Congenital Aniridia

Dewang Angmo, Bhaskar Jha, Anita Panda

Glaucoma Services, Dr RP Center for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

Correspondence: Anita Panda, Glaucoma Services, Dr RP Center for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India, e-mail: anitap49@yahoo.com

ABSTRACT

Aniridia is a rare bilateral condition that may have life-threatening associations. It occurs as a result of abnormal neuroectodermal development secondary to a mutation in the PAX6 gene linked to 11p13. This gene controls the development of a number of structures, hence the broad nature of ocular and systemic associations. This article presents a review of congenital aniridia including epidemiology, genetics, clinical features, ocular and systemic associations and management modalities.

Keywords: Aniridia, Subluxation, Glaucoma filtering surgery, PAX6 gene.

INTRODUCTION

Aniridia (Greek, absence of iris) is an uncommon hereditary bilateral congenital, panocular disorder affecting not only the iris but also the cornea, anterior chamber angle, lens, retina, and optic nerve as well with life-threatening associations. Its first description was given by Barrata in 1818. It is characterized by profound hypoplasia of the iris (Figs 1A and B) in frequent association with multiple ocular anomalies, such as peripheral corneal pannus and keratopathy, foveal hypoplasia, diffuse retinal dysfunction as seen on electroretinography, impaired acuity with nystagmus, cataract and ectopia lentis and optic nerve hypoplasia. These defects, in combination, usually cause a formidable barrier to normal visual function.

Often, the iris is vestigial (little more than a margin is present) and the eye appears to have colorless (only a larger than normal) pupil. It may be associated with systemic defects consisting of mental retardation, genital anomalies and Wilms’ tumor.1

Epidemiology: Incidence reported from studies are 1:64,000 to 1:96,000.1,2 Pedigree analyses have shown that two-thirds of children with aniridia have an affected parent.1,3

Mortality/Morbidity: All patients with aniridia are visually handicapped for their whole life. Complications like cataract and glaucoma reduce the vision furthermore. The patients with Wilms’ tumor have a reduced span of life. Aniridia itself is not a lethal disorder. However, miscarriages and a stillborn child have been the only results of a consanguineous mating between individuals with aniridia. It is possible that a homozygous mutation of the aniridia gene may be lethal. The morbidity of aniridia is significant because of the decreased vision and nystagmus.

Genetics: Aniridia can occur as the following:

- Autosomal disorder: Dominant and recessive
- Deletion of the short arm of chromosome 11, including band p13
- Sporadic case.

In the majority of cases with familial inheritance, an autosomal dominant inheritance pattern with almost complete penetrance has been demonstrated.1 However, variations in expression have also been seen to occur. Rarely, it may be transmitted in an autosomal recessive manner.4,5 Consanguineous

Figs 1A and B: (A) The peripheral iris rim and a clear view of the lens equator, (B) total aniridia with inferiorly subluxated lens
marriages have also been implicated in some studies. Of the sporadic cases of aniridia, two-thirds represent a new autosomal dominant condition. Regarding racial predisposition it has been seen that it does not exist.

As an isolated ocular malformation, aniridia is an autosomal dominant disorder, which is caused by a mutation in the PAX6 (paired box gene family) gene.

Patients with aniridia who have a positive family history are not at an increased risk for Wilms’ tumor. Two genetic loci for aniridia have been identified: one (AN1) on chromosome arm 2p and one (AN2) on chromosome 11 (Table 1).

**Miller Syndrome (WAGR Complex, 11p Syndrome)**

The association between aniridia and Wilms’ tumor is referred to as Miller syndrome. Approximately 30% of patients with sporadic aniridia develop Wilms’ tumor, usually before age 5 years. It is reported that 1.4% of patients with Wilms’ tumor have aniridia compared to one in 64,000 to one in 100,000 of the general population. Other associated features are genitourinary abnormalities, craniofacial dysmorphism, hemihypertrophy and severe mental retardation. These patients also have poorly lobulated low-set ears, prominent noses, and long narrow faces. The acronym WAGR (Wilms’ tumor, aniridia, genitourinary anomalies and mental retardation) describes some of the features of Miller syndrome.

Miller syndrome has been attributed to a deletion of band 11p13. Patients with sporadic aniridia should undergo a thorough physical examination and work-up by a family practitioner or pediatrician.

**Gillespie Syndrome**

Gillespie syndrome is the association of aniridia, cerebellar ataxia and mental retardation. It is autosomal recessive, occurring in approximately 2% of patients with aniridia. These patients have anatomical defects in the cerebellum and other parts of the brain, and they are not predisposed to developing Wilms’ tumor.

