult for a young child to be able to communicate because they were getting glare anyway and I think it is a drop in central vision that helps decide if the cataract is significant. For the second part when you put the implant in the bag which you have to do in aniridia, often the remaining anterior capsule will opacify and the less lens epithelial cell clearance you do or polishing you do, the more it will fibrose and become gray and I find that this does indeed reduce glare when this happens. I do not like to use artificial iris in children with aniridia because the rates of glaucoma and complications in my opinion and in my experience are too high.

8. **When do you start cyclosporine in young patients?**

   DBG: Starting of cyclosporine is useful when signs of inflammation are observed

   DW: rarely

   KKN: I Use cyclosporine 0.05% as soon as I think there is enough inflammation on the ocular surface to warrant suppression of this and to encourage wetting of the eye. Usually this is by the age of around 8 or 9 but definitely by the teenage years. In the earlier years I find that some topical FML as low dose as three times a week is sufficient to suppress inflammation. it is important not to underestimate the role of inflammation from dry eye on the deterioration of the keratopathy

9. **Success of trabeculectomy in aniridia?**

   DBG: Glaucoma in aniridia is with a bad prognosis however trabeculectomy get good results. The main problem may be recurrence of the high pressure

   DW: excellent after 5 years of age

   KKN: In my hands I tried avoid trabeculectomy in aniridia because I am worried about the lens moving forward and touching the cornea. I have colleagues who do trabeculectomy but it is not my preferred choice of procedure.

10. **From what age would you consider doing a trabeculectomy in children?**

    DBG: Could be as early as in congenital glaucoma

    DW: greater than five years of age

    KKN: see above

11. **Does it imply that we get a baseline OCT in all children with aniridia to get an idea of varying degrees of foveal hypoplasia?**

    DBG: If feasible yes

    DW: unnecessary, but of interest

KKN: see question 1 for answer

HS: While the degree of foveal hypoplasia is static, it is worthwhile to obtain a baseline OCT to identify and grade foveal hypoplasia in suspected or confirmed cases of aniridia.

12. **Is congenital or familial foveal hypoplasia part of the aniridia spectrum?**

DBG: Foveal hypoplasia is part of PAX6 mutation sporadic or family history

DW: No

KKN: almost always

HS: *PAX6*-related aniridia (including foveal hypoplasia within the phenotype) is inherited in an autosomal dominant manner and it can certainly be an explanation in such a case. Isolated foveal hypoplasia has been rarely reported in the literature in association with *PAX6*. It is more likely that foveal hypoplasia is seen in association with mild or forme fruste findings, since *PAX6* mutations can result in a spectrum of disease including an intact iris.

13. **Is there a possibility of Aniridia without foveal hypoplasia?**

DBG: Yes, however unusual

DW: No

NL: Rare cases may have no detectable foveal hypoplasia, but foveal/retinal function may still be affected.

KKN: very rarely

HS: In my centre's experience, we have not observed a *PAX6*-related aniridia without foveal hypoplasia. Other genotypes that can cause iris hypoplasia (such as *FOXC1, PITX2,* and other anterior segment genes) can cause iris abnormalities in the absence of foveal hypoplasia.

14. Could the corneal abnormality be due to limbal stem cell deficiency?

DBG: Yes, but not only as it is a deficiency of the stem cells niches

DW: yes, stem cells have decreased function

NL: We know that the limbal stem cell niche region does not properly develop or is degraded in cases of PAX6 mutation with progressive keratopathy. We do not know if the limbal stem cells are actually gone or if their function can somehow be preserved or recovered.

KKN: The cornea abnormality is due to limbal stem cell dysfunction for sure. whether it's because the limbal stem cells are not present I think is very unlikely, but we don't actually know. what we do know is that there must be limbal stem cells that are present because the keratopathy gets worse with age in most cases. it may be that the limbal stem cells function partially and that the addition of dry ocular surface, secondary inflammatory changes, inflammatory changes due to preservatives in the drops that we use, other trauma, other operations affecting the limbus and maybe even Rigorous eye rubbing because of allergic conjunctivitis may all play a role in making the limbal stem cells that are not fully functional completely dysfunction.

