A Rare Case With Aniridic Fibrosis Syndrome After Iris Diaphragm Intraocular Lens and Ahmed Valve Implantation in a Patient With WAGR Syndrome

WAGR Sendromlu Bir Olguda İris Diyafram Lensi ve Ahmed Valf İmplantasyonu Sonrası Gelişen Nadir Görülen Aniridik Fibrozis Sendromu

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ABSTRACT

Congenital aniridia is a rare, bilateral condition associated with foveal hypoplasia, nystagmus, cataract, glaucoma, keratopathy, and dry eye. Aniridic fibrosis syndrome is a newly recognized clinical entity characterized by progressive retrocorneal, cyclitic, or retrolenticular fibrosis which can lead to corneal endothelial decompensation, hypotony, and retinal detachment. A 6-year-old male presented with WAGR syndrome. At presentation he had mental retardation, nystagmus, bilateral rudimentary iris, and bilateral posterior polar cataract. Cataract extraction and implantation of an aniridia intraocular lens (IOL) was performed in the right eye. Glaucoma developed in the right eye approximately 2 months after cataract surgery. An Ahmed glaucoma valve was implanted in the right eye and prophylactic goniotomy was performed in the left eye. Nine months after glaucoma surgeries aniridia-associated keratopathy (AAK) was observed in both eyes (predominantly in the right eye). Keratopathy progressed during follow-up. At the 6th year follow-up aniridic fibrosis syndrome was detected in the right eye, with retrocorneal fibrotic membrane formation, inferior dislocation of the IOL, and endothelial decompensation. During the 6-years follow-up, intraocular pressure was controlled with 2 medications in the right and without medication in the left eye. The management of aniridia is often quite difficult because of the complex involvement of ocular structures. Although satisfactory results can be obtained with surgery for cataract and glaucoma, progression of AAK and development of aniridic fibrosis syndrome (especially in eyes with intraocular hardware) are the obstacles for good visual outcome. This is the first case of aniridic fibrosis syndrome reported from Turkey.

Key words: Aniridic fibrosis syndrome, congenital aniridia, WAGR syndrome.

ÖZ

Konjenital aniridi foveal hipoplazi, nistagmus, katarakt, keratopati ve kuru göz ile karakterize, nadir görülen ve her iki gözü birden etkileyen klinik durumdur. Aniridik fibrozis sendromu ise aniridi olgularında retrokorneal, siklitik veya retrolentiküler fibrozis ile karakterize, yeni tanımlanmış klinik durumdur. Aniridik fibrozis sendromu kornea endotel dekompanzasyonu, hipotoni ve retina dekolmanına neden olabilir. WAGR sendromu ile başvuran 6 yaşındaki erkek hastanın yapılan ilk muayenesinde mental retardasyon, nistagmus, her iki gözde rudimenter iris ve arka polar katarakt saptandı. Hastanın sağ gözüne katarakt cerrahisi ile birlikte aniridi intraoküler lens (IOL) implantasyonu yapıldı. Katarakt cerrahisinden yaklaşık 2 ay sonra sağ gözde glokom gelişti. Sağ göze Ahmed glokom valf implantasyonu, sol göze de profilaktik gonyotomi uygulandı. Glokom cerrahisinden 9 ay sonra, ağırlıklı olarak sağ gözde olmak üzere, her iki gözde aniridi ilişkili keratopati saptandı. Keratopati hastanın takipleri boyunca ilerlemeye devam etti. Hastanın 6. yıl takibinde sağ gözde retrokorneal fibrotik membran oluşumu, aşağı disloke IOL ve korneal endotel dekompanzasyonu saptandı. Bu bulgulara dayanarak sağ göze aniridik fibrozis sendromu tanısı konuldu. Hastanın 6 yıllık takibi boyunca göz içi basıncı sağ gözde iki ilaç ile sol gözde ise ilaçsız kontrol altındaydı. Oküler yapıların karmaşık tutulumu nedeniyle aniridi olgularının tedavisi zordur. Her ne

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kadar cerrahi ile katarakt ve glokom tedavisinde tatmin edici sonuçlar alınabilse de ilerleyici keratopati ve aniridik fibrozis sendromu gelişimi (özellikle göz içi implantı olan olgularda) iyi görsel sonuç alınabilmesinin önünde engel teşkil etmektedir. Bu olgu Türkiye'den bildirilen ilk aniridik fibrozis sendromu olgusudur.

