Case Report

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Bilateral Fixed Dilated Pupils after MicroPulse Transscleral Cyclophotocoagulation: A Case Report and Review of Urrets-Zavalia Syndrome

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ABSTRACT

MicroPulse transscleral cyclophotocoagulation (MP-TSCPC) is a relatively new procedure for treating refractory advanced glaucoma. It uses repetitive micropulses of diode laser in an "on-off" cyclic manner, delivered with the Cyclo G6 Glaucoma Laser System (IRIDEX Corp., Mountain View, CA). In this unique case, we report the only instance of bilateral Urrets Zavalia Syndrome (UZS) in medical literature following MP-TSCPC in a 33-year-old Asian female with refractory angle-closure glaucoma. The patient developed bilateral fixed dilated pupils (UZS) after the treatment. The treatment settings included 100 seconds of laser application (50 seconds superiorly and 50 seconds inferiorly). Treated areas were the superior and inferior 180 degrees of the eye, excluding the 3 and 9 o'clock positions. On the first postoperative day, vision and intraocular pressure (IOP) were stable. Six weeks postoperatively, the patient presented with fixed mid-dilated pupils bilaterally and a visual acuity (VA) of 20/200 and 20/300, despite discontinuing Atropine 1% for 42 days. The patient was given pilocarpine 2% for ten days without response; however, vision improved to 20/125 and 20/160 with refraction and a +4.50 add for near vision. One and a half years postoperatively, the patient showed spontaneous partial recovery of the fixed dilated pupils in both eyes, with sectoral paralytic iris superiorly. The overall pupils' size was smaller in both eyes compared to previous visits. This case outlines the patient's symptoms, treatment, and outcome while discussing the potential risk of UZS following MP-TSCPC in specific populations. Further research is needed to better understand and mitigate the UZS complication after MP-TSCPC.

Keywords

Urrets Zavalia Syndrome, MicroPulse transscleral cyclophotocoagulation, Fixed dilated pupil, Glaucoma.

Introduction

Urrets Zavalia Syndrome (UZS) is a rare but well-known complication characterized by a fixed dilated pupil after ophthalmic surgery [1]. The literature suggests that high intraocular pressure (IOP) during or immediately after surgery is a significant risk factor for UZS [2]. While penetrating keratoplasty (PK) is the most common surgery associated with this complication, other ophthalmic surgeries, such as deep anterior lamellar keratoplasty (DALK) and transscleral diode laser cyclophotocoagulation (TSCPC), have also been reported to cause UZS [2,3].

MicroPulse transscleral cyclophotocoagulation (MP-TSCPC) is a relatively new procedure for treating refractory advanced glaucoma with a better safety profile than traditional continuous

TSCPC [4]. However, recent studies have reported mydriasis as the most common complication following MP-TSCPC [5]. The underlying mechanism of UZS is not fully understood, but several theories have been proposed. The original theory of Urrets Zavalia suggested that an increase in IOP during or after surgery could lead to iris ischemia, damaging the constrictor iris sphincter muscle and producing a permanent fixed and dilated pupil [1]. Other proposed theories will be briefly discussed in this article.

Despite its recognition as a potential complication, there is currently no definitive treatment for UZS [2]. Prophylactic measures, such as intravenous mannitol 20%, have shown to decrease the incidence of UZS from 4% to 1.5% [2]. Iridectomy before surgery is controversial but has also been proposed to reduce the incidence of the pupillary block that was initially believed to be the cause of iris atrophy in UZS, although later studies have shown that angle closure is not present in most cases [2]. In the postoperative period, control of IOP and removal of air or gas in the anterior chamber (AC) may be helpful. Late management options for glare reduction include corneal tattooing, tented contact lenses, and artificial iris implants. In cases of focal atrophy with a pupil size of less than 6mm, miotics such as guanethidine and pilocarpine have been effective in UZS mydriasis [2].

In this case report, we present the only case of bilateral UZS in medical literature, following MP-TSCPC in a 33-year-old Asian female with refractory angle-closure glaucoma. Our case highlights the potential risk of UZS following MP-TSCPC in certain populations and underscores the need for further research to better understand and mitigate this complication.