A study of the PAX6 gene in Gillespie syndrome failed to find a mutation, suggesting that abnormalities in the PAX6 gene are not responsible for this syndrome.

**Pathophysiology**

Primary developmental arrest of the neuroectoderm and a secondary alteration of all three neural crest waves of the mesenchyme have been implicated in the pathogenesis of aniridia. The exact defect in iris morphogenesis giving rise to aniridia is unknown. Because the iris pigment epithelium, the iris musculature, the retina, and the optic nerve are derived from neuroectoderm, there may be a common embryologic origin for these anomalies. The pathogenesis may involve defective formation or excessive regression of various layers of the anterior segment caused by cellular or biochemical aberrations. This explains the combined anterior and posterior segment, neural ectodermal and mesenchymal defects. The iris stroma is hypoplastic, indicating an altered third neural crest wave of mesenchyme.

**Clinical Presentations**

1. Aniridia alone
2. Aniridia with other systemic abnormalities
   - Wilms’ tumor (20% cases)
   - Genitourinary abnormalities
   - Mental retardation
3. Aniridia with other ocular disorders
   - Albinism
   - Ectopia lentis (50%)
   - Spontaneous lens dislocation
   - Arcus juvenilis
   - Keratoconus
   - Cataract (50-85%)
   - Glaucoma (30-50%)
   - Nystagmus
   - Strabismus
   - Optic nerve hypoplasia (75%)
   - Pupillary membrane remnants.

**Age:** The age at presentations is generally infancy when the parents notice abnormally large pupil. Sometimes they may also complain poor vision and photophobia in early childhood along with nystagmus. Congenital glaucoma and aniridia usually are not associated at birth. The glaucoma develops at either the preteen or the teenage level.

Significant cataracts may occur before puberty. The risk for cataract increases with age with lens opacities observed in 50 to 85% of patients during the first two decades of life.

The clinical presentations/features are discussed one by one:

**Decreased Vision**

It is the most common symptom of the aniridia. Many series report that as many as 86% of affected individuals have 20/100 vision or worse in the better eye.

The causes of poor vision are:
- Foveal hypoplasia
- Cataract
- Glaucoma
- Corneal dystrophy
- Nystagmus
- Aberrations of light have also been indicated as a cause of early poor vision in aniridia
- Strabismus
- Ectopia lentis
- Optic nerve hypoplasia.

**Photophobia**

It is often present in affected patients and considered secondary to excessive light stimulation because of poor pupillary...
constriction. A characteristic facial expression in many children consists of narrowing of the palpebral fissure and furrowing of the brow.¹

Iris Abnormalities
Aniridia is still considered by some to be one of the colobomatous disorders.¹⁰

The abnormalities can be:
- Complete absence; as seen on oblique illumination
- Hypoplasia with irregular pupillary margins (atypical coloboma of pupil)
- Only root of the iris; visible on gonioscopy.

Iris abnormalities from almost total absence to mild hypoplasia of the iris may occur in affected individuals. Since a small portion of iris tissue can almost always be found on gonioscopic examination, the term “irideremia” better describes the condition than does aniridia.⁸⁻⁹ In addition, ocular colobomas and aniridia have been reported among individuals in the same family in the patients with aniridia. It is now known that iris thinning with a round; normal-appearing pupil may be found in family members of aniridics who, on further examination, show evidence of characteristic corneal or lenticular involvement of aniridia.⁹

Glaucoma
Congenital glaucoma with or without buphthalmos is rare in infants with aniridia, but the reported incidence of glaucoma later in childhood is 6 to 75%.¹¹⁻¹⁶

Although some infants have congenital angle anomalies (trabeculodysgenic anomaly) and early glaucoma, most glaucomas occur later in childhood or early adulthood with closure of the iridocorneal angle. As a result of its delayed onset, the clinical findings of megalocornea, buphthalmos and Haab’s striae are not found. Routine gonioscopic examination is important to detect anatomical changes in the angle structures that may progress to angle-closure. During the first few years of life, the trabecular meshwork appears open and is not covered by iris tissue. Grant and Walton believe that a progressive change in the angle structures occurs during the first two decades of life in those patients who will develop glaucoma.¹⁴ These changes consist of extensions of iris stroma, somewhat resembling anterior synechia, that reach across and attach anterior to the filtration area of the trabecular meshwork. These iris extensions may eventually form a sheet that covers most of the filtration area in patients who will develop glaucoma. The IOP elevation is presumed to occur at a later developmental stage, usually after the age of 5, or often in adolescence. The severity of glaucoma is directly correlated with the extent of progressive synechial angle closure by the pulled-up residual iris stump. Glaucoma secondary to intumescent lens changes or ectopia lentis (Fig. 1B) has been reported in aniridia.