Anahtar kelimeler: Aniridik fibrozis sendromu, konjenital aniridi, WAGR sendromu

INTRODUCTION

Congenital aniridia is a rare, bilateral condition caused by mutations of paired box gene 6 (*PAX6*) which is located at band 13 on the short arm of chromosome 11 (11p13) and it can occur in a familial or sporadic fashion.[1] Involvement of contiguous Wilms' tumor suppressor gene (*WT1*) can lead to WAGR syndrome, which is characterized by a Wilms' tumor, aniridia, genitourinary abnormalities, and mental retardation.[1]

Aniridic fibrosis syndrome is a newly recognized clinical entity in patients with congenital aniridia and characterized by progressive retrocorneal, cyclitic, or retrolenticular fibrosis that can lead to endothelial decompensation, intraocular lens (IOL) dislocation, hypotony, and retinal detachment.[2]

In this report we present the long-term outcome of cataract and glaucoma surgeries in a case of WAGR syndrome,ultimately developed aniridic fibrosis syndrome.

CASE REPORT

A 6-year-old male presented with congenital aniridia. His medical history included left radical nephrectomy because of a Wilms' tumor, followed by radiotherapy and chemotherapy at age 19 months.. At age 4 years he underwent right orchiectomy because of an undescended testis. Upon presentation he had mental retardation, nystagmus, bilateral rudimentary iris, and bilateral posterior polar cataracts (Figure 1A and 1B). Visual acuity assessment could not be performed because of mental retardation. Foveal hypoplasia was noted via fundus examination, but the peripheral retina and optic discs were bilaterally normal in appearance. His family history was negative for similar findings. Based on

