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Case report

Bilateral consecutive Xen gel stent surgery during pregnancy for uncontrolled early-onset primary open angle glaucoma

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ABSTRACT

Purpose: To report here a case of uncontrolled glaucoma during third-trimester of pregnancy that was treated successfully with bilateral Xen gel stent insertion.

Observations: A 35-year-old woman presented during the third trimester of pregnancy with bilateral uncontrolled primary open angle glaucoma. Her disc examination and visual fields were consistent with advanced glaucoma. After failed Selective Laser Trabeculoplasty and maximal medical treatment, including Acetazolamide, she was treated with bilateral consecutive Xen stent surgery with successful control of her intraocular pressure.

Conclusions and Importance: The use of Xen implant may have advantages over traditional trabeculectomy, especially during pregnancy, as the procedure is shorter, with less dependence on on-table antimetabolite and being minimally invasive with sparing of the conjunctiva.

1. Introduction

The management of glaucoma during pregnancy presents unique challenges because both medical and surgical treatment must take into consideration the needs of the mother as well the health of the growing fetus. We report here a case of medically uncontrolled glaucoma during third-trimester of pregnancy that was treated successfully with bilateral Xen gel stent insertion.

2. Case report

A 35-year-old woman of Middle-Eastern descent presented to the emergency department (ED) during the third trimester of pregnancy (week 35) with bilateral uncontrolled primary open angle glaucoma, which had been diagnosed two years earlier. Her intraocular pressure (IOP) had been well controlled with latanaprost monotherapy until recently. She has a strong family history of glaucoma with a cousin in Iraq also diagnosed at a young age. She had no other significant ocular history and was otherwise healthy. She previously delivered 3 other children by vaginal birth. Two months prior to her ED presentation, her private ophthalmologist had measured markedly elevated IOPs in both eyes, prompting escalation of her treatment with commencement of combined topical medical therapy and bilateral SLT. Despite treatment, her IOP remained uncontrolled.

The patient reported a recent gradual reduction in her vision, but no pain or redness. Her best corrected visual acuity (BCVA) was 6/6 in the right eye and 6/7.5 in the left. IOP measurements with Goldman applanation tonometry (GAT) was 48 mmHg in the right eye and 45 mmHg in the left eye, with central corneal thickness measurements of 604 μm (right) and 604 μm (left). Anterior segment examination was normal, with Grade 4 open angles. Disc examination revealed typical features of bilateral glaucomatous optic neuropathy with advanced cupping, worse in the left than the right eye, confirmed on OCT imaging. Her most recent 24-2 Humphrey Visual Field test from her private ophthalmologist showed right superior arcuate scotoma and left superior and inferior arcuate scotomas (Fig. 1). At this point, with markedly elevated IOPs, oral acetazolamide 250mg qid was added with the hope that her IOP could be sufficiently controlled to allow her to deliver via Caesarian section at 38 weeks, with a view to perform conventional incisional filtration surgery post delivery. However, on review the following day the IOP was 54 mmHg in the right eye and 51 mmHg on the left, necessitating urgent surgical intervention.

