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Congenital aniridia: clinical profile of children seen at the University College Hospital, Ibadan, South-West Nigeria

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Abstract

Purpose: To describe the clinical features of patients younger than 16 years with aniridia presenting to the Paediatric Ophthalmology unit of the Eye Clinic, University College Hospital, Ibadan, Nigeria.

Methods: The is a retrospective review of children with aniridia seen between May 2015 and April 2019 at the Paediatric Ophthalmology unit of the Eye Clinic, University College Hospital in Ibadan. Data on demographic characteristics, presenting complaints, ocular and systemic examination findings, and interventions were collected and descriptively summarised.

Results: A total of 28 eyes of 14 patients were studied. The mean age was 6.37 ± 4.98 years. Seven (50%) patients were male. Aniridia was diagnosed in first-degree relatives of nine patients. The most common complaint at presentation was poor vision in 11 (78.6%) patients. Objective visual acuity assessment was obtained in 22 (78.6%) eyes. Presenting visual acuity was worse than 20/60 in all 22 eyes and worse than 20/400 in 8 (36.4%) eyes. Refraction was performed in 17 (60.7%) eyes and revealed a mean spherical equivalent of –3.93 ± 5.99 diopters. Twenty (71.4%) eyes had corneal opacities, and lenticular opacities were seen in 15 (62.5%) of 24 eyes. Mean intraocular pressure (IOP) at presentation was 21.62 ± 10.4 mmHg; 12 (41.4%) eyes had elevated IOP at presentation. Ten (35.7%) eyes had cataract surgery and six (21.4%) eyes had glaucoma surgery.

Conclusion: Familial aniridia was common in this study, and most of the patients presented with moderate to severe visual impairment. The common ocular associations were refractive error, cataract, corneal opacity and glaucoma.

Keywords: aniridia, children, Nigeria, secondary glaucoma, sub-Saharan Africa

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Introduction

Congenital aniridia is a rare, bilateral disease that manifests as partial or complete absence of the iris tissue from birth. Incidence ranges from 1 in 64,000 to 1 in 100,000.[1] Mutations in the PAX6 gene are responsible for classic aniridia, whereas mutations in other genes such as CYP1B1, FOXC1, PITX2 and FOXD3 have been implicated in aniridia-like phenotypes.[2] The PAX6 gene is located on chromosome 11p13 in humans and expressed in the cornea, lens, iris and retina of developing and mature eyes; hence, mutations result in a pan ocular disease.[2,3]

Inheritance follows the Mendelian pattern with two-thirds of cases inherited in autosomal-dominant fashion. The remaining one-third are sporadic and arise from spontaneous mutations or deletions involving the PAX6 gene and its adjoining WT1 gene. The mutations result in the

WAGR syndrome, an acronym for Wilms tumour, Aniridia, Genitourinary abnormalities and Mental retardation.[3,4]

Visual morbidity from congenital aniridia is multifactorial, with contributions from corneal opacification, glaucoma, cataract, foveal and optic nerve hypoplasia.[5] The absence of iris tissue also compounds the visual morbidity causing glare and discomfort.[4] Although clinical presentation of this condition has been extensively described in other climes,[5–9] there are only a handful of reports on the clinical profile of aniridia in Africans.[10–12] The aim of this study is to describe the clinical profile of children with aniridia seen in the Paediatric Ophthalmology unit of the Eye Clinic, University College Hospital, Ibadan.

Materials and methods

This was a retrospective review of clinical records of children aged less than 16 years with aniridia seen over a 4-year period between May 2015 and April 2019. All patients were seen and diagnosed by at least one of the three paediatric ophthalmologists (M.O.U., B.A.O., A.M.B.) in the unit. Relevant information which included patient's demographic characteristics, family history, visual acuity, anterior segment and posterior segment findings, and interventions received was retrieved.

