First XEN implantation in Axenfeld-Rieger syndrome: A case report and literature review

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ABSTRACT

Purpose: To present the first report of a XEN45 gel stent implantation in a female with Axenfeld-Rieger syndrome (ARS), a rare congenital anomaly caused by abnormal neural crest migration during early embryogenesis. This shows promise as new minimally invasive therapeutic option in the treatment of secondary glaucoma in ARS. Observations: A 31-year-old female with known sporadic ARS was evaluated and treated at the Edith Wolfson Medical Center in Holon, Israel. The vision in her right eye was hand motion and 20/25 in the left eye. In the left eye the intraocular pressure (IOP) was up to 31 mmHg under maximal tolerated treatment. She refused Trabeculectomy or Glaucoma Drainage Device (GDD) surgery, but agreed to Minimally Invasive Glaucoma Surgery (MIGS). A Xen device was implanted in uneventful surgery. 15 months post operatively her IOP is 8 mmHg.

Conclusions: XEN implantation, when technically feasible, is a suitable procedure in ARS. This shows promise as new minimally invasive therapeutic option in the treatment of secondary glaucoma in ARS. This has particular significance as these patients often require surgery at a young age.

1. Introduction

Axenfeld-Rieger syndrome (ARS) is a rare congenital anomaly that includes ocular and systemic manifestations. It is the result of abnormal neural crest migration during early embryogenesis, making it a part of a spectrum of disorders known as anterior segment dysgenesis. 1

ARS was first described by Axenfeld and Rieger in the early 20th century. It is a fully penetrant, multigenic syndrome with variable expressivity. It most often follows autosomal dominant inheritance but can also be sporadic or de novo. The etiology in approximately 40%–70% of ARS cases correlate with mutations in Forkhead-Box C1 (FOXC1) and Pituitary Homeobox 2 gene (PITX2) genes, on chromosomes 6p25 and 4q25, respectively. Other genes reported to cause ARS include human forkhead transcription factor gene (FKHL7) on chromosome 6p25. 3

Ocular features in ARS involve the cornea (sclerocornea, megalocornea and posterior embryotoxon), a prominent and anteriorly displaced Schwalbe line), iris (corectopia, atrophy and hole formation) and anterior chamber angle (anterior insertion of the iris, tissue strands attached to Schwalbe’s line). 2,4 In addition, systemic findings can include cardiac, dental, craniofacial, and abdominal wall defects.1,4,5

More than half of the patients with ARS develop secondary glaucoma, which commonly become manifest in childhood or young adulthood. The elevated intraocular pressure (IOP) in ARS is due to inherent iridogoniodysgenesis and iris strands that obscure the angle structures. 6 Treatment begins with medical therapy, but often ultimately, surgical intervention is often required. 7

To the best of our knowledge, this is the first report of XEN implantation in an eye suffering from glaucoma secondary to ARS. In addition, 15 months follow up results are presented.

2. Case report

A 31-year-old female with genetically proven ARS with PITX2 sporadic mutation, has been followed in the Edith Wolfson Glaucoma Clinic since the age of 8. She also has systemic manifestations of ARS, including craniofacial dysmorphism, dental abnormalities and redundant umbilical skin. All other family members have been genetically tested and found to be free of the mutation.

At initial presentation the right eye (RE) had severe secondary glaucoma. Over the course of several years, she had undergone several surgical procedures in the RE with complications. The current vision is hand motion (HM) and IOP is in the low teens with topical treatment.

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The left eye (LE) maintained good IOP control for many years with topical medication and uncorrected 20/25 vision (see image 1). While the optic nerve appeared healthy on clinical exam, the optical coherence tomography (OCT) of the retinal nerve fiber layer (RNFL) (Heidelberg Engineering, Heidelberg, Germany) showed an average thickness of 73 μm, with inferior and superior thinning. Repeated 24-2 Sita Standard visual fields showed mild glaucomatous damage with an inferior nasal step and mean deviation (MD) of –5.00 dB, Pattern Standard Deviation (PSD) of 2.24 dB, measured by the Humphrey HFA II-i 750i field analyzer (Carl Zeiss Meditec, Dublin, CA).

Prior to surgery the IOP began to increase and reached up to 31 mmHg despite maximally tolerated treatment. Visual acuity remained 20/25. Gonioscopy demonstrated broad peripheral anterior synchiae (PAS) in the nasal, inferior and temporal quadrants, but the upper 90° allowed view of the scleral spur. The lens was clear. OCT RNFL now showed deterioration, with average thickness of 55 μm.

