Congenital iris ectropion as an indicator of variant aniridia

Aniridia and its variants may cause diagnostic difficulty especially when the iris is not wholly or partially absent.^{1,2} In congenital iris ectropion (also called ectropion uveae), the posterior pigment epithelium of the iris extends onto the anterior iris surface causing darkening around the pupil. We report a man and his infant son with variant aniridia and a mutation in the PAX6 gene, where the major anterior segment finding was iris ectropion.

Case report

A 30 year old man with bilateral iris ectropion, vision impairment, and nystagmus attributed to optic nerve hypoplasia, and his infant son also with poor vision, were examined. A search of the man's previous ophthalmic records indicated that at 6 weeks of age he had poor vision, nystagmus, myopia (−6.0 D), and small, anomalous optic discs. Ectropion uveae was noted in the records at age 9 years. A poorly developed foveal reflex was identified in his late teens. A magnetic resonance imaging (MRI) head scan at age 19 years was reported as normal. Inferior corneal pannus and raised intraocular pressure (mid 20s mm Hg) were identified in the patient's twenties. Visual acuity had remained around the level of "count fingers" all his life. Examination at 30 years of age revealed bilateral iris ectropion and corneal pannus, but no keratitis (fig 1A). There was bilateral optic nerve hypoplasia with tilted discs, temporal excavation, and peripapillary atrophy (fig 1C), as well as macular hypoplasia. There was no family history of ocular

disease, he had no siblings and his parents had normal ocular examinations.

The man's infant son had nystagmus, bilateral iris ectropion, persistent pupillary membranes, and anterior polar cataracts (fig 1B). Fundal examination revealed bilateral optic nerve hypoplasia with tilted discs, peripapillary pigmentary changes (fig 1D), and a poorly developed macular reflex. Vision was estimated at 1/60 using Teller acuity cards at 4 months of age.

With ethics approval and informed consent, in lymphoblast DNA from the man, the PAX6 coding exons were amplified (primers available upon request), and sequence analysis was performed. An A>T variant was detected at nucleotide 1630 of the cDNA M93650 (<http://pax6.hgu.mrc.ac.uk/About/pax6cdna.htm>). This mutation (X423L) changes the PAX6 stop codon 423 (TAA), to a leucine (TTA) and is present in patients with classic aniridia with iris absence, and others with minimal iris involvement.³ The mutation was present in the man's affected son, but not his wife or unaffected parents.

Comment

In this report we describe a man and his infant son with bilateral iris ectropion, hypoplastic anomalous optic discs and macular hypoplasia, with an X423L missense mutation in the PAX6 translation stop codon confirming a diagnosis of variant aniridia. A diagnosis of variant aniridia for the sporadically affected patient has significant implications for genetic counselling. Aniridia is an autosomal dominant condition. While the recurrence risk for the unaffected parents of a sporadic aniridia patient is low, the risk for the affected patients when they reach

adulthood of having an affected child is 50% (one in two).

Congenital iris ectropion has known associations with Rieger syndrome,⁴ Prader-Willi syndrome,⁵ and neurofibromatosis type 1.⁶ A patient with a Q422R PAX6 mutation was described who had bilateral iris ectropion and corneal opacities, but no optic nerve or macular problems.⁷ Iris ectropion was present in some members of a large family with autosomal dominant keratitis and a splice site mutation in the PAX6 gene.⁸ Findings in infancy in the man in this case report focused on the presence of hypoplastic anomalous optic discs. Optic nerve hypoplasia has a wide differential diagnosis, and while early literature on aniridia indicated the occurrence of hypoplastic optic discs,⁹ a diagnosis of aniridia may not be immediately considered in a patient who lacks absence of the iris. Our report highlights iris ectropion as a strong anterior segment indicator for variant aniridia.

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Figure 1 Anterior segment and fundus photographs in the affected individuals. In the anterior segment of the man (A) iris ectropion of varying amount involves the entire pupillary margin, and inferior and superior corneal pannus is present, and in his infant son (B) there is milder iris ectropion with an irregular pupillary margin, hypoplastic sphincter pupillae, slight nasal iris sectoral hypoplasia, and pupillary membranes arising from the collarette. Optic nerve changes in the man (C) include small and tilted discs with peripapillary atrophy, and in his son (D) include mild optic nerve hypoplasia with tilting and peripapillary atrophy with pigmentary changes.

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Fourth time lucky: a case of multiple recurrence of a macular hole

We present the case of a patient who has undergone four macular hole operations for late multiple recurrences. The same experienced ophthalmologist confirmed the presence of each macular hole and performed each operation.