Visual acuity was measured in preverbal children with age-appropriate methods, and Snellen's chart was used to assess visual acuity in verbal children. Visual acuity values were converted to LogMAR, and visual acuity of light perception was assigned a LogMAR value of 2.7. All children had a detailed anterior segment examination with either the handheld or the table-mounted slit lamp bio-microscope. The diagnosis of aniridia was made when there was: complete absence of the iris or presence of rudimentary iris tissue.

Intraocular pressure was measured with the Goldman applanation tonometer in older children and under sedation with the use of Perkins tonometer in younger children. The diagnosis of glaucoma was made when the intraocular pressure (IOP) was greater than 21 mmHg with other additional evidence: glaucomatous disc damage, buphthalmos or enlarged cornea. The children were considered to have elevated IOP alone when IOP was greater than 21 mmHg in the absence of the other signs listed above. Cornea pathologies were classified as congenital cornea opacities if the opacities occurred from birth or aniridia-associated keratopathy (AAK) if the cornea involvement developed later in life. It was, however, difficult to retrospectively grade the AAK as there were no clinical photographs to review. Refraction and fundoscopy were performed for patients with clear media.

The study adhered to the tenets of the Declaration of Helsinki for studies involving human subjects. Ethical approval (NHREC/05/01/2008a) was obtained from the institutional review board of the University of Ibadan/University College Hospital, Ibadan ethical committee.

Data were collected using SPSS version 21(IBM, Armonk, NY, USA), cleaned and descriptively summarised.

Results

Sociodemographic characteristics

Of the 5172 new patients seen within the study period, 16 (0.31%) were diagnosed with aniridia. A total of 28 eyes of 14 patients were studied; 2 patients were excluded due to missing records. There was an equal number of male and female. The median age at presentation was 96 months with an interquartile range of 84.5 months. The mean follow-up period was 19.6 ± 20.17 with a range of 0–56 months (Table 1). There was history of poor vision in first-degree relatives of 11 patients (78.6%) of which 9 (64.3%) had relatives diagnosed with aniridia. The study included three siblings with aniridia.

Presenting complaints

Poor vision was reported in 22 (78.6%) eyes, and this was the most common presenting complaint. Other complaints were jerky eye movement (6 eyes, 21.4%), whitish speck (5 eyes, 17.9%), cloudy vision (4 eyes, 14.3%), aversion to light (4 eyes, 14.3%) and enlarged globe (4 eyes, 14.3%).

The following ocular examination findings are summarised below and presented in Table 2: visual acuity, refractive status, cornea, lens and optic nerve findings.

Visual acuity

In total, 22 eyes of 11 (78.6%) patients had objective visual acuity assessment with Snellen's chart,

Table 1. Demographic and clinical characteristics of 14 patients with aniridia.

Variable	Frequency (%)
Gender	
Male	7 (50)
Female	7 (50)
Age at presentation	
Mean	6.37 (± 4.98) years
Range	5 days to 16 years
Median	5.5 years
Interquartile range	6.6 years
Duration of follow-up	
Mean	19.6 (± 20.17) months
Range	0–56 months
Median	12 months
Interquartile range	37 months

while visual fixation pattern was assessed in the other 6 (21.4%) eyes. Of the 22 eyes with objective assessment of vision, visual acuity was worse than 20/60 but ⩾20/200 in 11 (50%) eyes, worse than 20/200 but ⩾20/400 in 3 (13.6%) eyes and worse than 20/400 in 8 (36.4%) eyes of which one patient had vision of light perception. The mean LogMAR visual acuity was 0.95 ± 0.54 (0.6–2.7)

Refractive status

Refraction was performed in 17 (60.7%) eyes. The mean spherical equivalent was –3.93 ± 5.99 (−14 to +7) dioptre sphere (DS). Myopic astigmatism was observed in 11 eyes (64.7%), hyperopic astigmatism in 3 (17.6%) eyes, simple myopia in 2 (11.7%) eyes and mixed astigmatism in 1 (5.9%) eye.