Cataract
Cataracts (Fig. 2) occur frequently and at a young age in aniridics.¹⁷ Lens opacities develop in 50 to 85% of patients, usually during the first two decades of life. Subtle changes may be present in the lens at birth, and these can progress to significant opacities by middle age.

Types of cataracts are as following:
- Anterior polar
- Pyramidal
- Nuclear
- Lamellar
- Cortical.

Anterior and posterior lens opacities noted after birth do not usually cause significant visual difficulty. Cortical, subcapsular, and lamellar opacities often develop by the teenage years and may require lens extraction. Areas of clear space may be present in the cataractous lens, which allows for relatively good vision. In these patients, cataract surgery is best delayed, since the risks of glaucoma, developing or progressing, and foveal hypoplasia in aniridic eyes outweighs the small potential for visual improvement.

Ectopia Lentis
Ectopia lentis (Figs 1B to 3) has been reported in up to 56% of patients with aniridia. Segmental absence of zonules is a possibility but zonules are morphologically normal. The high incidence of ectopia lentis in aniridia may eventually be attributed to defects in their molecular structure.¹⁸⁻¹⁹

Corneal Defects
These can be seen in the following forms:
- Pannus (Fig. 3)
- Epithelial ulcers
- Arcus juvenilis
- Microcornea.

Progressive corneal opacification and pannus occur in most patients, developing as early as age of 2 years. In majority of individuals aniridic keratopathy manifests in the first decade of life as thickened irregular epithelium of the peripheral cornea.
The epitheliopathy is typically accompanied by fine superficial neovascularization (Fig. 3). Initially, fine radial vessels invade the superficial layers of the peripheral cornea at the 6 and 12 o’clock positions, and then involve the whole circumference. This process may initially involve epithelial and subepithelial layers, and later on may progress to involve the entire thickness of cornea. Overtime subepithelial fibrosis and stromal scarring predisposes aniradic patients to recurrent erosions, corneal ulceration and chronic pain. This corneal “dystrophy” associated with aniridia may progress in a variable manner to completely cover the cornea, further compromise vision requiring corneal transplantation. Since, the corneal abnormality is vascularized and inflamed, it cannot be included among the group of diseases known as dystrophies.

Microcornea has been reported in association with aniridia. The cause for the keratopathy is still not clear. It is thought to be resulting from dysfunction of limbal stem cells which originates from following observations:

1. The clinical morphology of the limbus in aniridic patients has been shown to be abnormal. These patients lack the palisades of Vogt. These palisades serve as a marker for corneal stem cell differentiation. The absence of this important limbal structure suggests localization of the epithelial abnormalities in aniridic patients to the limbus.
2. Healthy corneal epithelium is a stratified squamous epithelium that contains no goblet cells or other conjunctival specific elements. In aniridic patients, goblet cells are present in significant numbers in the peripheral corneal epithelium.

**Posterior Segment Disorder**

It consists of optic nerve hypoplasia and foveal hypoplasia; optic nerve hypoplasia has rarely been reported in aniridic patients. True aplasia to even mild anomalies can be seen in the patients with aniridia. Mild cases can be noted if careful comparisons are made between the widths of the superior or inferior retinal arteriole prior to its bifurcation with the disk size. While the normal disk/arteriole ratio in an adult eye is $14.6 \pm 2.4$, in hypoplastic disks the range is from 6.1 to less than 14.6. True aplasia of the optic nerve is although rare in the general population, but can be found in these patients. The association between poor retinal development and aniridia is not surprising, since the iris epithelium and musculature, and the retina, are derived from neuroectoderm.

**Foveal Hypoplasia**

Foveal hypoplasia is a devastating feature of some cases of aniridia, with patients having nystagmus from an early age, and a visual acuity potential of only about 20/200. This should make the physician cautious about the visual results from cataract extraction or penetrating keratoplasty. In some patients, foveal hypoplasia may be so subtle that fluorescein angiography may be necessary to demonstrate lack of the foveal avascular zone. Approximately, 75% of patients with aniridia have some degree of optic nerve hypoplasia. The macula and optic nerve are usually normal in patients with Gillespie syndrome.

**Strabismus and Refractive Errors**

Strabismus is common in aniridic patients and mostly it is esotropia. Asymmetric visual loss in aniridic children may occur from amblyopia secondary to strabismus or anisometropia. High refractive errors are not uncommon and a careful cycloplegic refraction is necessary in affected children. This can be either myopia or hypermetropia. Visual acuity may improve if clinical suspicion is high for amblyopia and appropriate optical correction and occlusion therapy begins early in the child’s visual development.