15. Has anyone tried an artificial iris or a tinted IOL?

DBG: It is important to understand that artificial iris or integrated IOL iris are not recommended because of the major risk of severe increased glaucoma and corneal opacification. They can be used in acquired aniridia as traumatic aniridia

KKN: I have not. The reason is that I have found too many complications in children who are sent to me for a second opinion where an artificial iris has been used. I also think that the problem is that the tinted implants can have an effect on the developing nervous system in a child under the age of eight that reduces their contrast sensitivity and I am somewhat concerned about this. What I do know is that even the colored contact lenses with a clear aperture in the middle sometimes tend to cause more inflammation than I see otherwise.

16. **Does this PAX6 related keratopathy stain with fluorescein?**

DBG: Yes, however no fluo. staining at beginning in periphery

DW: Yes

NL: Yes, and there is a clear trend in the increase in Oxford Staining Score with age and with grade of keratopathy.

KKN: Yes, it most certainly does and you can see that early staining at the limbus. When you see this it is really important to be very aggressive about lubrication about the consideration of anti-inflammatory drops such as FML and also depending on the age the use of topical cyclosporine.

17. **My understanding is that humanoptics artificial iris can't be used in phakic eyes - as it is tucked under the ant. capsule? Is this right?**

DBG: True however not recommended for congenital aniridia

DW: no experience with this

KKN: I am sorry I have no experience with this artificial iris.

18. **Which knife is used for this prophylactic procedure?**

DBG: Storz

DW: Storz SP7-62233

KKN: I have never used a goniotomy knife and I use instead a disposable 25-gauge needle on visco elastic. This means that I don't have to worry about getting the knife sharpened and I have always done my goniotomies that way so that's what I use.

19. **Is there a particular age after which the success rate of the goniosurgery surgeries declines?**

DBG: Probably only adapted in very young children

DW: probably over 2-3 years

KKN: So the number that I have done is much less than doctor Walton. However, I think the key is to do the surgery before the glaucoma sets in because once the glaucoma sets in then it's like the trabecular meshwork is damaged and releasing the attachment doesn't really help.

20. **What's the end point of successful goniosurgery?**

DBG: IOP stabilized

DW: no acquired glaucoma

KKN: Since it is prophylactic, the end point is that even if you have to add drops the glaucoma remained stable and you do not have to intervene with other types of surgery.

21. **Ken: Were you using a Thorpe Goniolens in the Video just shown?**

KKN: I used a Barkan Hoskins lens which I got from ocular instruments.

22. **In patients with late glaucoma, what would be the drainage procedure of choice in view of the keratopathy and risk of mitomycin use, if trabeculectomy is considered?**

DBG: Trabeculectomy

DW: trabeculectomy

KKN: I do not do a trabeculectomy for these cases. I would use a drainage valve and my choice is the Ahmed.

23. **Why not wait till glaucoma develops before doing a goniosurgery?**

DBG: I wait because of the risk of increasing cataract

DW: goniosurgery will fail later

KKN: see answer to question 20

24. **Is IOP the single parameter for success in these cases (prophylactic gonio)?**

DBG: Not only axial length is important

DW: yes

KKN: This depends on the age of the child. In older children around eight 9, 10 and older then the intraocular pressure is the parameter that you are measuring. In younger children axial length, corneal clarity, corneal diameter and the intraocular pressure matter. Clearly all of these parameters are more important in children under the age of four but can be important even up to the age of eight or nine in my experience.

25. **Are contact lenses contraindicated in aniridia because of the eye surface disease?**

DBG: Yes, can cause trauma of the limbus

DW: usually, yes

NL: regular contact lenses can worsen the epithelial and ocular surface damage and inflammation, as well as increase the risk for hypoxia.