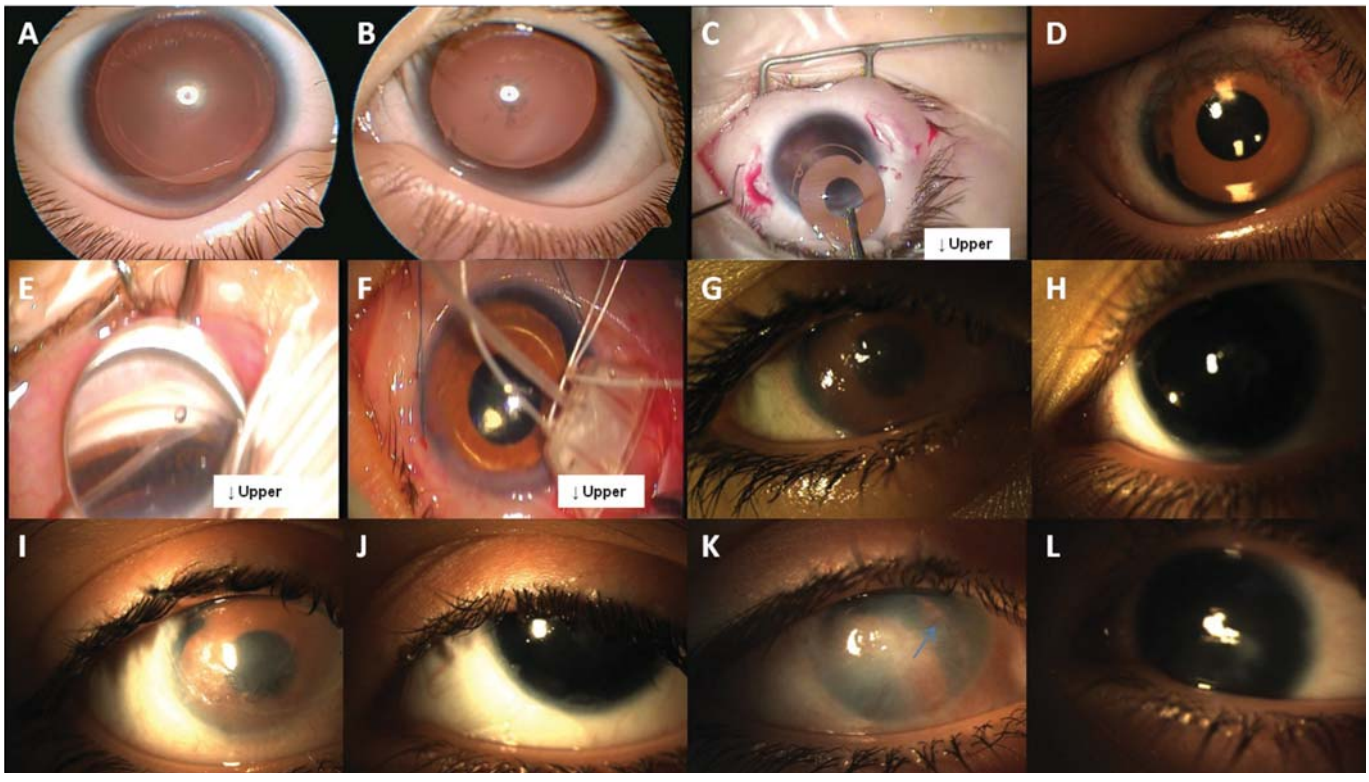

Figure 1. *Pre- and postoperative photographs*

Notes: *Preoperative images of the patient's right (OD) (**A**) and left eye (OS) (**B**) show bilateral aniridia and cataract wtih clear cornea. Intraoperative (**C**) and postoperative (**D**) images of iris diaphragm IOL implantation after cataract extraction (OD). Intraoperative image (**E**) of goniotomy (OS). Intraoperative image (**F**) of AGV implantation (OD). Anterior segment photographs 1 year after OD (**G**) and OS (**H**), 2 years after OD (**I**) and OS (**J**) and 6 years after glaucoma surgeries OD (**K**) and OS (**L**) . Progressive corneal opasification and edema is seen especially in the right eye. At 6 years of follow up, inferior dislocation of IOL is seen (**K**) in the right eye (arrow shows IOL haptic).*

Abbreviations: AGV, Ahmed glaucoma valve, IOP, intraocular pressure

the ocular findings and medical history, the patient was diagnosed as WAGR syndrome.

Cataract extraction was performed and an iris diaphragm polymethylmethacrylate IOL (Morcher GmbH, Stuttgart, Germany) was implanted in the ciliary sulcus (Figure 1C and 1D). Ocular examination was performed under general anesthesia three weeks after cataract surgery. Intraocular pressure (IOP) was 38 mmHg in the right and 10 mmHg in the left eye with Perkins tonometer. Central corneal thickness was 780 m in the right and 654 m in the left eye. Dorzolamide and timolol in combination twice daily was initiated to the right eye.

Ocular examination under general anesthesia was repeated three months after cataract surgery. IOP was 52 mmHg in the right and 15 mmHg in the left eye. At the same session, while under general anesthesia, prophylactic goniotomy was performed on the left eye (Figure 1E). Ahmed glaucoma valve (AGV) implantation with adjunctive use of Mitomycin-C (0.2 mg / mL, for 2 min) was performed at the superotemporal quadrant of the right eye one week after goniotomy (Figure 1F). The patient was then followed-up for 6 years.

Nine months after AGV implantation, persistence of corneal epithelial defects and corneal vascularisation were noted in the right eye. Amniotic membrane transplantation (AMT) was performed to restore ocular surface integrity. The same procedure was repeated 1 and 2 months later. Despite AMT, and meticulous use of artificial tear drops and bandage contact lenses, corneal opacification progressed (Figure 1G, 1I). The left eye also had limbal stem cell deficiency and developed corneal leukoma, but remained clearer than the right eye (Figure 1H, 1J). During the 6-years follow-up period, IOP was under control (15- 21 mmHg) in the right eye with dorzolamide-timolol eye drop twice daily and without any medication in the left eye.