Cornea status

Corneal opacity was present in 20 (71.4%) eyes: 4 (20%) of these had congenital cornea opacities and the remaining 16 (80%) had AAK. This included varying degrees of cornea scarring from subepithelial haze (2 eyes, 10%) to mild stromal scarring (13 eyes, 65%) and dense scarring (5 eyes, 25%). Of the 20 eyes, 13 (65%) had pannus and 1 eye had bullous keratopathy following previous cataract surgery. The other corneal finding was prominent, anteriorly displaced Schwalbe's line (posterior embryotoxon) in two (7.14%) eyes of the same patient.

Lens status

The lens status was documented in 26 of 28 eyes, of which 11 (42.3%) had clear lenses, 14 (53.8%) eyes had lens opacities and 1 eye was aphakic from a previous surgery performed about 12 years earlier. Microspherophakia was seen in four (16.7%) eyes and it co-existed with lens coloboma in one of them. Four (16.7%) eyes (of two patients) had ectopia lentis. Two eyes had dense corneal opacities which precluded the view of further ocular structures.

Fovea

Foveal examination was reported in 20 (71.4%) of the 28 eyes, 6 (21.4 %) eyes had media opacities which precluded the view of the posterior segment, while 2 (7.1%) eyes did not have a fundus examination documented at the time of this study. Of the 20 eyes examined, 6 (30%) were observed to have hypoplastic fovea.

Glaucoma

The mean IOP at presentation was 21.6 ± 10.4 mmHg with a range of 8–50 mmHg. IOP was elevated in 12 (42.9%) eyes with a mean IOP in these eyes of 30.4 ± 8.5 mmHg. A diagnosis of glaucoma was made in 11 of these eyes, while 1 eye with elevated IOP was not diagnosed with glaucoma because of the absence of other features of glaucoma. Of the 11 eyes with glaucoma, 6 eyes presented with other features of congenital glaucoma, namely, enlarged cornea, corneal oedema, tearing and photophobia, while 1 eye had aphakic glaucoma.

Other clinical features

Other findings on ocular examination included strabismus in 5 (17.9%) eyes of four patients, nystagmus in 18 (64.3%) eyes and ptosis in 5 eyes (17.9%).

Systemic evaluation

None of the patients was found to have an abdominal mass on clinical examination or on abdominal ultrasonography. One patient had atrial septal defect on echocardiography.

Table 2. Ocular examination findings in patients with Aniridia.

Examination findings	Frequency (%)
Mean LogMAR VA($n = 22$ eyes)	0.95 (±0.54)
Mean spherical equivalent ($n = 18$ eyes)	–33.93 (±5.99) dioptre sphere
Strabismus ($n = 5$; 17.9%)	
Esotropia	4 (80)
Exotropia	1 (20)
Cornea size ($n = 28$)	
Normal	16 (57.1)
Small sized	8 (28.6)
Large sized	4 (14.3)
Lens opacity ($n = 14$)	
Anterior polar	1 (7.1)
Cortical	2 (14.3)
Nuclear	4 (28.6)
PSC	5 (35.7)
Anterior polar + PSC	1 (7.1)
Posterior polar	1 (7.1)
Optic nerve finding ($n = 21$)	
Normal	15 (71.4)
Disc pallor	3 (14.3)
Pallor + Cupping	3 (14.3)

PSC, posterior subcapsular.

