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Glaucoma Management in an Early Adulthood Axenfeld-Rieger Syndrome: A Case Report

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ABSTRACT- Glaucoma, the consequence of Axenfeld–Rieger syndrome(ARS) can develop in 50% of patients. It can cause complete permanent blindness if not givenappropriate management.A twenty-one-year-old woman came to the clinic with blurred vision in both eyes since thelast 3 years, pain in both eyes and headache since the last 2 years and previously medicated. Visual acuity (VA) was 1/60 in both eyes and intraocular pressures (IOP) were 46 mmHg and 37 mmHg respectively. The right eye (RE) showed prominent Schwalbe's line, posterior embryotoxon, corectopia, pseudopolycoria, and diffuse irisstromal hypoplasia. The left eye (LE) showed iris hypoplasia. Gonioscopy revealed iris adhesions in both eyes.Size of cup to disc ratio (CDR) was 0.7with peripapillary atrophyand myopic crescent in the LE. HumphreyVisual Field (HVF) showed an arcuate defect superiorly, multiple defects ininferior quadrantof the RE and superior arcuate, nasal step in the LE. Non-ocular abnormalities consisted of configuration craniofacial dysmorphism hypertelorism, telecanthus, mid-facial hypoplasia, paraumbilical skin tags, microdontia, hypoplasia,and partial anodontia. We planned trabeculectomy with 5-fluorouracil for both eyes (BE). It has been done in LE. LE uncorrected visual acuity becomes 5/60 and the IOP reduce to 9 mmHg in the 14th day of surgery. Glaucoma in Axenfeld–Rieger syndrome could be treated by trabeculectomy with 5FU.

Keywords: **Axenfeld-Rieger Syndrome, glaucoma, trabeculectomy, 5-fluorouracil**

I. INTRODUCTION

Axenfeld–Rieger syndrome (ARS) was first describe by an ophthalmologist, Theodor Axenfeld from German in 1934. In 1924, Reiger, another ophthalmologist, described the similar case with addition on disorder of the iris. Axenfeld-Rieger syndrome has a small incidence in worldwide, 1:200,000, so it makes this disease become a very rare autosomal dominant (AD) disorder. The disorders of this syndrome consist of spectrum that showed not only in ocular but also including: craniofacial, dental, and periumbilical abnormalities(Agarwal et al., 2019). There are three groups of Axenfeld-Rieger Disorders, which are: Axenfield anomalyfor patients with posterior embryotoxon and peripheral anterior adhesions, Rieger anomalyfor patients with ocular phenotypes including peripheral, anterior adhesions, iris hypoplasia, polycoria, corectopia, and posterior embryotoxon, and Rieger Syndrome patients with Rieger anomaly and systemic malfunctions. For that reason, these groups seem overlapping even with the same gene mutations, which is why the Axenfeld-Rieger group of disorders is called Axenfeld-Rieger Syndrome (ARS)(Seifi& Walter, 2018)

The ARS patients have a lifetime risk of developing glaucoma due to the anomalies in the iridocorneal angle and drainage structures of the eye. It seems that the severity of anomalies not correlated with the age of patients. It was reported that 50% ARS patients with difference onset of age will develop glaucoma. The appropriate guidelines to follow up such case is still unclear(Souzeau et al., 2017)Here, we report a case of a 21-year-old Indonesian woman diagnosed with ARS.

CASES

A twenty-one-year-old women referred to our clinic with suspect ARS and ocular hypertension that already receivedtopical and systemic glaucoma medicationsfor one month. She complained of blurred vision in her both eyes since the last 3 years, pain in BE and headache since the last 2 years also protrusion of eyes since the last 1 year.There were no history of family or siblings with the same condition. Uncorrected visual acuity was 1/60 in BE, IOP 46 mmHg in the RE and 37 mmHg in the LE.Slit lamp biomicroscope of the eye revealed prominent Schwalbe's line, posterior embryotoxon, corectopia, pseudopolycoria and diffuse iris stromal hypoplasia in the RE while iris hypoplasiaand pupil unround on

the LE(Figure 1).Gonioscopy revealed multiple iris adhesions in the REandiris adhesion in nasal and inferior quadrants also Schwalbe's line in superior and temporal quadrantsin LE (Figure 2).