At the 6th year follow-up, inferior dislocation of the IOL and endothelial decompensation were detected in the right eye (Figure 1K). Ultrasound biomicroscopy revealed no contact between the IOL and cornea, but retro-corneal fibrotic membrane formation in the right eye (Figure 2). The membrane was adhered to the posterior surface of the cornea. No adherence to the iris or IOL was detected. Membrane formation was not detected in the left eye. B-scan ultrasonography of both eyes showed echo-free vitreous and an attached retina. Based on these finding, aniridic fibrosis syndrome was diagnosed in the right eye. Because of mental retardation, flash visual-evoked potential (flash-VEP) was performed to analyse visual function. Signal conduction was present in both eyes with relatively good amplitude in the left eye (Figure 3).

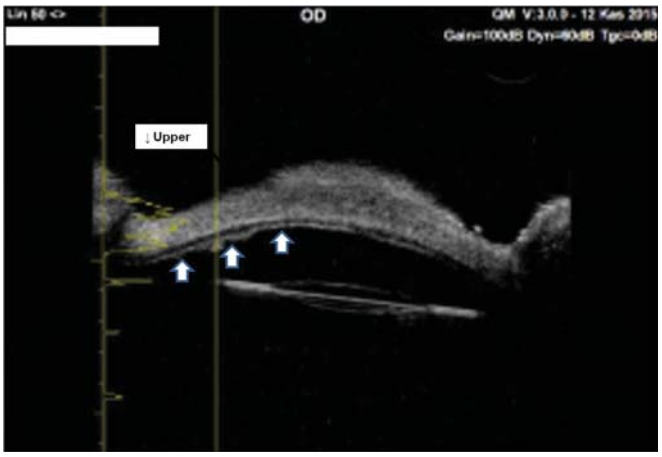

Figure 2. *UBM imaging of the right eye shows corneal surface irregularity, sub-epithelial fibrosis, retrocorneal fibrotic membrane formation (arrows), inferiorly dislocated IOL with no IOL-cornea touch.*

DISCUSSION

Netland et al.[3] reported that between patients with congenital aniridia, 83% had nystagmus, 71% had cataract, 46% had glaucoma, and 45% had keratopathy. Medical and surgical treatment of aniridia is difficult because of the complex involvement of ocular structures. Iris deficiency is associated with glare, photophobia, and low visual acuity.[1]

Glaucoma usually develops during the first 2 decades of life in patients with congenital aniridia.[1] Glaucoma is thought to occur because of developmental abnormalities in the iridocorneal angle and synechia-like attachments of the iris stroma to the trabecular meshwork associated with progressive anterior rotation of the iris.[1] Prophylactic goniotomy is a very effective method for preventing glaucoma before forward extension of the iris.[4] Once glaucoma is developed, it is usually difficult to control IOP both medically and surgically and glaucoma drainage devices are good options for controlling IOP in such cases.[1,5]

Aniridia associated keratopathy (AAK) develops secondary to limbal stem-cell deficiency and it is characterized by thickening and vascularization of the peripheral cornea which gradually advance to the central cornea and result in recurrent corneal erosions, ulcers, sub-epithelial fibrosis, and ultimately total corneal conjunctivalization and opacification.[1] Ocular surgery, especially excessive manipulation of the limbus, and use of topical antimetabolites can lead to early disruption of the fragile corneal epithelium balance.[1]

Aniridic fibrosis syndrome is a newly recognized clinical entity in patients with congenital aniridia that was first described by Tsai et al.[2] The syndrome is characterized by progressive retrocorneal, cyclitic, or retrolenticular fibrosis which can lead to endothelial decompensation, IOL dislocation, hypotony, and retinal detachment.[2] Aniridic fibrosis syndrome is strongly associated with a history of ocular surgery and presence of intraocular hardware (IOLs, tube shunts, and artificial irises).[2,6] A possible mechanism for the