KKN: The short answer is yes. However, in certain circumstances you can fit hybrid lenses that have a scleral skirt and therefore the pressure on the limbus is reduced. In my career I can think of three or four adults who have preferred to use a contact lens but that was partly because they wanted to try and deal with the discomfort of the ocular surface disease that they had. They of course realized that the contact lens itself could make the ocular surface worse but that was their choice.

26. What about posterior optic capture in Aniridia?

KKN: This technique must be something that the surgeon is familiar with because if during the operation the anterior capsule opening is much bigger than the optic diameter if you do not capture the optic in the posterior capsular opening, that optic will move forward. Since there is no iris, the optic will end up hitting the endothelium of the cornea and causing corneal decompensation post up. Therefore, the technique of posterior optic capture is something that people should have as a skill if they are going to tackle these cases. Some of my colleagues would say that you should do the optic capture in aniridia every single time. I do not do that but I have certainly done it as I demonstrated in the webinar when the need arises.

27. Can you please comment about the risks / benefits of using tinted or coloured contact lenses in aniridia?

DBG: trauma of the limbus and increase risk of keratopathy and corneal opacification

DW: unnecessary

NL: general risks of contact lenses listed above should be considered.

KKN: see answer to question 25

28. Are natural tears / tears naturale eye drop products safe to use?

DBG: Yes, if preservative free

DW: yes, if preservative free

KKN: Whichever artificial tear you use try and make it preservative free. The reason is that preservatives can induce inflammation themselves and it is the inflammation that causes the damage.

29. Once the children present with glaucoma, what is the preferred surgical procedure?

DBG: Trabeculectomy or goniosurgery considering the age

DW: less than 5 years of age tube, greater than 5 years of age trab.

KKN: Depending on the age and depending on the circumstances and behavior of the child I will sometimes use cyclo diode laser to try and control the pressure and let the child get a little bit older so that they understand what we're doing. My preferred technique surgically then is a drainage tube. Please remember that while in a textbook it may be true that a drainage tube is the best thing to do, in life, in reality the behavior of children, the care and attention the child will get are dependent on the child's behavioral manners and the parents social and family situation. It is our job as pediatric ophthalmologists to assess these and make sure that just because we know that a tube is the correct thing to do by the textbooks that buying some time with cyclodiode laser is a justifiable thing to do. When I use I cyclodiode laser to buy time, I tend to do one inferior quadrant or two inferior quadrants but never the superior quadrants because that is where I tend to place the tube. Do not place the tube in an area that has had cycler diode laser previously.

30. We have seen aniridia in neonatal onset glaucoma. Would the surgical procedure differ in different ages of onset?

DBG: No goniotrabeculectomy

DW: Tube; if trabecular meshwork open, then goniotomy

KKN: Neonatal onset glaucoma in aniridia is probably one of the most difficult types of glaucoma to treat. I think it is important under these circumstances to recognize what the anterior chamber depth is. If the anterior chamber depth is very shallow an it often is in these cases, then whatever you do, you have to be prepared to either damage the cornea, damage the lens or damage both. For this reason, in neonatal glaucoma due to aniridia I again tend to use cyclodiode laser to get the child even six months older or even up to a year older to see if the anterior chamber depth deepens and then I place a tube.

31. **In aniridic glaucoma presenting with a superiorly subluxated cataractous lens, what would be the best way forward?**

DBG: Phaco first and then treating glaucoma if necessary

DW: remove lens first

KKN: This is a tough case and I think it's always difficult without being able to examine the child to advise appropriately. I think that what I would say in general is that if a lens is subluxated and cataractous it is likely that it would have to be removed. In this particular case it sounds like the child would have to be left aphakic. As I said very difficult to advise without knowing the details of the exam but the prognosis here seems to me to be pretty poor for visual rehabilitation Unless the child will wear glasses. If there was glaucoma, then I would remove the lens doing anterior vitrectomy and place a tube but again Please remember that it is difficult to comment on specific cases.

32. How do you do the peripheral iridectomy in subscleral trabeculectomy?

DBG: No iridectomy if no iris root

DW: with difficulty

KKN: I do not do a trabeculectomy in aniridia. And of course remember that in aniridia the Irish may only be a very small stump so you may not need to do an iridectomy.