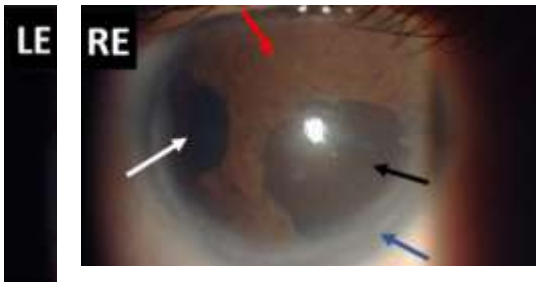

Figure 1. RE the anterior eye segment on the right eye showed prominent Schwalbe's line, posterior embryotoxon (blue arrow), corectopia (white arrow), pseudopolycoria (black arrow) and diffuse iris stromal hypoplasia (red arrow). LE the anterior eye segment on the left eye showed iris hypoplasia (green arrow) and pupil unround (yellow arrow).

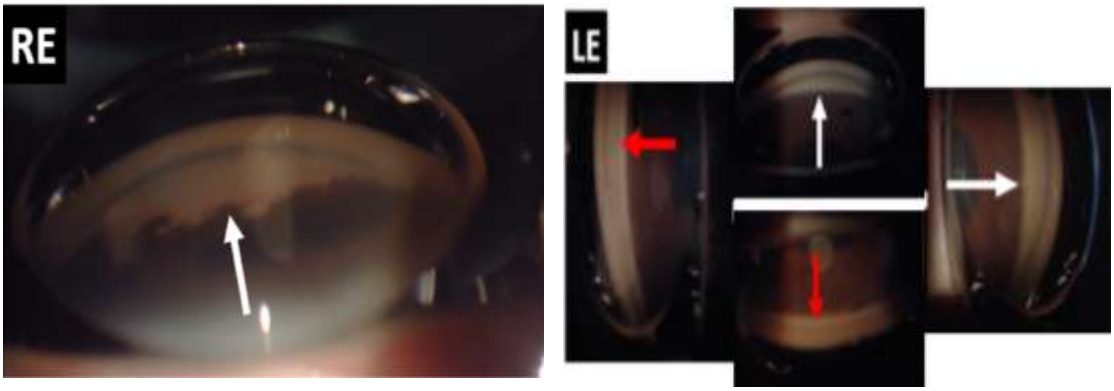

Figure 2.RE gonioscopy revealed on the right eye showed multiple iris adhesions (white arrow). LE Gonioscopy revealed on the left eye showed iris adhesions in quadrants nasal and inferior (white arrow), Schwalbe's line in quadrants superior and temporal (red arrow).

Humphrey Visual Field (HVF) test showed a superior arcuate and multiple defectin inferior quadrants of the RE. It also showedsuperior arcuate and nasal step in the LE (Figure 3).Cup Disc Ratio was 0.7 with peripapillary atrophyand myopic crescent in the LE. (Figure 4). It was difficultto evaluate CDR in the RE due to the pupil condition in this eye.

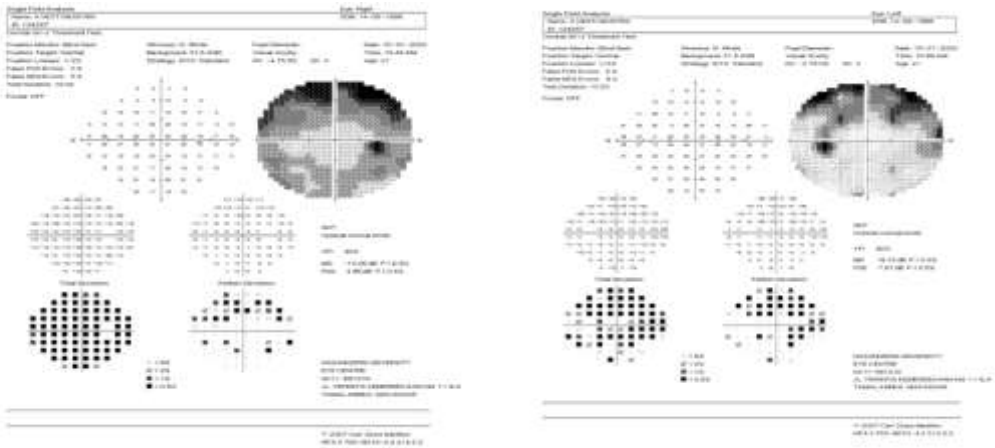

Figure 3. HVF, central 30-2 threshold test showed outside normal limits and general reduction in both eyes