Case Presentation

We present a case of bilateral Urrets Zavalia Syndrome (UZS) following MicroPulse transscleral cyclophotocoagulation (MP-TSCPC) (Figure 1A, 1B) in a 33-year-old Asian female with a known case of Best-like retinal dystrophy with Best 1 gene positive. The patient presented with high intraocular pressure (IOP) and advanced disc cupping in both eyes due to acute angle-closure glaucoma. Nd: YAG laser peripheral iridotomies (PI) were carried out in both eyes, followed by bilateral Ahmed glaucoma valve implant (AGVI) surgeries for uncontrolled IOP despite maximum tolerated medical treatment. The patient was subsequently referred to our glaucoma service.

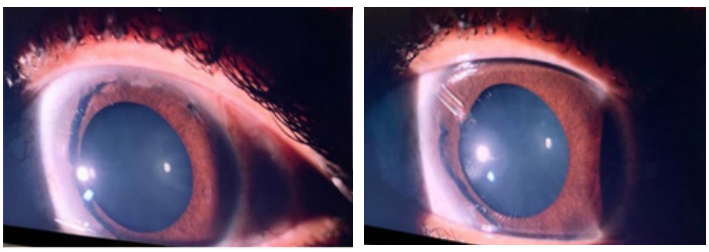

Figure 1A: Right eye post MP-TSCPC, **Figure 1B:** left eye post MP-TSCPC

At presentation, the best-corrected visual acuity was 20/125 in the right eye and 20/100 in the left eye, and IOP was 15/14 mmgh OD and OS respectively. The patient disclosed being in her first trimester of pregnancy, and Xalatan was discontinued. Follow-up after six days showed elevated IOP at 25/21 mmgh OD and OS respectively. The Central corneal thickness was 585 µm & 581 µm in the right and left eye respectively, axial length was 23 mm in both eyes. Slit-lamp examination of the anterior segment revealed large lenses with the shallow anterior chamber and patent PI's. Both pupils were reactive to light and accommodation and fundus examination showed flat retina with no retinal tears and a 0.9 cup/disk ratio in both eyes. The Goldman visual field showed progression compared to 2017 results. The patient was subsequently discussed at the monthly division meeting, and lensectomy+ECP OU was decided to be the best course of action. However, the patient's internal medical specialists advised against any invasive procedure due to the risk of premature labor. Therefore, the surgery was cancelled, and the patient was referred to a general hospital for medical attention.

The patient was followed up during her pregnancy, during which IOP was consistently borderline high. Two months after delivery, the patient presented with a worsening of visual acuity to 20/300 OU and IOP at 28/21 mmgh OD and OS respectively on full topical medication (Xola TID + Alphagan TID + Xalatan QHS + Timolol BID all drops used OU). After a detailed discussion of the benefits and risks of all possible management options, the patient and doctor decided to proceed with MP-TSCPC in both eyes due to its less invasive nature and fewer overall side effects.

Before the procedure, the patient received a retrobulbar block for each eye, and the 810 nm laser (G6, Iridex) was used with the MicroPulse P3 handpiece. Treatment settings were 100 seconds (50 seconds superiorly and 50 seconds inferiorly), with treated areas being the superior and inferior 180 degrees of the eye, excluding the 3 and 9 o'clock positions. Approximately 4 to 6 passes were done per session on both superior and inferior hemispheres, and power was 2500mW. Subconjunctival dexamethasone (2 mg/0.5 ml) was given after applying the laser.

On the first postoperative day, the patient had an unremarkable examination with stable vision and no significant anterior chamber (AC) inflammation observed, with an IOP of 17 mmHg in both eyes. She was discharged on prednisolone acetate 1% eyedrops four times daily for the first week, then tapered weekly over four weeks, Atropine 1 % TID for two weeks with the initial continuation of pre-laser anti-glaucoma drops (topical Brinzolamide 1% twice daily, and timolol 0.5% twice daily, and brimonidine 0.15% three times daily).

