Bilateral sporadic aniridia: review of management

CASE REPORT

Abstract

Purpose: To report a rare case of bilateral sporadic aniridia in an African child and review the management modalities.

Presentation: We report a case of bilateral sporadic aniridia with horizontal nystagmus, axial cataract optic disc, and fovea hypoplasia in a 5-year-old female patient. She was managed conservatively. Various modalities of treatment are reviewed.

Keywords: aniridia, sporadic, nystagmus, cataract, glaucoma, keratopathy, tattooing, syndrome, fovea hypoplasia and optic disc hypoplasia

Introduction

Aniridia may be congenital or traumatic. Post-traumatic aniridia has been reported following a domestic accident in which total desinsertion of the iris occurred after a contusive trauma associated with the rupture of the eye globe.[1]

In congenital cases, the term aniridia is a misnomer as a rudimentary iris is usually present peripherally. It is often difficult to manage. It is not as common as other congenital eye diseases such as buphthalmos and cataract.[2,3]

It has been reported to have an incidence of between 1:64,000 and 1: 100,000[4,5] and it may occur in isolation or be associated with a number of syndromes such as WAGR (Wilm's tumor, bilateral sporadic aniridia, genitourinary abnormalities and mental retardation).[4] It is even rarer in Africa. Two thirds of all cases are familial, and one third is sporadic.[6] Aniridia occurs as a result of mutations in paired box gene 6 (PAX6) on band p13 of chromosome 11 though there are few reported cases with no identified mutation of PAX6.[7] The PAX6 gene is a developmental ocular gene and mutations result in panocular changes.

These changes include alterations in corneal cytokeratin expression, cell adhesion and stem-cell deficiency.[8] It also has a fibrotic nature which may result in failure of many interventions such as penetrating keratoplasty and filtration surgery.

The aim of this report is to highlight the various modalities of management of aniridia and challenges of management in a developing country.

Presentation

A 5-year-old female presented at our clinic. Her mother complained that her daughter was unable to see well, saw white specks and always walked with her chin lowered in a head-down position since birth. She was delivered by spontaneous vaginal delivery after an uneventful pregnancy. A twin sister died at birth. Nutrition was exclusively

breastmilkuntilthepatientwas6monthsoldwhenshewas introduced to other food and artificial milk. Her developmental history was within normal limits.There was no history suggestive of a similar problem in her family.

Herheadwastilteddowninanattempttoshyawayfrom light. Examination of both eyes revealed a visual acuity of count fingers. Figure 1 shows the right eye of the patient. There was pendulous horizontal nystagmus, clear cornea, rudimentary irises, axial lens opacities, hypoplastic optic discs and fovea hypoplasia. The intraocular pressure with Perkin's tonometer was 16 mmHg and 18 mmHg in right and left eyes respectively.

Pediatricassessmentdidnotrevealanyotherabnormality. Urinalysiswasnormal.Abdominalultrasonographyrevealed thattheliverandspleenwerewithinnormallimits;bothkidneyshadnormalsonographicappearanceandwerenormalin sizeandposition,measuring78mmby32mmand82mm by 31 mm on the right and left respectively.There was no intra-abdominal mass.

Shewasplacedonlubricantgel,oculentachloramphenicol nocte and advised to rest in dark shade.

Discussion

Aniridiaisacomplexdisorderthatusuallyresultsinimpaired vision from multiple causes including aniridia associated keratitis (AAK), cataract, glaucoma, foveal hypoplasia, nystagmus and retinal detachment. It is associated with a numberofsyndromes,includingWAGR.Treatmentisusually ineffective despite the understanding of the genetics and pathology of the condition.The high rate of failure of surgicalinterventioniscausedbythecondition'sprofibrotic nature.Indevelopingcountries,nonavailabilityofmaterial andhumanresourcesnecessaryforthemanagementofthe cases and poverty especially of the patient in this report worsenthe picture.The patient could not afford the necessary investigations such as fundus photography, optical coherence tomography, let alone any treatment.

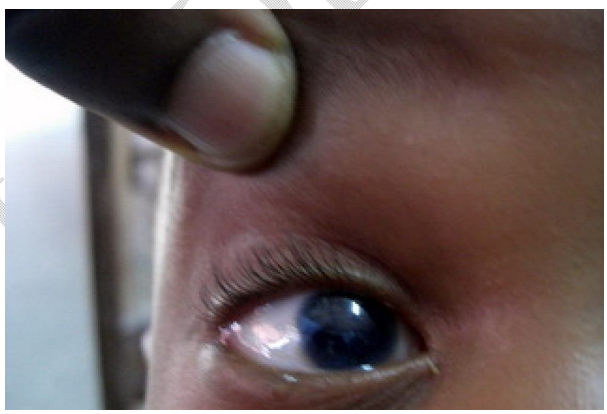

Figure1 Showstherighteyeofthepatientwithrudimentaryiris,largepupillaryspaceand cataract.