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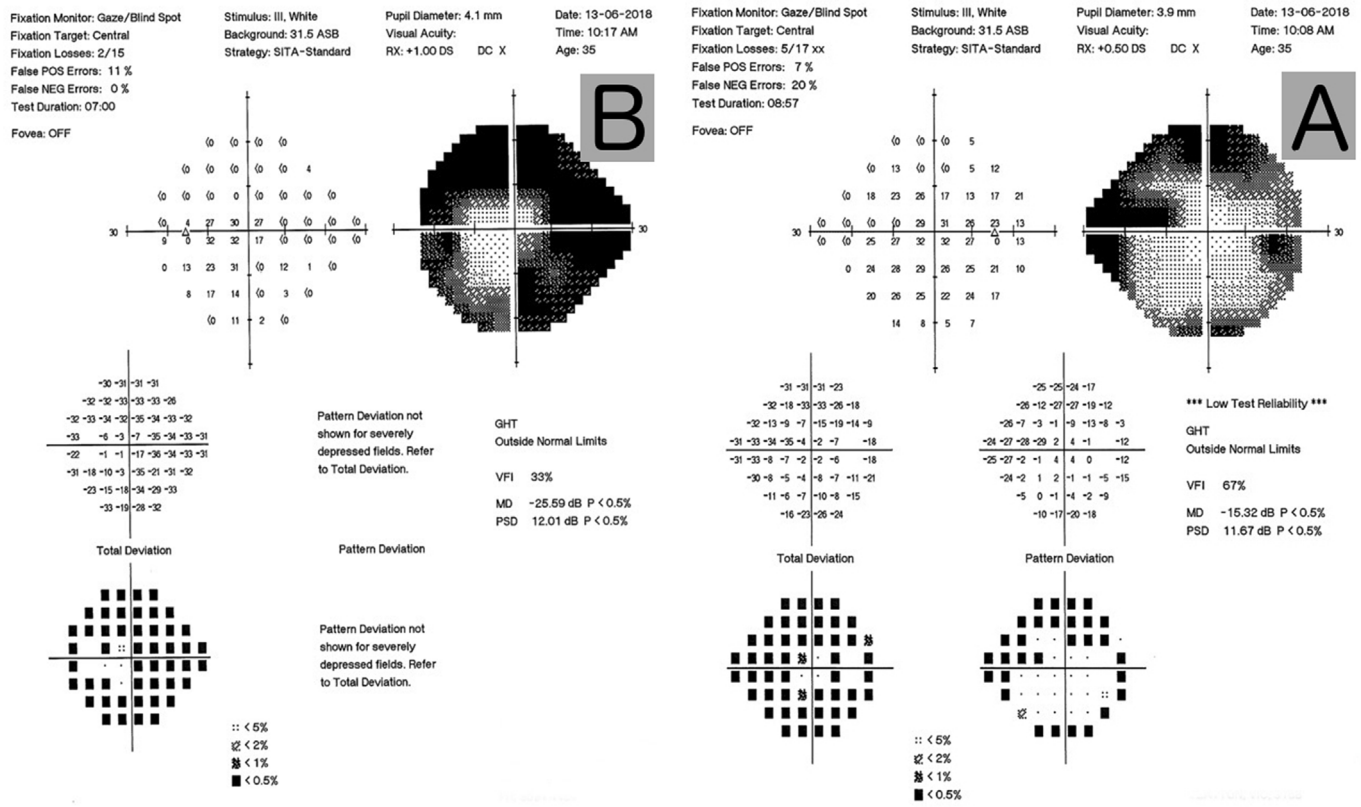

Fig. 1. 24-2 Humphrey Visual Field of the right (A) and left (B) eye.

After consideration of the risks and benefits of various approaches to surgery, bilateral consecutive bilateral Xen gel stent implantation surgeries without Mitomycin C were performed several days apart, with the left-sided surgery performed first as this eye has more advanced glaucoma.

Surgical technique of Xen gel stent insertion was a modification of that described elsewhere.[1] Patient received local anesthetic with sub-Tenon Lignocaine 2% and Ropivocaine 1% (50:50) mixture approximately 10–15 minutes prior to procedure. Two small marks were made with sterile marker 3 mm from the limbus in the superior-nasal aspect of the conjunctiva to identify the approximate exit point for gel stent. Instead of using Mitomycin C, injection of 0.2mL of dexamethasone (4mg/mL) was used to perform subconjunctival hydrodissection. The subconjunctival space above Tenon's fascia is maintained by injecting small amount of Healon GV just under superficial conjunctival layer, this ensures that the Xen gel stent is injected into this desirable space. An inferior-temporal main limbal corneal wound was made with keratome, and an inferior-nasal side-port was made with side-port blade. Anterior chamber was filled with Healon GV. Xen stent was injected with delivery device as per manufacturer instructions. Immediately following delivery of the stent there is excess length of gel stent in the anterior chamber, this was rectified by grasping the gel stent using a vitreoretinal forceps and advance the stent until desired length. Healon GV was then removed with irrigation/aspiration cannula and subsequently subconjunctival dexamethasone was delivered. Acetazolamide and glaucoma drops for the left eye were discontinued.

On Day 1 post-operatively, the left eye was hypotonous (4 mmHg) with a shallow anterior chamber (AC) (See Fig. 2). Initial management was with atropine and reduction of dexamethasone eye drops frequency. By Day 3 the IOP remained 4 mmHg with significant peripheral iridocorneal touch requiring reformation of the AC with Healon GV, which resulted in reversal of the hypotony, deepening of the AC and an IOP of 14 mmHg. When surgery was performed on the right eye,

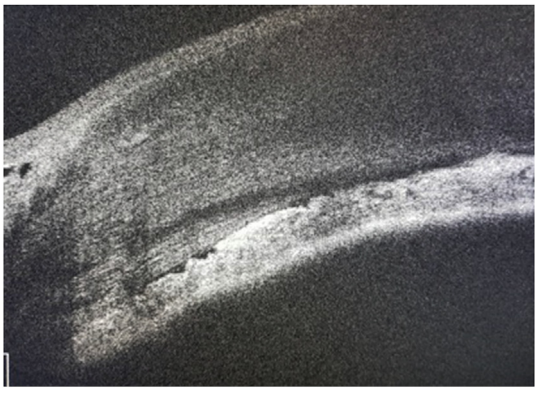

Fig. 2. Anterior segment OCT of left eye on post-operative day 3 showing shallow anterior chamber with iridocorneal touch.