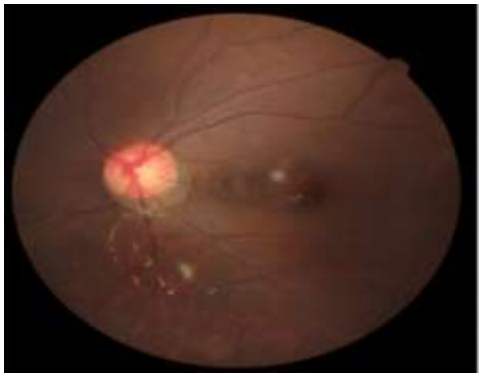

Figure 4. Funduscopic examination showed CDR 0,7 with peripapillary atrophyand myopic crescent in the LE.

Non-ocular abnormalities consisted of a configuration craniofacialdysmorphismhypertelorism, telecanthus, mid-facial hypoplasia and there were partial anodontia besides microdontia and hypoplasia and paraumbilical skin tags (Figure5).

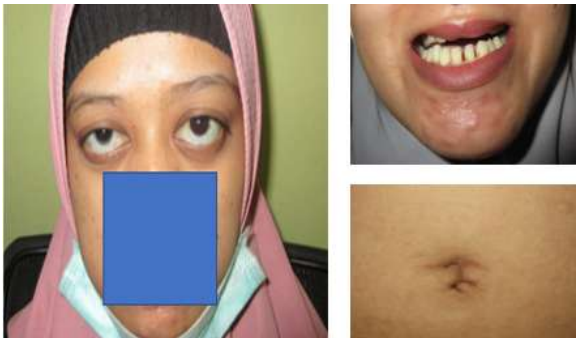

Figure 5. The systemic traits of the reported patient. Craniofacial dysmorphism: hypertelorism, telecanthus, mid-facial hypoplasia and microdontia, hypodontia, partial anodontia and paraumbilical skin tags

We diagnosed the patients as ARS with secondary glaucoma based on the findings. Even after with added other medical therapy, both intraocular pressures (RE: 45 mmHg and LE: 37 mmHg) were uncontrolled with maximum medical pharmacologic therapy so we decided to do trabeculectomy in both eyes, with the LE first. A fornix-based trabeculectomy was done with 5-FU (50 mg/ml) on sponge soaked applied between the sclera and the conjunctival flap for five minutes. After removing the sponge, the eye was copiously irrigated with Ringer Lactate to remove any residual 5-FU before we do the next step of trabeculectomy. The triangular scleral flap was reapproximated to its bed with 10.0 nylon and conjunctiva closed in a single layer running suture of 8-0 polyglactin. Topical antibiotic, homatropine and povidone iodine were given topically before we ended the surgery.

Systemic glaucoma medication and topical glaucoma medications for the LE were stopped after the surgery. Topical corticosteroid administered intensively (8 times daily) initially and tapered every week. Topical antibiotic and cycloplegic agent (homatropine) were used for 3 weeks. Topical glaucoma medication continued for the fellow eye. Frequent office visits were planed in the first postoperative month (1^{st} day, 3^{rd} day, 1^{st} week).

The first day examinations after trabeculectomy intheLE showed IOP 5 mmHg, uncorrected visual acuity (UCVA) 5/60, normal anterior chamber depth, witha bleb evaluation (Indiana bleb score):medium height, horizontal extent > 4 hours, moderate vascularity and negative leakage on seidel test (Figure 6). The examination in second weeks postoperatively showed IOP 9 mmHg, UCVA 5/60, normal anterior chamber depth with bleb evaluations: medium height, horizontal extent> 2 -4 hours, mild vascularity, seidel leakage negative. We did not find any early complications such as: wound leaks, hypotony, shallow or flat anterior chamber and serous or hemorrhagic choroidal effusions after the surgery.

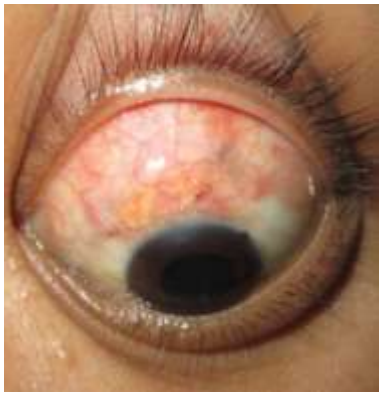

Figure 6. The first day after trabeculectomy with bleb evaluation: medium height, horizontal extent> 4 hours, moderate vascularity, seidel leakage negative.