Interventions received

Six (42.9%) patients had spectacles prescribed and 11(39.3%) eyes were commenced on IOP-lowering medications. Six (21.4%) eyes of four patients had glaucoma surgery, while 10 (35.7%) eyes of six patients had cataract surgery. Of the four eyes that had trabeculectomy as primary surgery, two (50%) subsequently had tube surgery as a result of bleb failure, one eye (25%) became phthisical as a complication of surgery and one eye (25%) did well with IOPs ⩽15 mmHg after trabeculectomy. Further details on medical and surgical interventions are presented in Tables 3 and 4

Discussion

The majority of patients in our study had history of a first-degree relative with aniridia. This is not unexpected as autosomal-dominant inheritance has been reported to account for two-thirds of cases.[1–3,6,13] They also had no systemic associations as is the case with sporadic aniridia which is often syndromic.[14] It can therefore be inferred with some measure of confidence that these cases are likely to be of autosomal dominance inheritance even though genetic studies were not carried out. This underscores the need for genetic counselling of affected individuals who intend to have children. Although genetic testing services are not readily available in Nigeria, detailed history, pedigree charting and good clinical skills are indispensable in arriving at a diagnosis and genetic counselling. However, it is vital to use a combination of genetic and clinical diagnosis for a more accurate and holistic management of these patients. This is especially so for diagnosis and prognosis of the disease.[15,16] Investment in resources and infrastructure for genetic studies is therefore essential.

We observed that all the patients in our study had moderate to severe visual impairment. This is not unusual as severe visual morbidity in aniridia is a common clinical feature, especially in the presence of cornea opacities, glaucoma, lens opacities and foveal hypoplasia which were present in the majority of our patients.[6–8,17] Furthermore, visual impairment is known to have a negative impact on quality of life as well as the outcome of care.[4] In addition, the fact that most of the patients had delayed presentation for care at a mean age of 6.37 years predisposed them to poor visual outcome after treatment as a result of amblyopia.

Keratopathy is a major contributor to vision loss in aniridia, and its prevalence and severity increase with age.[6,13,18] Our finding of corneal involvement in over two-thirds of patients is comparable to the results of other studies.[5,9] Mayer and colleagues[13] reported that more than 55% of patients 10 years and younger had keratopathy, and all patients in the fifth decade of life had AAK. On the contrary, a lower prevalence of 45% was reported by Netland and colleagues.[19] However, this difference in frequency may be explained by the fact that the diagnosis of keratopathy in the study by Netland and colleagues[19] was based on reported symptoms. The authors acknowledged a possible underestimation of keratopathy as asymptomatic

cases may have been missed.[19] Thorough slit lamp examination may increase the prevalence of keratopathy as early stages may be easily missed. Treatment of keratopathy in our cohort was quite challenging as we had no facility for limbal stem cell therapy although this has not been shown to give consistently good outcomes.[20] On the contrary, keratolimbal allograft when combined with penetrating keratoplasty in patients with stromal scarring has been reported to give a better visual outcome.[13]

The reported prevalence of glaucoma co-existing with aniridia is usually about 50%, with a range of 6–75%.[2,13,17] Mayer and colleagues[13] reported that in patients aged 10 years and younger, the presence of glaucoma reduced the proportion of people who had visual acuity ⩾6/60 from 100% to 86%. In this study, almost half of the patients had elevated IOP at presentation; 35.7% and 7.1% were diagnosed with glaucoma and elevated IOP, respectively. A comparative prevalence of 28.8% for elevated IOP and 18.3% for glaucoma at presentation was reported by Balekudaru and colleagues.[21] Patients with glaucoma co-existing with aniridia often have very high IOP. Mean IOP for this subset of patients in our study was 30.42 ± 8.5 mmHg compared with the overall mean of 21.6 ± 10.4 mmHg for all eyes. This is similar to findings by Balekudaru and colleagues[21] with reported mean IOP of 33.9 ± 8.6 mmHg at diagnosis and Gramer and colleagues[17] with reported maximum mean IOP of 32.6 mmHg.