**Nystagmus**

Pendular nystagmus is present in the majority of aniridics. Most investigators believe that nystagmus is secondary to macular hypoplasia. The presence of nystagmus should alert the physician to the likelihood of foveal hypoplasia. The other causes of nystagmus and poor vision in infancy are the characteristic iris defect and lack of foveal reflex in aniridia. Mild cases may be difficult to detect because of nystagmus, and corneal or lens opacities.

**Differential Diagnosis**

- Rieger syndrome with iridocorneal dysgenesis
- Congenital coloboma of the iris
- Surgical iris coloboma
- Hereditary iris hypoplasia
- Traumatic iris injury
- Bilateral congenital mydriasis
- AGR triad—sporadic (bilateral or unilateral) aniridia, genitourinary abnormalities and mental retardation
• Corectopia
• ICE syndromes
• Anterior cleavage syndromes
• Colobomatous microphthalmia.

**Investigations**

**Gonioscopy**

Grant and Walton studied detailed angles assessment in aniridic children.\(^{25}\) They noted that the angles of aniridic patients without glaucoma are free from iris attachments to the trabecular meshwork and that the iris remnant is in the normal iris plane, which is perpendicular to the axis of the eye. The angles of aniridic patients developing glaucoma show increased confluence of irregular attachments from the iris stroma to the angle wall. They found that in most of the eyes the peripheral stump of iris gradually extended anteriorly to cover the filtration portion of the trabecular meshwork (Figs 4A and B) eventually leading to synechial angle closure. Typically, later in childhood the filtration area of the trabecular meshwork is covered by extension of abnormal iris tissue forward on to the trabecular meshwork, and therefore rising the intraocular pressures.\(^{25}\) Therefore, gonioscopy is must to find out the progression of angle closure glaucoma. If the iris stump is enlarging it is an indication of prophylactic goniotomy.

**Schirmer’s test**: To find out associated dry eye.

**Ultrasound biomicroscopy**:\(^{26}\) This is helpful in imaging, especially in cases of opaque cornea. Ultrasound biomicroscopy imaging demonstrates shallow anterior chamber, irregular corneal thickness, hyperechoic lesion of the corneal stroma and short, thin ciliary body (ciliary body hypoplasia). It also shows peripheral residual iris stump. Ultrasound biomicroscopic imaging demonstrated that not only iris hypoplasia but also ciliary body hypoplasia exist in aniridia. Anterior inclination of the ciliary process was also found, which was thought to be at least partly responsible for the shallow anterior chamber.

**Impression cytology**: To find out abnormal cells in the epithelium. The presence of caliciform cells in corneal impression cytology defines the instability of the lacrimal film and an epithelial defect.

**FFA**

Intravenous fluorescein angiography shows an early vascular loop in the remaining iris and late leakage from the pupillary margin; this may be a helpful finding in those cases where the diagnosis of aniridia is not apparent because of a round, more normal-appearing pupil. The posterior pole of aniridic patients shows persistence of vessels in the normally avascular zone of the macula.

**Electrophysiological Tests**

The electroretinographic (ERG) signal amplitudes in patients with visual acuity of 20/60 or worse are abnormally low, while some patients with better acuities may have abnormally high a:b wave ratios. Prolonged latencies of the b wave peaks (implicit times) were also demonstrated in some patents; no ERG findings have been consistent enough to be useful diagnostically.

The electrooculogram (EOG) has usually been normal.

**Lab Studies**

Chromosomal deletion is detected by cytogenetic testing with the use of high-resolution banding.

Submicroscopic deletions of the Wilms’ tumor gene are recognized with a fluorescent in situ hybridization (FISH) technique.

High-resolution chromosome studies are obtained in sporadic cases to determine if there is a deletion of band 11p13.

Serial renal ultrasound examinations are indicated in patients through age 7 years, especially for those with a deletion of band 11p13 or those with a negative family history of aniridia and normal chromosomes.

**Histologic Findings**

Histologically, small portions of the iris are always present; the ciliary body is usually hypoplastic; and the anterior chamber
angle may be normal, immature (i.e. incompletely developed), or malformed. Histopathologic examination of advanced cases of aniridia reveals only stubs of iris tissue that lack dilator and sphincter muscles, both neuroectodermal derivatives. In eyes enucleated from older patients, extensive peripheral anterior synechia that cause the iris stump to adhere to the posterior corneal surface have been observed.

Retinal lipoidal deposits in the peripheral retina have been reported in three patients suggests that the underlying defect may be in the metabolic pathway of fats, which results in storage of an abnormal lipid compound in the tissues.