A B-scan ultrasound for axial length examination on BE was performedafter trabeculectomy on LE. It wasresulted 26 mmon RE (this eye has not been done any surgery) and 24 mm on LE (already had trabeculectomy) (Figure 7).Unfortunately, we did not perform B-scan ultrasound before the surgery for the LE because the technical problem with the B-scan on that day.

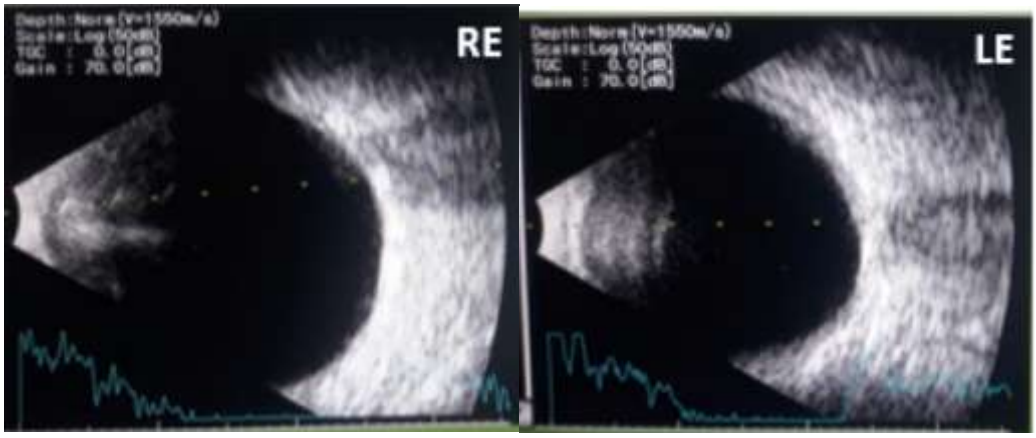

Figure 7. RE B-scan showing an axial length of 26 mm before surgery. LE B-scan showing an

II. DISCUSSION

Axenfeld-Rieger syndromeis the syndrome that comes from anterior segment dysgenesis of neural crest that characterized by the alteration in the peripheral cornea, iris, and anterior chamber angle, where other ocular and systemic features is not necessarily occured.(Rao et al., 2018)

It is usually bilateral, asymmetric or even rarely unilateral. This is associated with iris hypoplasia, which is the condition of underdeveloped iris tissue.There was iris hypoplasia,corectopia, and polycoria in this patient. Hypoplasia is an underdeveloped iris tissue condition. Corectopia refers to the displacement of the pupil. The pupil position deviated from its normal pupil, central position and is likely to be associated with high myopia or ectopia lentis. Progressive ectopia can be associated with the Axenfeld-Rieger spectrum as well as iridocorneal endothelial (ICE) syndrome.

Polycoria is a rare condition characterized by full-thickness tears through the changes of the iris that happened to patients with ARS, with the range of being subtle to being profound. In some cases, this condition is related to the location of the pupil, corectopia, and polycoria that can produce abnormal interolerance to visual perception of light (photophobia) and cosmetic tissue. This situation may also lead to anterior displacement of Schwalbe's line, which cause abnormality of the cornea to posterior embryotoxon as the dominant trait and as the key factor in ARS diagnosis, where patients with this condition have no cornea abnormalities such as cornea opacity, sclerocornea or megalocornea(Seifi& Walter, 2018)

Glaucoma can be the cause of blindness to these patientswithin several years of time. The blockage of Schlemancanal, due to anterior displacement of Schalbe's line,leads to the increasing of intraocular pressure. It triggers physical changes at the optic nerve head. The compression of optic nerve axonal at the laminal cribrosa, the blockage of the axoplasmic flow, and interference in retrograde neurotrophin transport to RGCsleads to retinal ganglion cells (RGGs) death and blindness if it is left untreated (Seifi & Walter, 2018).

The angle of ARS patients' eye can be obtained open angle or closed angle, as in the research souzeau et al suggested thatif one of a family member is diagnosed with PCG and five family members are diagnosed with POAG. This may indicates that genetic architecture is the contribution that come from FOXC and PITX2(Souzeau et al., 2017). Song et al reported that Gonioscopy suggested iridocorneal adhesion from the anterior angle of the right eye quadrant in the patient's eye.One of our limitationswas that we did not carry out examination on other family members.