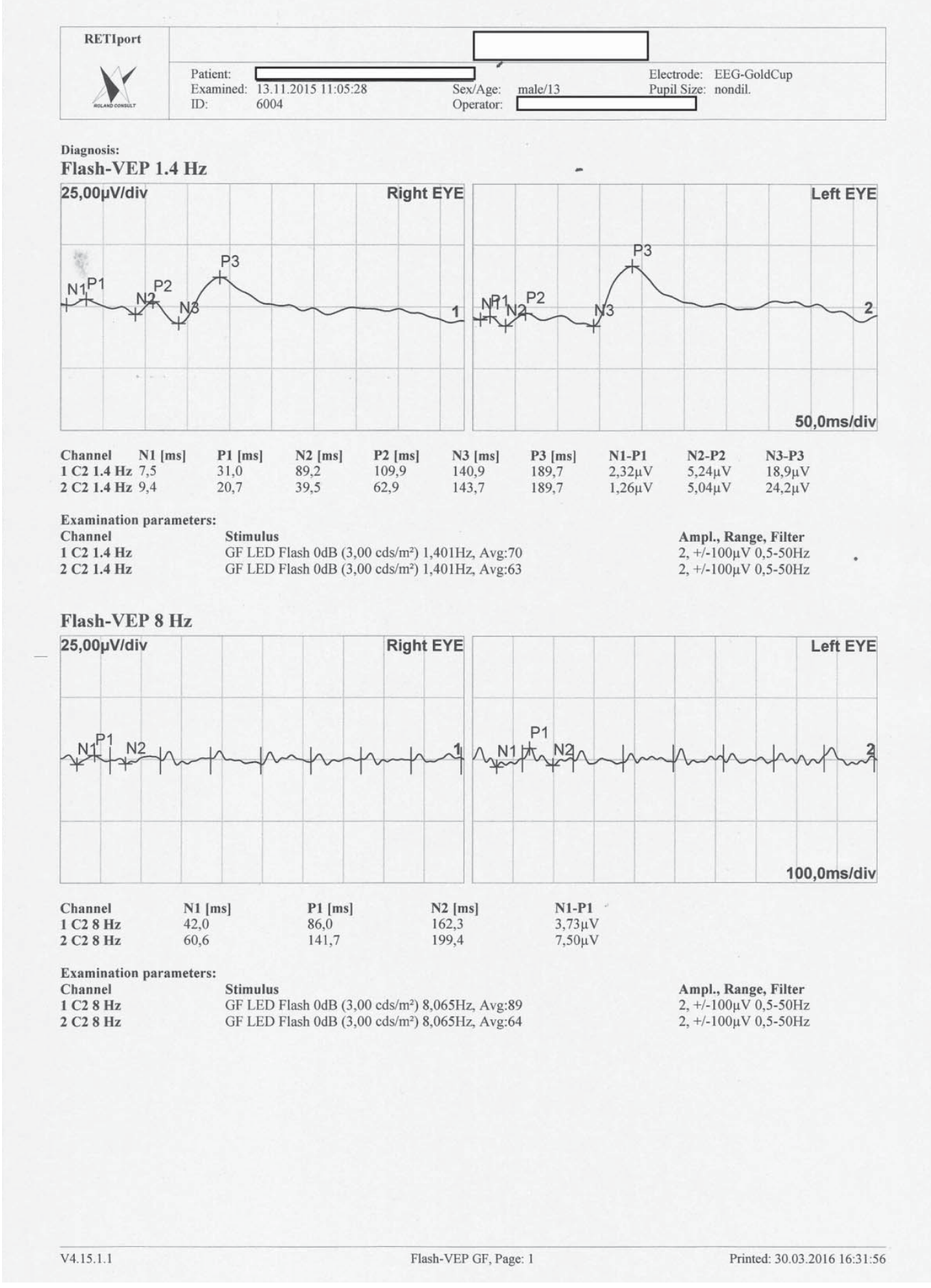

Figure 3. *Flash-VEP results of both eyes shows signal transduction is present in both eyes with relatively good amplitude in the left eye*

development of aniridic fibrosis syndrome is the proximity or touching of intraocular hardware on immature vessels in the rudimentary iris and the hardware could provide a stimulus and scaffold for the development and extension of the fibrotic membrane.[2]