Systemic Investigations
Abdominal ultrasound: To rule out associated Wilms’ tumor
Genitourinary referral: To find out associated anomaly
IQ evaluation: For mental retardation.

TREATMENT
Glaucoma
This is difficult and the prognosis guarded. Prophylaxis is directed toward the prevention of glaucoma, which includes the following:
- Medical treatment with miotics
- Surgical separation of the iris from the trabecular meshwork in selected cases.

Medical treatment is frequently the initial approach, although it is usually eventually inadequate. The medical treatment is directed toward control of intraocular pressure, which includes the topical use of the following:

Miotics: Miotics often are tried first; they improve aqueous outflow by contracting the ciliary muscle. However, the induced myopia may not be well-tolerated by young patients. Adrenergic agonists, beta-blockers, and carbonic anhydrase inhibitors also may be tried, but they often are ineffective long-term as the patient becomes refractory to them. Whenever a new medication is to be instituted, a trial should be performed, adding and removing only one medication at a time.

Beta-blockers
- Sympathomimetics
- Carbonic anhydrase inhibitors.

Argon laser trabeculoplasty: It has been described in the patients with aniridia. Nelson performed the procedure in four of his patients and all had good control of IOP.1 Poor results have been obtained with laser trabeculoplasty.1

Surgical Procedures
No convincing opinion exists as to which surgical procedure is the treatment of choice for aniridic glaucoma; none has been considered reliable and predictable in efficacy. Surgical procedures for the treatment of aniridic glaucoma include the following:

1. Goniotomy is useful if performed before the development of irreversible synechial closure. This early surgical therapy has some risk to the crystalline lens and zonules because the surgery is performed from the anterior approach. It was reported by Barkan11 in the 1950s to control IOP in one patient with aniridia followed for 9 months. Since that time, however, multiple authors have reported disappointing outcomes with IOP control from goniotony.25,27

2. Trabeculotomy may be safer than goniotony since it relies on the posterior approach (ab externo). The tissues can be defined more clearly, and accurate surgery can be performed. However, failures are common. Adachi et al41 found that in 12 eyes, which initially underwent trabeculotomy, 10 eyes (83%) obtained good IOP control (defined as an IOP of 21 mm Hg or lower) after the first or second trabeculotomy with a mean follow-up of 9.5 years. In eyes that underwent other procedures first (i.e. goniotony, trabeculectomy, trabeculectomy with trabeculotomy and Molteno implant), only three of 17 eyes (18%) obtained good IOP control. They concluded that in eyes with aniridia and uncontrolled glaucoma, trabeculotomy is the preferred initial surgical intervention. Their patient population, however, developed glaucoma and underwent surgery at an earlier age than most patients with aniridia. Of the 29 eyes that had glaucoma surgery, 14 eyes had glaucoma surgery in the first year of life. This is inconsistent with the general belief that many patients with aniridia develop glaucoma later in childhood (i.e. between ages 5 and 15) because of progressive angle closure, and that glaucoma in infancy is rare in aniridic patients. The success rate reported by Adachi et al includes patients who had an IOP of 21 or lower, with or without medications. In fact, only three of 12 eyes (25%) treated with initial trabeculotomy achieved IOP control without medications. Wiggins and Tomey27 did not have as much success with trabeculotomy in treating aniridic glaucoma as the two eyes that underwent this procedure in their large series did not achieve successful IOP control.

3. Filtering procedures: Most surgeons operate for trabeculectomy after a few attempts at goniotomy or trabeculotomy. There is a greater danger of injury to the crystalline lens and to disturbance of the vitreous along with vitreous loss in trabeculectomy because of the absence of iris. The surgical complications of direct lens injury, lens or vitreous incarceration in filtration sites can be considerably reduced with the use of intracameral viscoelastic perioptatively. Several other studies, however, have reported poor IOP control after trabeculectomy in eyes with glaucoma associated with aniridia. Grant and Walton reported poor IOP control (defined as pressure > 22 mm Hg or the need for further surgery) in nine eyes of seven patients treated with filtering surgery for glaucoma.
5. Cyclodestructive procedures have also been reported in the Glaucoma drainage devices therapy. Thus, glaucoma drainage implants have a role in trabeculotomy, laser trabeculoplasty, and cyclotherapy. Many of these eyes had multiple prior IOP drops. Vision remained stable in 25% of eyes, improved in 63% of eyes, and decreased in the one eye that experienced a complication, retinal detachment. Wiggins and Tomey also reported a high rate of success with glaucoma drainage implants in advanced cases of aniridic glaucoma, in that 83% of the eyes that underwent this procedure had a postoperative IOP < 21 mm Hg with no visually devastating complications. Many of these eyes had multiple prior IOP lowering procedures including trabeculectomy, trabeculotomy, laser trabeculoplasty, and cyclotherapy. Thus, glaucoma drainage implants have a role in aniridic glaucoma and can be used as an initial surgical approach or in advanced cases with extensive prior surgical attempts at IOP lowering.