The treatment of glaucoma in aniridia is often difficult, with some patients requiring multiple surgeries and medications to achieve optimal IOP control.[22] Our results and those of similar studies show that anti-glaucoma medications are often inadequate for IOP control, as most patients require surgery.[6,19,22] Visual outcome has been reportedly poor in the long term despite surgical and medical interventions. Identified risk factors for poor outcome include higher baseline IOP, greater number of surgeries, presence of limbal stem cell deficiency and a positive family history of aniridia.[21,22]

Cataract is also a common finding in aniridia, which may not be visually significant at diagnosis.[6,13,17,19] Half of the eyes in our study had cataract similar to reports from other studies.[13,17,19] Although the proportions of cataract reported by these studies were higher than ours, this disparity may be attributed to the younger age group in our study compared with other studies with reported mean age >25 years.[13,17,19] In our study, 16.7% of cases had ectopia lentis similar to that reported in the study by Gramer and colleagues.[17] Deficiencies in the molecular composition of zonules have been proposed as the cause of ectopia lentis in aniridia.[17]

Table 3. Medical and surgical interventions in patients with aniridia.

Type of intervention	Frequency (%)
Spectacles ($n = 14$)	
Prescribed	6 (42.9)
Not prescribed	8 (57.1)
Anti-glaucoma medications ($n = 11$)	
Timolol	2 (18.2)
Brinzolamide	2 (18.2)
Latanoprost	2 (18.2)
Timolol/Dorzolamide combination	5 (45.5)
Cataract surgery ($n = 10$)	
Lensectomy + AV	4 (40)
SICS + PPC + AV	2 (20)
SICS + PCIOL	3 (30)
Explantation of dislocated lens	1 (10)
Primary glaucoma surgery ($n = 6$)	
Trabeculectomy	4 (66.7)
Glaucoma drainage device	2 (33.3)

AV, anterior vitrectomy; PCIOL, posterior chamber intraocular lens; PPC, primary posterior capsulotomy; SICS, small-incision cataract surgery.

Cataract surgery is a common procedure in patients with aniridia and may result in some improvement in vision.[13,23] In our study, 71.4% of patients with cataract had surgery; this is similar to findings of Mayer and colleagues.[13] Special intraocular lenses (Morcher and Ophtec intraocular lens) which reduce symptoms of glare and photophobia have been produced for use in cataract surgery in aniridia.[17] Our patients had standard intraocular lenses due to non-availability of these special intraocular lenses in our environment

The prevalence of foveal hypoplasia in literature varies widely from as high as 94.5% to as low as

Table 4. Patients' demography, clinical characteristics and surgical interventions.

Initials	Age (months)	gender	Family history	Siblings in study	Eye	Nystagmus	Strabismus	Buphthalmos	Cornea involvement	lens	IOP (mmHg)	Glaucoma	Surgical intervention
MS	29	F	+	No	R	+	–	+	AAK, corneal oedema	Coloboma, MSP, PPC	35	+	Trabs
					L	+	–	+	AAK, corneal oedema	Clear, MSP	19	+	Trabs. &Lens explantation
FD	3	M	+	No	R	–	–	+	CCO, corneal oedema	Poor view	25	+	Awaiting glaucoma surgery
					L	–	–	+	CCO, corneal oedema	Poor view	24	+	Awaiting glaucoma surgery
OA	192	F	X	No	R	+	–	–	AAK, bullous keratopathy	Aphakic	35	+	–
					L	+	–	–	AAK	APC	50	+	Tube surgery
QD	168	M	+	No	R	+	Exotropia	–	AAK	Clear	–	–	–
					L	+	–	–	AAK	Cortical cataract	–	–	–
SO	132	F	+	No	R	+	Alternating esotropia	–	Clear	Clear	10	–	–
					L	+	Alternating esotropia	–	Clear	Clear	20	–	–
OE	36	F	–	No	R	+	–	–	Clear, microcornea	APC, PSC	16	–	–
					L	+	–	–	Clear, microcornea	Clear	14	–	–
RA	72	M	–	No	R	–	–	–	AAK	PSC	34	+	Awaiting glaucoma surgery
					L	–	–	–	AAK	Clear	23	+	Awaiting glaucoma surgery
AO	18	F	+	Yes	R	+	Alternating esotropia	–	Clear	PSC	10	–	SICS + PPC + AV
					L	+	Alternating esotropia	–	Clear	PSC	10	–	SICS + PPC + AV