viscoelastic was left in the AC at the end of the case in anticipation of postoperative hypotony. However, an IOP check 2 hours post operatively showed IOP had increased to 60 mmHg and excess Healon GV was "burped" under sterile conditions at the slit lamp until IOP reduced to 30 mmHg. The IOP next day for her right eye again as reduced to 4 mmHg with shallow AC. Despite some viscoelastic remaining in the eye, the next day the AC remained shallow with an IOP of 4 mmHg, for which initial conservative treatment with atropine and a reduced frequency of dexamethasone drops was chosen, with close monitoring planned. However, the patient was not able to attend her follow-up appointment as she required hospital admission for monitoring of high blood pressure in pregnancy and possible pre-eclampsia. The diagnosis of pre-eclampsia was later ruled out and while in hospital the patient developed spontaneous dilation of cervix and went into labour. She delivered her infant by emergency uncomplicated Caesarean section at 37.5 weeks. When she was reviewed in hospital, her IOP had risen to

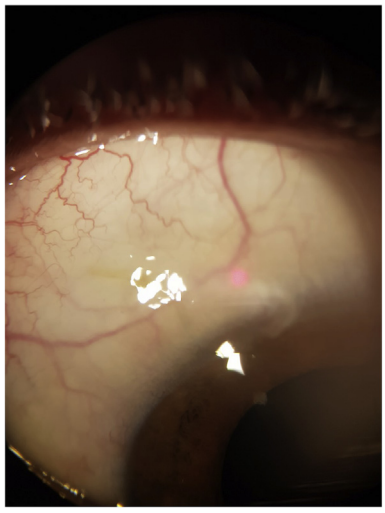

Fig. 3. Slit lamp photo, post operative day 3 appearance of the left eye bleb.

12 mmHg with a slightly shallow AC. Three days later she was discharged from hospital with an IOP in the right eye of 14 mmHg and a deep AC. She had non-vascularised, shallow and diffuse filtration bleb in both eyes (Fig. 3).

In the post-operative period several needling procedures with subconjunctival injection of 5-fluorouracil were required to treat early bleb encystment. Two months post surgery IOP was controlled 14 mmHg in both eyes, with deep anterior chambers and visual acuities of 6/6 both eyes. Table 1 summarizes all post-operative events.

3. Discussion

Glaucoma surgery in pregnancy has special risks and considerations including the risk of various topical/systemic medication on the growing fetus, the risks of local and general anaesthesia, the position of the patient during surgery and contraindication of antimetabolite use in pregnancy.

Medical management of IOP during pregnancy is difficult because many of the topical IOP lowering medications are classified as Category C (meaning animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans). The only exception is brimonidine, which is category B (animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women). Oral acetazolamide at high doses is associated with birth defects in animal studies, however relatively high dosage of acetazolamide use in patients with idiopathic intracranial hypertension showed no significant adverse outcomes.[2] It is important that patients are made aware of the potential side effects that their treatment may have to their growing fetus. Towards the third trimester of pregnancy, the risk of birth defects is much lower than in the first trimester. In late pregnancy the concern is more about the effect that systemic absorption of the medication can have on a newborn, such as central nervous system suppression by brimonidine or bradycardia from beta-blocker medications. Due to the complexities, pregnant women may consider local treatment with SLT laser to reduce or avoid medication use. However, in our patient SLT was ineffective.

Table 1
Timeline of post-operative events.

Left eye Xen	- No intra operative complications
Post Op Day 1	- IOP 4 mmHg with shallow AC - Treated medically
Day 5	- IOP 4 mmHg with iridocorneal touch - AC reformation with healon GV
Day 6	- IOP 14 mmHg with deep AC
Right eye Xen (Day 9 post op)	- Viscoelastic left in AC - 2h post op IOP 60 mmHg - Excess healon was burped
Post Op Day 1	- IOP 4 mmHg with shallow AC - Treated medically
Day 2	- Same IOP and AC
Day 5	- Did not attend follow up visit as admitted to hospital for high blood pressure
Caesarean section	
Day 8 - review in hospital post delivery	- Right IOP 12 mmHg - AC still slightly shallow
Day 11 – day of discharge	- Right IOP 14 mmHg - Deep AC
2 weeks post op – bilateral needling on slit lamp	- Bilateral early encystment, right IOP 25 mmHg, left 15 mmHg
1 month post op – right needling	- Right IOP 23 mmHg, left 11 mmHg
2 months post op	- IOP 14 mmHg OU - Remained stable

IOP = Intra-ocular pressure, AC = Anterior chamber.