6. Goniosurgery: Chen and Walton described a different approach to aniridic glaucoma, using goniosurgery to prevent the development of glaucoma in selected young patients with aniridia. They reported the use of a modified goniosurgery in 55 eyes of 33 patients with aniridia, all of whom met inclusion criteria (i.e., age greater than 1 year of life and the presence of particular gonioscopic findings). Eyes that were felt to be good candidates for prophylactic goniosurgery included aniridic eyes with greater than half the circumference of the posterior trabecular meshwork covered by extensions of tissue from the peripheral iris, or eyes with progressive covering of the trabecular meshwork by iris tissue. Eyes with aniridia and IOP mm Hg, or eyes with less severe gonioscopic changes were not considered good candidates for prophylactic goniosurgery. These selected eyes that were felt to be at high-risk for the development of glaucoma because of progressive iris changes then underwent a modified goniosurgery. In this modified goniosurgery, a goniolysis knife was used to remove the abnormal tissue spanning between the iris and the trabecular meshwork. Care was taken to avoid injury to the trabecular meshwork. Similar to goniosynechialysis surgery, this iris tissue is peeled away from the wall of the angle. Unlike goniolysis surgery, no incision through the trabecular meshwork or into Schlemm canal is made. Chen and Walton reported successful prevention of glaucoma in 89% of patients treated with this prophylactic goniosurgery (i.e., IOPs were < 22 mm Hg without medications at last follow-up). Additionally, the remaining 11% of patients who associated with aniridia. Nelson and Spaeth noted that in five of 14 patients with glaucoma associated with aniridia, IOP remained uncontrolled after trabeculectomy. Okada and associates reported successful IOP control in young aniridic patients after filtering surgery. In their study, 17 trabeculectomies and three trabeculectomies with mitomycin C were performed on 10 eyes of six patients younger than 40 years, followed up for a mean of 14.6 months (range, 2-54 months). The mean duration of successful IOP control (defined as pressure lower than 20 mm Hg with or without glaucoma medications) after filtering surgery was 14.6 months.

4. Glaucoma drainage devices: The choice of the techniques and the order, in which they are used, depends upon the peculiarities of the case and the perception of the surgeon. Use of luminal occlusive suture, which can be removed later, has greatly improved the success of this procedure and enhanced the safety. Arroyave et al studied five patients with aniridia (8 eyes) who underwent placement of glaucoma drainage devices (7 eyes had Baerveldt implants and 1 a double plate Molteno implant) at an average age of 92 months and who were followed up for an average of 19 months. Insertion of the glaucoma drainage implant was the initial glaucoma surgery in six of the eight eyes in this study. They reported a success rate of 100% at 6 months and 88% at 1 year, with success defined as IOP ≤ 21 mmHg, with or without medications, with no visually devastating complications or need for reoperation for glaucoma. The patients experienced a decrease in average IOP from 35 mm Hg preoperatively on an average of one glaucoma medication to 14.9 mm Hg postoperatively with no eye drops. Vision remained stable in 25% of eyes, improved in 63% of eyes, and decreased in the one eye that experienced a complication, retinal detachment. Wiggins and Tomey also reported a high rate of success with glaucoma drainage implants in advanced cases of aniridic glaucoma, in that 83% of the eyes that underwent this procedure had a postoperative IOP < 21 mm Hg with no visually devastating complications. Many of these eyes had multiple prior IOP lowering procedures including trabeculectomy, trabeculotomy, laser trabeculoplasty, and cyclotherapy. Thus, glaucoma drainage implants have a role in aniridic glaucoma and can be used as an initial surgical approach or in advanced cases with extensive prior surgical attempts at IOP lowering.
underwent the procedure subsequently developed glaucoma with elevations of IOP that could be controlled with two glaucoma medications or less. These results were based on an average follow-up of 9.5 years, and there were no complications of surgery. This is in contrast to the literature, which reports the incidence of glaucoma in aniridia to be about 50%.

Glaucoma occurs in about half of all cases of aniridia and is difficult to control with medications and surgery. Different surgical approaches have been attempted with only limited success. The most successful approach may be to prevent aniridic glaucoma by performing goniosurgery in selected eyes with progressive angle changes. For aniridic glaucoma, glaucoma drainage devices may be more successful in lowering IOP and may have fewer complications than trabeculectomy and cyclodestructive procedures.