Managementofaniridia

Aniridia is better managed if the pathology is well understood.Aniridia occurs as a result of mutations in PAX6 on bandp13ofchromosome11.Thesemutationscauseabnormalities in many parts of the eye. However, there are few reported cases with no identified mutation of PAX6.[7]

PAX6mutationsresultinalterationsincornealcytokeratinexpression,cell adhesion,andstem-celldeficiency.[8]These resultinafragilecorneaandaniridia-associatedkeratopathy (AAK).Abnormaldifferentiationoftheangleorprogressive angle closure from synechia usually results in glaucoma. Cataract development with associated fragile lens capsule mayalsobefound.Theirisisdeficient.Theopticnerveand foveaareoftenhypoplastic,andtheretinamaybeproneto detachment.Manyinterventionsincludingpenetratingkeratoplasty and filtration surgery usually fail because of the fibrotic nature of this disease.

Aniridia-associatedkeratopathy

PAX6playsacrucialroleinthedevelopmentofthecornea. It regulates the expression of cytokeratins 3 and 12 which form the intermediate filament proteins of the corneal epithelial cells.[9]These cytokeratins perform a vital role in cell-to-cell binding or adhesion, and in anchoring cells to theunderlyingbasallamina.Inaniridia,thereisadecreased expressionoftheadhesionmolecules:desmogleine, β-catenin,andγ-catenin.Thisgivesrisetospacesbetween the corneal epithelial cells.[10] There is also a deficit in the cellsurfaceglycoconjugatesignatureinthecornea[11]resultinginareductionoftheabilityofcellstomigrateinwound healing.Thislossofcytokeratinsandcelladhesion,coupled with glycoconjugate defects, result in an extremely fragile cornealsurfacethatissusceptibletorecurrenterosionsand ulcerations thereby causing AAK which occurs in 20% of cases.Limbalstem-celldeficiencyhasalsobeenimplicated inAAK.[12]AAK contributes significantly to the visual loss in aniridia.The clinical features usually appear in the first decadeof life.Thickening and vascularization start from the cornealperipheryandlateradvanceintothecentralcornea. AAK is often worse after surgery that interferes with the limbalstemcellsoraftertheuseoftopicalantimetabolitesto treataniridia-associatedglaucoma.[4]AAKisthereforecaused byacombinationoffactors:Limbalstem-celldeficiency,

abnormally differentiated epithelium, abnormal cell adhesion and impaired healing response. The symptoms of AAK include photophobia, dry eye, red eye, and epiphora. The patient reported has always had her head tilted down since birth because of photophobia. There is meibomian gland dysfunction and an abnormal tear film, with reduced tear break-up time and reduced tear meniscus.[13]

Management

This includes the use of preservative-free lubricants and darkglassesforphotophobiaintheearlystages.Inmoderate keratopathy,serumdropsandamnioticmembranetransplants maybeused.Thiswillfacilitatethesurvivalandexpansion ofsurvivinglimbalstemcells.[14]Autologousserumeyedrops hasbeenfoundtoimprovethekeratopathyinpatientswith mild or moderate severity. In these patients, autologous serum eye drops ~~was~~were found to be superior to conventional therapywithartificialtearsforimprovingtheocularsurface and subjective comfort.[15]

In severe cases, limbal stem cell transplantation is necessary.[16]The prognosis of penetrating keratoplasty is poor because of the frequent recurrence of the same pre-graft corneal changes, followed by subsequent graft failure.[17,18] Thisismostlikelycausedbytheprimaryabnormalityinthe limbalstemcellsoftherecipientcornea.Ontheotherhand, homologouslamellar limbo-keratoplasty appears to be quite effectiveinAAK.[19,20]Itssuccessrateisincreasedbytheuse ofsystemicimmunosuppressantscomparedtousingtopical immunosuppressantsalone.Bostonkeratoprosthesisisanew approachtomanagingAAK.[21]Thismay reduce the incidence of recurrent graft rejections in AAK.

Glaucoma

Glaucomainaniridia,usuallyoccursduringthepreadolescent orearlyadolescentyears.[22]Itisthoughttobeduetodevelopmentalabnormalitiesinthedrainageangleoftheeye,which obstruct the outflow of aqueous humor.