The use of antimetabolite for both trabeculectomy and Xen gel stent is off label. Antimetabolite is classified as category D (There is positive evidence of human fetal risk based on adverse reaction data or studies in humans) with a risk of birth defects from systemic absorption. The literature on surgical glaucoma treatment during pregnancy is limited. Pickering et al. reported a case of successful trabeculectomy without application of antimetabolite in a pregnant woman.[3] Razeghinejad et al. reported one case of trabeculectomy without Mitomycin C and 2 cases of tube shunt surgery in patients with uncontrolled glaucoma during pregnancy.[4]

Other options for minimally invasive glaucoma surgery (MIGS) as iStent or Hydrus, although not requiring antimetabolite use was not chosen for several reasons. Firstly these trans-trabecular devices are highly unlikely to reduce IOP from pre-operative level of > 40 mmHg down to the target pressure of low teens, secondly these devices are not available in our institutions, thirdly these devices are not yet approved for stand-alone use without cataract surgery in Australia therefore not suitable in this young patient.

Published series of Xen gel stent commonly use 0.1 mg/mL or 0.2 mg/mL injected Mitomycin C.[5] While the outcomes of trabeculectomy without antimetabolites have been well described,[6] the long term outcomes of Xen45 without Mitomycin C application are unclear. Early Xen studies with higher diameter Xen140 or Xen63 without antimetabolite reported good IOP reduction but up to 43% needling at 12 months.[7] However, in this case, the ability of the Xen gel stent to achieve good IOP long enough for patient to deliver her baby safely, especially if she were to have a vaginal delivery and still preserve her superior and superior-temporal conjunctiva for future incisional surgery is particularly advantageous.

Early studies of the Xen gel stent demonstrated unacceptably high rates of hypotony with increasing inner luminal diameter (i.e. the Xen63 and Xen140)[7]. More recently, Grover et al.[1] reported the safety of Xen45 Gel Stent in 65 patients after 12 months. No intra operative complications were reported. Post-operative adverse effects were mostly mild or moderate and transient and included nonpersistent loss of best corrected visual acuity and transient hypotony (IOP < 6 mmHg) in about 25% of the patients, that neither required surgical intervention nor had clinically significant consequences. 87% had resolved by day 27. Our patient in this case experienced early hypotony without maculopathy or choroidal effusion, however shallow anterior chamber with iridocorneal touch requiring reformation. Younger age as well as hormonal changes during pregnancy can influence the globe rigidity and might have been contributing factors to the hypotony in this case.

It is unclear in this patient what effect the pregnancy had on the IOP. Several studies have shown that intraocular pressure typically decreases during pregnancy.[8] There are several proposed mechanisms to explain this IOP reduction, including greater aqueous outflow facility due to hormonal changes, lower episcleral venous pressure due to

decreased systemic vascular resistance, and metabolic acidosis resulting from gestation.[9] However the course of glaucoma during pregnancy is variable. There are no large studies regarding IOP in pregnant glaucoma patients. One small study of 15 women examined glaucoma progression during pregnancy. The authors found no increase in IOP or visual field progression in 57% of subjects. However, 18% of the women demonstrated progressive visual field loss, while an additional 18% demonstrated IOP elevation without visual field progression.[10]

Given the high level of intraocular pressure in our patient, there may be an argument that this patient could have benefited from bilateral same day Xen gel stent. The several days delay in surgery for the second eye, during which acetazolamide had to be ceased because of the post operative hypotony in the first eye, may lead to additional optic nerve damage. Bilateral same day trabeculectomy is almost never performed due to the risk of unexpected post-operative complications. Given the reported relative safety of Xen gel stent in preventing early hypotony,[1] bilateral insertion may become possible for patients who require urgent IOP lowering in both eyes. However, Xen gel stent is not without its post-operative complications, as demonstrated in this case some patients require anterior chamber reformation for early anterior chamber shallowing,[11] and cases of endophthalmitis are being reported.[12,13] Therefore, authors still advise that for patients who require prompt bilateral surgical IOP lowering should still have consecutive surgery performed several days apart, depending on severity of glaucoma.

After delivery, several needling procedures with subconjunctival injection of 5-fluorouracil were required to treat early bleb encystment. The passage of cytotoxic drugs in human milk has been poorly studied. Limited information from oncology patients[14] indicated that maternal intravenous infusion at a dose of 200mg/square meter daily produces undetectable levels in milk. The single subconjunctival dose used during needling is much lower (5mg in 0.1mL).

In conclusion, this case describes the use of the Xen implant that may have advantages over conventional trabeculectomy in this setting as the procedure is shorter, with less dependence on intra-operative antimetabolite and is minimally invasive with sparing of the conjunctiva for additional surgery post-partum if needed.

3.1. Patient consent

The patient consented to publication of the case orally. This report does not contain any personal information that could lead to the identification of the patient.

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Disclosures

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Authorship

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

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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.2019.100510.

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