**Corneal Problems**

1. Penetrating keratoplasty may be indicated for corneas that have opacified from pannus or in the cornea that becomes sufficiently opaque. Surgical results from penetrating keratoplasty are quite poor because of the abnormal stem cells and highly vascular host. Therefore, visual results are marginal (one to two lines improvement in Snellen acuity) and the prognosis is guarded because of rejection and underlying amblyopia or other structural defects. Kremer et al reported recurrence of ocular surface abnormalities in 91% of treated eyes and rejection of corneal grafts in 64% of patients. Gomes documented graft failure in 100% of patients requiring repeat penetrating keratoplasty for recurrent aniridic epithelial disease.

2. Keratolimbal allograft: These have been tried to address the problem of limbal stem cell deficiency. Results have been found encouraging.

3. Amniotic membrane transplantation is a very effective procedure, although its effect is transitory, for restoring the ocular surface integrity in patients with congenital aniridia and moderate limbal deficiency.

4. Stem cell transplantation: Ocular surface stem cell transplantation is a new therapy aimed at correcting stem cell deficiency and has been highly successful in treating the corneal disease associated with aniridia. The goal of the surgery is to transplant normal stem cells from donor eyes to the stem cell deficient aniridic eye.

5. A recent analysis of patients treated demonstrates the establishment of a stable ocular surface in 90.5% of aniridic patients treated with appropriate immunosuppression. Of these patients, approximately one-third were spared the need for subsequent corneal transplantation. In those patient in which significant scarring had already occurred prior to stem cell transplantation, corneal transplantation was performed and was successful in 85% of patients on appropriate immunosuppression.

6. Autologous serum has also been proved in these patients.

**Cataract**

Lens opacification may require cataract extraction. Before operating, however, the ophthalmologist should attempt refraction through the aphakic portion of the pupil if the lens is subluxated. Either extracapsular or phacoemulsification surgery may be used, depending on the stability of the zonules.

**Management of Cataract**

- In-the-bag lens implantation in cases without lens dislocation
- In-the-bag IOL placement with intracapsular ring, when there is slight lens displacement
- Lens extraction followed by contact lens correction, if the lens is grossly out of place.

Cataract extraction can be difficult and is often accompanied by vitreous loss or further deterioration of the cornea. Dense cataract removal may result in some improvement in visual acuity. Lensectomy performed with an aspiration-cutting instrument has been recommended. Capsule-supported intraocular lenses are not appropriate for patients with ectopia lentis. The use of intraocular lens implants in children is an evolving field, and their use in patients with aniridia is still not very clear.

A combined approach for both glaucoma and cataractous subluxated lens: In the bag limbal lensectomy with Ahmed glaucoma valve implantation.

**Surgical Technique**

**“In the Bag” Limbal Lensectomy**

The surgery is done through limbal ports, which are made using 20 G microvitreoretinal (MVR) blade, at 9 and 2 o’clock position for superiorly subluxated lens (Fig. 5). A third port is made at 4 and 5 o’clock position for the anterior chamber maintainer.

MVR blade is used to make an opening in the anterior lens capsule followed by hydrodissection with hydrodissection cannula. Vitrectomy cutter of phacoemulsification system is used in I/A-Cut mode (in which irrigation and aspiration comes before cutting). Vitrectomy probe is inserted into the anterior chamber and then through the opening in anterior capsule into the lens (Fig. 6).

Second port is used for irrigation cannula to maintain chamber. All the cortical matter is aspirated and then capsular bag is taken with the help of vitrectomy cutter in the same mode. Now a thorough anterior vitrectomy is done in Cut-I/A mode (Fig. 7).

**Ahmed Glaucoma Valve Implantation**

Adequate surgical exposure is dependent on proper placement of a traction suture. A 6-0 polyglactin (Vicryl) or silk traction suture on a spatulated needle is placed through superficial cornea near the superior limbus and attached to the drape beneath the eye.
A fornix-based conjunctival–Tenon capsule flap is created, usually in the superotemporal quadrant to expose the sclera bed (Figs 8 and 9A). The flap is slightly elevated to allow for blunt dissection between Tenon and episclera with blunt Westcott scissors. Radial relaxing incisions on one or both sides of the conjunctival flap can improve surgical exposure.

Whenever possible, the superonasal quadrant should be avoided to reduce the risk for strabismus/motility problems. The Ahmed drainage device, when placed in the superonasal quadrant, has also been shown to come within 1 mm of the optic nerve.46

With Ahmed valved implants, balanced salt solution must be irrigated through the tube using 27 gauge cannula (Fig. 10), before the insertion into the anterior chamber, to ensure that the valve opens properly.