33. **How do you prevent shallow or flat AC following Trabe. in a Child?**

DBG: Follow up

DW: anterior chamber reformation with viscoelastic or tie the tube

KKN: part of the reason why I don’t do trabeculectomy in aniridia

34. Best way to measure IOP given anatomic changes?

DBG: Icare IOP with corrected pachymetry

DW: applanation

KKN: I think it's important that whatever you use to measure the pressure that you'd use the same instrument all the time. It's also important to use corneal diameter, the clarity of the cornea and the axial length in the younger children, especially those under the age of four. As far as which instrument is the most accurate I think it's really difficult to be certain but I tend to end up using Goldman applanation tonometer in the older children and I tend to use the i-care in the younger children.

35. Ken: Do you use punctal plugs & restasis in ALL children with Aniridia? If not, do you have any selection criteria?

DBG: Probably not

KKN: So I think this is a progression of management. I will use punctal plugs if I cannot get ahold of preservative free artificial tears. I will use cyclosporine 0.05% if I think that there is inflammation. The main goal is to have a quiet looking wet eye.

36. Role of corneal transplants?

DBG: As stem cells deficiency corneal transplant re-opacified quickly

DW: always fail

NL: corneal transplantation, without long-term stable and functioning limbal stem cells, will provide only temporary improvement in vision (perhaps 1 – 2 years) before the keratopathy returns. Some patients have multiple transplants after repeated failures. Long-term immunosuppression is needed and this can be difficult for the patient and can have side effects. There may also be a risk of triggering aniridia fibrosis syndrome.

KKN: This is a good question but a tough one to answer. By the time you get to the need for a corneal transplant it means that the limbal stem cells definitely are not functioning well and if you're going to do a corneal transplant you have to think about doing some kind of limbal stem cell transplant also. This means that you're going to need long-term immune suppression. I think the prognosis really even after Limbal stem cell transplant and corneal transplantation is not great and for that reason by the time you get to a corneal transplant you really are at a very difficult and lost stage in the management of these cases.

37. Does strabismus or nystagmus surgery help or have a negative impact in some way?

DBG: No negative impact if you care ocular surface

DW: rarely appropriate

KKN: I think this is the one situation where you really do want to avoid Limbal peritomy because you don't want to damage any remaining or partially functioning limbal stem cells. Therefore, if you do strabismus surgery or nystagmus surgery I would recommend that you do phonics based incisions in the conjunctiva.

38. What should we think if we find unilateral aniridia?

DBG: As shown it still could be PAX6 mutation

DW: check cornea for evidence of hereditary aniridia or not

NL: In our experience congenital aniridia is always bilateral, although the degree of ocular involvement and rate of progression can vary among both eyes.

KKN: Unilateral aniridia is extremely rare. It is usually very asymmetric so I would look at the other eye that appears to have no aniridia and look for iris hyperplasia. If it is genuinely unilateral aniridia then there's another cause and it's not likely to be packed six related. Again I would look for subtle signs such as posterior embryotoxon.

HS: *PAX6*-related aniridia is typically bilateral. Other anterior segment disorders and genes can show variable expressivity between the eyes and it may be worth considering mutations in other genes (*FOXC1, PITX2*, chromosomal abnormalities including these genes) if the phenotype appears very asymmetric.

39. Can we prevent corneal damage as child with aniridia grows up?

DBG: Yes, artificial tears preservative free

DW: no

NL: In those with classical PAX6 aniridia, it is important to maintain a healthy ocular surface without dryness or inflammation for as long as possible. We do not yet know if it is possible to delay or prevent corneal damage over time; controlled long-term studies with specific therapies are lacking.

KKN: The short answer is yes. Please see the previous questions about the ocular surface and keeping the eye wet and non-inflamed. These factors will play a big role in stopping the progression of corneal damage though you're not going to be able to stop that progression in all likelihood.