GrantandWalton[23]havefoundthatthestromaoftheiris extendsforwardsontothetrabecularmeshwork(TM)inthe formofsynechia-likeattachmentsintheearlystages,which later become a homogenous sheet, resulting in eventual angle closure.Thediagnosisismadebyexaminationoftheangle forevidenceofclosure,intraocularpressure(IOP)measurement,opticnerveexamination,andvisualfieldassessmentin anolderchild.Measurementofcentralcornealthicknessis alsoimportantbecausethishasalargeimpactontheaccuracy of tonometric readings.Aniridic patients may have cornea upto100μmthickerthantheaverage[24,25]makingtonometry unreliable in these patients. The treatment of glaucoma associated with aniridia is difficult. Grant andWalton[23] found that38.7%respondedtomedicaltreatment,includingmiotic eyedrops.Ofthosethatwereresponsivetomedicaltreatment, 50.0% required oral carbonic anhydrase inhibitors. Unsatisfactoryresultshavebeenreportedwithcasestreatedwithargon lasertrabeculoplasty(ALT).[26]Diodelaserphotocoagulationis also ineffective.[27] Surgical treatment like medical treatment is challenging and includes trabeculectomy +/− antimetabolites, prophylacticgoniotomy, therapeuticgoniotomy, cyclocryotherapy and guarded filtration surgery.Prophylacticgoniotomy has beenfoundtobequiteeffectiveinthepreventionofglaucoma inpatientswithaniridia.[28]Theaimistoseparatetheabnormal extensionsofirisstromafromtheanglewall,thuspreventing closure of the angle.Trabeculectomy has been found to be effective in the treatment of aniridic glaucoma.[26]

Cyclocryotherapyiseffectiveinloweringbutseriouscomplicationswhichincludephthisisbulbi,progressive cataractandlossofvisioncanfollowit[27]makingitunsuitable for use as a first-line treatment.[29]

Guardedfiltrationsurgery(GFS)usingAhmedMolteno andBaervaldtimplantshasbeenfoundtobeveryeffective inobtainingcontrolinaniridicglaucomawithsuccessrates ranging from 66% to 100%. GFS may however be associatedwithcomplicationssuchasprolongedhypotony,retinal detachment,migrationofthetube,erosionofthetubethrough the conjunctiva and fibrosis of the anterior chamber.[30]

Irisdeficiency

The iris deficiency associated with aniridia leads to disturbance of vision associated with glare and photophobia.

Management

Severalmeasureshavebeentakentoovercomethesesymptomswhichincludeeyelidsurgery,cornealtattooing,[31]and implantationofartificialirides.[32]Artificialirisimplantshave been found to diminish visual discomfort such as photophobia.[33]However,glaucomahasbeenfoundtobethemost importantcomplicationafterthisprocedurethoughimplantation of the iris prosthesis in the capsular bag may reduce this complication, but this requires a large capsulorrhexis and presents a surgical challenge.

The use of a black diaphragm intraocular lens (IOL) to correctbothcongenitalandtraumaticaniridiahasbeenadvocated.[19,34,35]TheselensesincludetheMorcheraniridiaIOLtypes 67F and 67G, the aniridia ring type 50C and the coloboma diaphragmtype 96G.They canbe placedin the ciliarysulcusif thereisadequatesupport,oraresuturedtrans-sclerally.

Complications reported included postoperative uveitis, secondary glaucoma, clinically significant macular edema (CSMO), chronic endothelial cell loss, progression of corneal epithelial disorders and hyphema.[19,34]

Cataract

Thisisacommonassociationwithaniridiaasfoundinthisreport. Nelsonetalfoundcataractin50%–85% of patients with aniridia.[22] Cataract extraction is often necessary with or without IOL insertion. However, the anteriorcapsuleofaniridiacataractshasbeenfound to be very fragile,[36] hence, care must be taken during surgery to avoid capsular complications. The use of ablack diaphragm IOL consisting of an opaque diaphragm surrounding the transparent optic has recorded satisfac- tory results.[37,38]

Posteriorsegmentabnormalities

Optic nerve hypoplasia and macular hypoplasia are common findings and these contribute to visual malfunction in aniridia.[22]Opticnervehypoplasiaisfoundinapproximately 10%ofcases.[39]Pendularhorizontalnystagmusasfoundin this report, occurs in most patients, secondary to macular hypoplasia. Aniridia may also be associated with retinal tears and detachments. Retinal detachments occurred in four eyes of three children as a result of giant retinal tears in one study.[40] These were treated with vitreolensectomy and silicone oil injection with two of the eyes recovering useful vision.

Opticalcoherencetomography(OCT)hasbeenfoundto be useful in the diagnosis of foveal hypoplasia in children with aniridia.[41]

Nonavailabilityofmaterialandhumanresourcesnecessary for the management of the developments in follow up coupled with poverty of the parents especially of the child inthisreportwhocouldnotaffordthevariousinvestigations suchasfundusphotographandOCTmayaffecttheprognosis in developing countries.

Conclusion

Aniridiaisacomplexdisorderthatinvolvesmanypartsofthe eyeandwhichmayresultinimpairedvisionfrommultiple causes.Understandingthemanagementoftheconditionand availability of necessary manpower and material needs useful inmanagementwillgoalongwayinassistingtheoccasional cases that are seen in developing countries.

Disclosure

Theauthorsreportnoconflictsofinterestinthiswork.

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