The external plate is then tucked posteriorly into the sub-Tenon space (Fig. 9C) and is sutured to sclera with nonabsorbable 9-0 Prolene or nylon sutures through the anterior positional holes of the plate, with the anterior border at 8 to 10 mm posterior to the limbus.

The tube is then cut, bevel up, to permit its extension 2 to 3 mm into the anterior chamber (Fig. 9C). It is best to maintain
The anterior chamber is then entered with a 23 gauge or a 22 gauge needle, parallel to the iris plane/stump (Figs 11A and B). The needle creates a watertight seal, preventing leakage around the tube, and thus reducing the risk for postoperative hypotony.47

The angle at which the needle enters the anterior chamber is critical, because it is important that the tube, which will pass through this needle track, is positioned between cornea and iris, without touching the cornea.

The tube is then inserted into the anterior chamber via the needle track using nontoothed or specially designed tube-insertion forceps, but these generally are not necessary (Figs 12A and B). The tube can be secured to the sclera by using a nonabsorbable suture, such as 9-0 prolene or nylon.

The anterior chamber may need to be deepened with balanced salt solution, or viscoelastic, via the paracentesis, and the tube is checked for proper position in the anterior chamber. To avoid the potential complications related to tube erosion, a rectangular patch of preserved sclera 5 × 7 mm is sutured over the tube at the limbus (Figs 13A and B).49 Processed pericardium (Tutoplast), donor sclera, dura and fascia lata are also available commercially for this purpose. It is also possible to use autologous sclera or to place the tube under a partial-thickness scleral flap similar to a trabeculectomy procedure.

The conjunctiva is then sutured back to its original position using 8-0 Vicryl sutures (Fig. 14). Once again vitrectomy status is checked, triamcinolone acetate can be used for this purpose.
Anterior chamber is formed after hydrating the ports. Subconjunctival steroids and antibiotics are injected at the completion of the procedure in a quadrant away from the surgical site.

Iris Abnormalities

Various methods have been used to overcome the disabling effects of iris deficiency, including eyelid surgery, colored contact lenses, corneal tattooing and implantation of artificial irides. The most commonly used prosthetic iris devices are the Morcher aniridia IOL types 67F and 67G, the aniridia ring type 50C, and the coloboma diaphragm type 96G. Types 67F and 67G are used in traumatic or congenital aniridia either in the ciliary sulcus, if there is adequate capsular support, or trans-sclerally sutured in the absence of capsular support. Morcher 67G aniridia IOL and type 50C is designed for endocapsular implantation in cases of traumatic or congenital aniridia. For a total reconstruction of the missing iris, two rings have to be implanted and turned against each other to form a complete ring, and then an additional foldable lens is inserted.

Type 96G is used in the capsular bag in cases of sector iris defects up to 90°. Iris defects between 90° and 180° could be managed by inserting two such devices. One version consists of an artificial black iris attached to a standard polymethylmethacrylate intraocular lens. This type of iris is best used when suturing of the lens is required to secure the lens in place. An advantage of this implant is that it is very stable.

Treatment of Photophobia, Nystagmus and Strabismus

Patients should be given the following things:
- Tinted or iris contact lenses
- Tinted spectacle lenses
- Tinted intraocular lenses (IOLs).

By the above measures, reducing the amplitude and frequency of nystagmus is possible. In cases of strabismus, patching of the favored eye is indicated to treat amblyopia. Cycloplegic refraction should be performed, and appropriate correction should be given. Strabismus surgery may be indicated at an early age to enhance binocularity.

Treatment of Refractive Errors, Strabismus and Amblyopia

Careful refraction and complete correction must be done to decrease the risk of amblyopia. Usually, the potential visual acuity in both eyes should be symmetrical. When the vision is unequal without structural difference, vigorous amblyopia exercises should be performed in the worst eye.

Binocularity can be achieved if macular hypoplasia is not severe. Strabismus surgery is indicated at an early age.

Consultations

- Banded chromosome analysis on the patient and both parents
- Linkage analysis when large families are available.
Genetic Counseling

- All patients with aniridia should be referred for genetic counseling. A full family history should be sought, with specific attention to ocular abnormalities, low vision, genitourinary abnormalities, Wilms’ tumor and mental retardation.
- A full physical examination should be performed concentrating on the genitourinary system. Imaging of the abdomen and brain, preferably MRI, is indicated.
- Chromosome analysis of the patient and family and genetic analysis of the PAX6 gene should be performed.
- Parents and close relatives should have a careful ocular examination performed.
- Fluorescein angiography of the iris and fundus may reveal subtle abnormalities not found clinically, e.g. abnormalities of the iris collarette and foveal avascular zone.

REFERENCES