Given the poor result of past glaucoma surgeries in the RE, and her difficult experiences, the patient was extremely reluctant to undergo any surgical intervention in her left eye. Nevertheless, after deliberation the patient was willing to undergo a minimally invasive glaucoma surgery. Therefore, We chose to use a XEN45 gel stent (Allergan Inc., CA, USA), which is a 6 mm long stent with a 45 μm inner lumen diameter hydrophilic tube implanted ab-interno.8–10

The XEN45 implantation was done under topical anesthesia using lidocaine 2% and oxybuprocaine hydrochloride 0.4%. The skin was disinfected with povidone-iodine 10% and a sterile covering and eyelid retractor was inserted. Gonioscopy was done showing open angle at the target sector in the nasal upper quadrant. After marking the upper conjunctiva with a 3-mm limbal distance using a caliper, a subconjunctival injection of 0.1ml Mithramycin C (MMC, 0.3 mg/1ml) to the target sector was applied. A clear cornea self-sealing incision of 2 mm size at the 5 o’clock position and a second small paracentesis at 9 o’clock position were done. Viscoelastic (Biolon, Hanita, Israel) was injected into the anterior chamber. While stabilizing the eye with the Vera hook over the nasal paracentesis, the XEN45 gel stent was entered through the temporal inferior corneal incision into the chamber angle on the opposite site between 11 and 12 o’clock. When the XEN-implantation bevel was visible in the previously marked area, under the conjunctiva, the gel stent was carefully injected. The implant system was then removed. The implant was clearly visible in the correct position by gonioscopy. The viscoelastic material was then removed from the anterior chamber. The corneal incisions were hydrated and the eyelid retractor removed (See video, supplemental digital content 1, which demonstrates the surgical procedure).7,11

On the first postoperative day, IOP was 10 mmHg with no topical antiglaucoma medication. There was an elevated diffuse bleb, minimal inflammatory signs and no hyphema in the anterior chamber. Over the course of the following fifteen months, the IOP has remained stable, around 8–10 mmHg in multiple exams (see image 2). No needling procedures or subconjunctival injections of anti-fibrotic agents were needed and no anti glaucoma medication added. After a gradual decrease in topical steroids (prednisolone acetate), she remains with no topical treatment. The UCVA, OCT RNFL and Humphrey 24-2 perimeter have remained stable.

3. Discussion

We present a case of XEN45 gel stent implantation in an only good eye of a young female with ARS, showing good IOP control for 15 month post-operatively.

ARS encompasses a heterogeneous group of developmental disorders, which affect the anterior segment of the eye, often leading to secondary glaucoma, with median age at diagnosis of 13.5 years old.12 The treatment of glaucomatous eyes with ARS syndrome is challenging, due to the anatomical obstructions. Topical and systemic anti glaucoma medication often fail, consequently surgical treatment is needed in order to achieve IOP control. It is estimated that more than 70% of patients with ARS associated glaucoma require multiple surgeries.10

Controversy exists regarding the procedure of choice in ARS.7 Shields et al. suggested that angle surgery, such as goniotomy or trabeculotomy would not be successful in ARS, although it is the first-line in many pediatric glaucomas. Zependa et al. found that trabeculectomy with anti-fibrotics and Baerveldt glaucoma drainage device (GDD) have shown the greatest success in ARS. On the other hand, trabeculectomy exposes the patient to a life-long risk of bleb-related infections, which is particularly important in young people with many years ahead of them. The Baerveldt GDD is not available in our country, and other options, such as, Ahmed drainage device was reported to have a poor success rate of a mere 25%.10

Minimally Invasive Glaucoma Surgerie (MIGS) are becoming more and more common, gradually changing the surgical management in many glaucoma cases. There are various MIGS devices on the market but our experience has been primarily with the XEN45. Although Xen implantation also creates a bleb, it has the significant advantage of being a less invasive procedure compared to trabeculectomy, with reports of a favorable safety profile.13 In addition, we have had very good results in our patients to date with a low complication rate. We have found good IOP control from immediately after the operation but resort to needling with 5 Fluorouracil (5FU) in the clinic when needed later on. No such interventions were needed in this case.

Moreover, XEN45 has previously been reported as a promising

![Image 1. Pre operative photo of the LE illustrating iris atrophy and corectopia.](image1.png)

![Image 2. photo of the LE taken at post-operative day 6 illustrating the position of the yellow-gold subconjunctival XEN45 implant at the superior nasal quadrant.](image2.png)
option in eyes with morphological irregularity, such as ICE syndrome. This led us to believe that it would be the most suitable surgery in this case especially given the extreme reluctance to undergoing any surgery at all.

It is important to emphasize that if it fails, XEN45 implantation does not preclude additional surgery, such as trabeculectomy or GDD, making it a good option for a stepwise approach. A pre-trabeculectomy surgical step is specifically advantageous in younger patients, as they are likely to need additional filtration surgery over the course of their lifetime. This was further amplified in our young patient, who had lost vision in the fellow eye and was unwilling to consider any traditional glaucoma operations.

4. Conclusions

To conclude, in our patient with ARS we have achieved excellent visual and IOP control results to date, with follow up period of 15 months. This XEN45 procedure has a very high safety profile with a low level of postoperative complications, making it a suitable option for patients who fear a major invasive surgery. Xen implantation seems to be a possible solution in other anomalies of the angle, with the caveat that about a quarter of the angle should be open and accessible. More clinical studies and longer follow up are required for more comprehensive knowledge.

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Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Consent for publication

Written informed consent was obtained from the patient for publication of the medical data and accompanying images.

Ethics approval and consent to participate

Not applicable.

Availability of data and materials

The datasets analysed in this study are not publicly available due to protection of medical data privacy but are available from the corresponding author on reasonable request.

Authors’ contributions

LM data curation, investigation, writing- original draft, review & editing, visualization-surgical video editing, photo images, project administration.

RI data curation, investigation, writing- original draft.

LN- writing-review & editing, resources.

MKL performed the operation, conceptualization, supervision.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2022.101486.

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