(continued)

Table 4. (continued)

Initials	Age (months)	gender	Family history	Siblings in study	Eye	Nystagmus	Strabismus	Buphthalmos	Cornea involvement	lens	IOP (mmHg)	Glaucoma	Surgical intervention
AI	36	M	+	Yes	R	+	–	–	AAK	Nuclear, ectopia	16	–	Lensectomy + AV
					L	+	–	–	AAK	Nuclear, ectopia	22	–	Lensectomy + AV
AZ	108	F	+	Yes	R	–	–	–	Clear	Clear, ectopia	18	–	Lensectomy + AV
					L	–	–	–	Clear	Clear, ectopia	20	–	Lensectomy + AV
IH	0.2	F	–	No	R	–	–	+	CCO, corneal oedema	Clear, MSP	30	+	Trabs & tube surgery[a]
					L	–	–	+	CCO, corneal oedema	Clear, MSP	36	+	Trabs& tube surgery[a]
JK	60	M	+	No	R	+	–	–	AAK, microcornea	PSC	32	+	Tube surgery, SICS + PCIOL
					L	+	–	–	AAK, microcornea	PSC	15	–	–
BA	108	M	+	No	R	+	–	–	AAK, microcornea	Nuclear cataract	16	–	SICS + PCIOL
					L	+	–	–	AAK, microcornea	Nuclear cataract	14	–	SICS + PCIOL
AD	108	M	x	No	R	–	–	–	AAK, microcornea	Cortical cataract	08	–	–
					L	–	–	–	AAK, microcornea	Clear	10	–	–

+, present; –, absent; AAK, aniridia-associated keratopathy; APC, anterior polar cataract; AV, anterior vitrectomy; CCO, congenital corneal opacity; ectopia, ectopia lentis; IOP, intraocular pressure; L, left; MSP, microspherophakia; PCIOL, posterior chamber intraocular lens; PPC, primary posterior capsulotomy; PSC, posterior sub-capsular cataract; R, right; SICS, small-incision cataract surgery; Trabs, trabeculectomy; x, unconfirmed.
[a]Secondary glaucoma procedure.

3.3%.[6,17,18] Foveal hypoplasia was found in about a third of the eyes of patients who had posterior segment examination. In a case series of congenital aniridia with cataract by Wang and colleagues,[23] all cases had foveal hypoplasia on optical coherence tomography (OCT). Low prevalence in some studies may be due to a variety of factors such as underreporting, difficulty with posterior segment examinations from corneal and lens opacification, and young age of patients at diagnosis which may have made performance of investigations such as OCT difficult.[6,19] Foveal hypoplasia may also be subtle, necessitating a fluorescein angiography to show abnormalities of the foveal avascular zone.[24]

Nystagmus is a common finding in aniridia, with a prevalence as high as 80% in some studies.[6,13,17,18] Nystagmus occurs as a result of bilateral early-onset sensory deprivation. Its occurrence in aniridia has been linked to foveal hypoplasia.[1,25] In our study, nystagmus was found in a large proportion (64.3%) of the patients.

Conclusion

Familial aniridia with a possible autosomal-dominant pattern of inheritance is the predominant type of aniridia observed in our practice. In addition, a wide variety of the typical ocular features which include moderate to severe visual impairment, keratopathy, cataract and glaucoma were observed. The diversity of ocular findings in aniridia makes the management challenging and necessitates a multispecialty approach. We advocate that a clinical consultation of all patients with aniridia should include detailed pedigree charting, and comprehensive ocular and systemic examination until ophthalmic genetic services are readily available in Nigeria.

Conflict of interest statement

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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