There have been 56 cases of ARS seen for more that 10 years with the total 17 eyes from 11 cases (M=2, F=9), with unclassified ADS identified among them. All cases are known to be developmental or Glaucoma with juvenile open angle glaucoma, while one was diagnosed as primary angle glaucoma closure outside reported by Rao et al (2018)Gonioscopy in this patient revealed iris adhesions in the RE. The LE revealed iris adhesions in quadrants nasal and inferior, Schwalbe's line in quadrants superior and temporal.iris adhesionswork to connect iris and the anterior angle, which can also be concludes that there are three phenotypes that relate more with PITX2 mutations, such as craniofacial dysmorphism, dental malformation, and umbilical defects. There are also several features that are seen conducted with dental malformation including hypodontia, adentia, or peg-shaped teeth, such as hypertelorism, telechantus, flat nassal bridge, mid facial hypoplasma, shortening of the maxilla and mandible(Chrystal& Walter, 2019).

Topical treatment was unsuccessfully brought IOP to normal in our patient.There are two essentials way of performing the surgery, those are classic trabeculectomy (with or without 5-FU) or filtration surgery with glaucoma shunt implantation, which means that trabeculectomy is performed because the lack of natural iris. This may be the indication why several surgeons still prefer to perform trabeculectomy for better results.

Left eye UCVA increased from 1/60 pre op to 5/60 on the first day after trabeculectomy + 5-FU. There are some reasonable explanations can be found in some circumstancessuch as the age of the patients and how the optic nerves are able to sustain the blood flow with elevated IOP, longer than ones on elderly patients. Swanson and colleagues have proposed that retinal ganglion cells may undergo a period of reversible dysfunction preceding apoptosis(Muhsen, 2018) the maintenance of the same BCVA of 20/30 one year after the surgery and other trial also stated that some patients are stable for more than 6 months without any additional topical therapy(Kozomara et al., 2015)

The increase in IOP also affects the size of the axial length and patients with myopia. Axial elongation associated increase in glaucoma prevalence as 28.1% in a medium to highly myopic study population (Jonas et al., 2017). The vision improvement of this patient couldbe because the axial length (AL) of the left eye is nearing normal (24 mm). The AL of fellow eye that have not been operated was 26 mm. Trabeculectomy typically yields lower postoperative IOPs and a greater reduction in AL (Pakravan et al., 2017). We cannot conclude this reasoning due to lack of documentation of axial length of LE before surgery, there was no equipment available on that day.

Laser procedures as the options of managing ARS relate to glaucoma are not very useful unless we want to use it to relief iatrogenic pupillary block or for cyclo-destruction in refractory cases. Strungaru H.M., Irina Diru, Walter M. A, elaborate that glaucoma in ARS patients do not respond perfectly on conventional therapies in gaining lower IOP, which also come to the result that ARS patients with glaucoma need surgical intervention. (Chrystal & Walter, 2019).

In many cases, trabeculectomy is more preferable is some congenital diseases. More efficient surgical procedure for glaucoma treatment when combined with careful post-surgical care, which is also known as trabeculectomy with 5-FU.(Lindemann et al., 2017)Trabeculectomy is known to have more advantages in treating secondary glaucoma because some rare genetic diseases that affect the eyes and it can give no or little complications post operativity and with good result.

The effectiveness of trabeculectomy to control the IOP in long term depends on bleb. Bleb failure can happen because of the scarring from any level: conjunctivae, tenon, episcleral, scleral flap and internal ostium. Trabeculectomy augmented with antimetabolites/ anti proliferative agents such as Mitomycin C or 5-fluorouracil may be used in failed angle surgeries. Antimetabolite are used during the procedure in

order to reduce bleb failure by minimize and delaying scar tissue formation, enhancing filtration and maintaining the functional bleb. The follow up of patients is needed because the probability of complications, such as: blebitis, endophthalmitis, cataract, avascular filtering blebs, thinning of conjunctiva, hypotony, anterior chamber reaction and endothelial toxicity if mitomycin-C enters into the eye (Radhakrishnan et al., 2014)

III. CONCLUSION

Glaucoma develops in 50% of ARS cases. In our patient's,there were significant increased visual acuity. LE UCVA was 5/60 post-surgery, before surgery it was 1/60. TheIOP decreased on the first day of surgery and persisted until the 14th day of surgery. There were no early postoperative complications. It showed that trabeculectomy with antiproliferative agents like 5-fluorouracil and carefulpost-surgical care is an efficient surgical procedure for glaucoma treatment in ARS.

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