Preoperatively, in the right eye the cornea was clear, surgeries were uneventful, and glaucoma was controlled during the follow-up under 2 medications. Nonetheless, corneal epithelial decompensation was observed 9 months after surgery and rapidly progressed to total corneal opacification. We think that both the large corneal incision for IOL implantation and use of Mitomycin-C before AGV implantation played role in the early deterioration of limbal stem-cell balance. Although iris diaphragm IOLs remain the most commonly used prosthetic iris devices, their primary disadvantage is the need for a large corneal incision. AAK also developed in the fellow eye in which goniotomy was performed, but remained relatively stable, and IOP was controlled without medication. Although cataract was present in this eye, cataract surgery was not performed because of the fragility of the stem-cell balance and the unsatisfactory results in the right eye.

Keratoplasty alone has low success rate in the management of AAK in congenital aniridia because of limbal stem cell deficiency.[1] Before keratoplasty, allograft limbal stem cell transplantation should be considered in this type of patients.[2] Type 1 Boston keratoprosthesis is an alternative procedure.[7] In this report, the patient is still in his childhood and has mental retardation so we are not sure if the patient can take care of himself properly after surgery for ocular surface reconstruction. His left eye has relatively better visual function and we have an impression that any more surgical intervention will deteriorate AAK and aniridic fibrosis syndrome. Also, no posterior extension of the fibrotic membrane and no retinal detachment were detected. Because of these reasons we did not plan any surgical further surgical intervention for subluxated IOL or for keratopathy. Limbal allograft stem cell transplantation and keratoplasty with the excision of the fibrotic membrane may be considered in the future according to the patient's clinical status.

In conclusion, although satisfactory results can be obtained with surgical treatment of cataract and glaucoma, progression of AAK remains problematic. To preserve the limited corneal stem-cell reserve, surgeries should be performed with minimal trauma to the limbal region and glaucoma surgeries should be considered without the use of adjunctive antimetabolites, even if no signs of AAK were observed preoperatively. Aniridic fibrosis syndrome is a rare condition that can lead to severe complications and ultrasound biomicroscopy is a useful method for its early diagnosis. To the best of our knowledge this is the first case of aniridic fibrosis syndrome reported from Turkey.

REFERENCES / KAYNAKLAR

1- Lee H, Khan R, O'Keefe M. Aniridia: current pathology and management. Acta Ophthalmol 2008; 86: 708-15.

2- Tsai JH, Freeman JM, Chan CC, Schwartz GS, Derby EA, Petersen MR, et al. A progressive anterior fibrosis syndrome in patients with postsurgical congenital aniridia. Am J Ophthalmol 2005; 140: 1075-9.

3- Netland PA, Scott ML, Boyle JW 4th, Lauderdale JD. Ocular and systemic findings in a survey of aniridia subjects. J AAPOS 2011; 15: 562-6.

4- Chen TC, Walton DS. Goniosurgery for prevention of aniridic glaucoma. Arch Ophthalmol. 1999; 117: 1144-8.

5- Arroyave CP, Scott IU, Gedde SJ, Parrish RK 2nd, Feuer WJ. Use of glaucoma drainage devices in the management of glaucoma associated with aniridia. Am J Ophthalmol 2003; 135: 155-9.

6- Kothari M, Rao K, Moolani S. Recurrent progressive anterior segment fibrosis syndrome following a descemet-stripping endothelial keratoplasty in an infant with congenital aniridia. Indian J Ophthalmol 2014; 62: 246-8.

7- Bakhtiari P, Chan C, Welder JD, de la Cruz J, Holland EJ, Djalilian AR. Surgical and visual outcomes of the type I Boston Keratoprosthesis for the management of aniridic fibrosis syndrome in congenital aniridia. Am J Ophthalmol 2012; 153: 967-71.