Case report

A 55 year old female myope, −3.75 D right eye and −3.5 D left eye, was referred to the vitreoretinal clinic with a 2 month history of right visual disturbance. On presentation, her visual acuities were 6/9 right eye and 6/60 left eye. Fundal examination and fluorescein angiography showed a right stage I macular hole and a left stage IV macular hole. As the left macular hole was long standing, it was decided not to operate on this eye. Two months later the right visual acuity was reduced further to 6/36 because of progression to a stage II macular hole and she underwent a right vitrectomy and 18% C₃F₈ gas tamponade. At the time of surgery, the posterior hyaloid was detached and the absence of an epiretinal membrane was confirmed but no inner limiting membrane (ILM) peel was performed. Following this and each subsequent vitrectomy, the patient postured face down for 2 weeks. Postoperatively, right visual acuity improved to 6/6 but 8 months later the hole reopened, and her right visual acuity dropped to 6/18. A further vitrectomy and 20% C₃F₈ gas tamponade was carried out. During this, a silicon tipped aspiration needle was used to confirm the absence of vitreous at the macula and a barbed blade used to show that no epiretinal membrane was present. The hole closed and the vision improved to 6/12. Two years later the patient underwent uneventful right phacemulsification cataract surgery with posterior chamber intraocular lens implantation and her acuity was restored to 6/9. After another 2 years right visual acuity fell to 6/36, the hole had reopened. The patient underwent a third macular hole operation consisting of ILM peel and 18% C₃F₈ tamponade. The hole remained closed and the vision improved to 6/9 for a further 3 years when the hole reopened and the vision decreased to 6/24. A fourth procedure was performed consisting of trypan blue

assisted ILM peel to two disc diameters from the hole and 18% C₃F₈ gas tamponade.

When last seen, 16 months after surgery and 9 years after presentation, the right visual acuity was 6/12 and the macula hole confirmed as closed on ocular coherence tomography.

Comment

Previous studies have shown that repeat macular hole surgery is successful in closing recurrent macular holes and improving vision.^{1,2} Late reopening of successfully closed macular holes has been reported to occur in between 4.8% and 6.9% of eyes.^{3–4} The success of repeat surgery did not depend on whether the hole reopened early or late as in this case.^{1,2} A third recurrence of a macular hole is a less common event. The results of repeat macular hole surgery are better in those eyes in which one of the previous operations had successfully closed the macula hole.¹ In those eyes that had previous successful surgery the mean final visual acuity was 20/40. By comparison, in those eyes in which surgery failed to close the macula hole, the success of final closure rate was 56% and the mean final visual acuity was 20/100.⁵

The pathophysiology for failure of closure and reopening remain unclear. Early failure is thought to result from the lack of formation of a stable glial plug that is essential for hole closure.⁶ The causes for late reopening remain unclear as in this case, it may be a spontaneous event.^{2,7} Some authors have suggested that chronic cystoid macular oedema, cataract surgery, or the development of an epiretinal membranes resulting in tractional forces may be involved.^{2,4} This was not the case in this patient.

In summary, this case suggests that the visual outcome can be favourable following multiple repeat macular hole operations especially if there has been previous successful closure.

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MAILBOX

Vision restoration therapy and raising red flags too early

Vision restoration therapy (VRT) has been the subject of considerable controversy,^{1–3} and with Horton's latest editorial³ it has now turned rather personal. The editorial is filled with numerous inaccuracies and misrepresentations and this cannot go unanswered. Just as a scientific debate should not focus on fiction but on facts, comments by critics must be evaluated with the same rigor as the original work itself. Only by keeping track of all of the scientific evidence rather than by a personal and limited review of some selected facts will we get closer to the truth.

Firstly, it is a fundamental misrepresentation by Horton that we are trying to "salvage neurons" at the fringe of a lesion. Rather, we believe that VRT activates surviving neurons in areas of residual vision (ARVs)—that is, areas that are partially damaged.^{4–7} Repetitive use through daily training increases neuronal activation,⁸ which is greatly enhanced by attentional processes.⁹ No neuron is "salvaged."

It is correct that at the time Horton wrote his editorials no one had published studies on eye movements. But since then the first eye movement studies have been published in abstract form. It actually turns out that eye movements, when measured with an eye tracker, are not altered after VRT.¹⁰ There is also other indirect evidence, which is incompatible with the hypothesis that eye movements explain visual field improvements:

- Fixation performance in standard automated perimetry is an accepted quality control measure and our patients typically show >90% stable fixation, which is measured by counting the number of hits at fixation. Because this does not change after VRT (it usually improves slightly, see Kasten et al.,⁴ Poggel et al.,⁹ Reinhard et al.,¹¹ Mueller et al.,¹² and Sabel et al.¹³) it is unlikely that patients moved their eyes more after VRT.
- Horton erroneously believes that temporal field loss prevents blind spot measurements. This is true only for one eye. In our studies, the position of the blind spot remains unchanged in monocular measurement after VRT.¹³ Thus, neither eccentric fixation occurred after VRT nor are there more large saccades after VRT.¹⁰ The position of the blind spot is a reliable parameter of eccentric fixation.¹⁴
- If eye movements were responsible for the visual field shifts, then the entire visual field border should shift in parallel. In most patients this is not the case. The border of the visual field may shift in one place (say the lower quadrant) and remain invariant in another (upper quadrant). Also, highly localised border shifts are induced by attention cues,⁹ and horizontal border shifts may occur in the absence of border shifts at fixation. All of these observations are not compatible with the proposal that eye movements cause the visual field border shifts. In fact, in the periphery the border shifts tend to be more pronounced, which is explained by the cortical magnification factor—that is, by visual cortex architecture.