However, six weeks post-operation, the patient reported experiencing difficulty with reading and was found to have fixed, mid-dilated pupils bilaterally with no reaction to light and accommodation. Despite being off cycloplegic agents for more than 42 days, visual acuity was measured at 20/200 and 20/300

in the right and left eyes, respectively, and the patient's IOP was 14 and 10 mmHg in the right and left eyes, respectively. The patient was started on Pilocarpine 2% BID for ten days but did not respond to treatment. The patient was followed up on multiple occasions and still had fixed, dilated pupils in both eyes, in addition to complaining of near vision difficulties. The patient was controlled on anti-glaucoma drops, including topical Brinzolamide 1%, timolol 0.5%, and brimonidine 0.15%, and required a +4.50 add for near vision.

At her last visit, which was one and a half years after undergoing mTSCPC, the patient had a spontaneous partial recovery of the fixed, dilated pupils in both eyes with sectoral paralytic iris superiorly, and the overall pupil size was smaller than previous visits in both eyes (Shown in Figures 2A, 2B) with normal optic disc (Shown in Figures 3A, 3B).

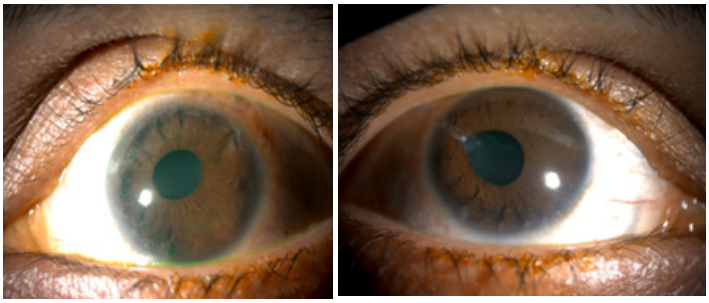

Figure 2A: Right eye, **Figure 2B:** left eye (after 1.5 years of the MP-TSCPC procedure).

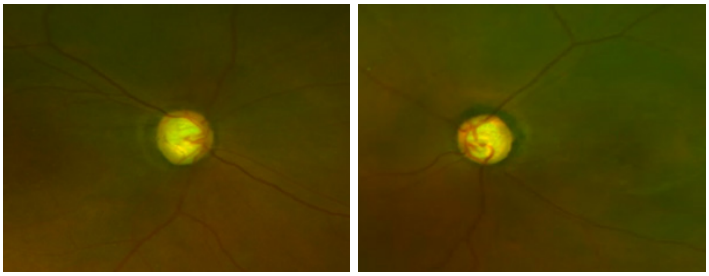

Figure 3A: Right eye, **Figure 3B:** Left eye (Optic nerve photo of both eyes at last visit).

In this case, we present a patient with bilateral UZS after MP-TSCPC, a relatively new and less invasive procedure for treating refractory advanced glaucoma. The patient's course of symptoms, treatment, and outcome were outlined, along with a discussion of potential risk factors and management options. This case report highlights the need for further research to better understand the potential for UZS as a complication of MP-TSCPC in a specific population at higher risk.

Discussion

Urrets Zavalia Syndrome (UZS) is a complication characterized by fixed dilated pupil following ophthalmic surgery. Its pathogenesis is not fully understood, and several theories have been proposed, including iris ischemia due to a postoperative elevation of intraocular pressure (IOP), permanent damage to the sympathetic fibers supplying the iris sphincter muscle, or direct damage to the iris during laser delivery. High IOP during or immediately after surgery is a known risk factor for UZS [1,2].

Presentations of UZS may include pupil dilation and fixation, peripheral synechia, posterior subcapsular opacities, iris ectropion, pigment dispersion, and glaucomfleken. Progression to secondary glaucoma has been observed in one-quarter of cases, although it is not considered a definitive characteristic of UZS [7].

UZS has been reported to occur after various ophthalmic procedures, with varying degrees of incidence. A review by Magalhães of all published UZS cases until 2014, including 30 series and approximately 110 cases, found that Penetrating Keratoplasty was the most common surgery associated with UZS, comprising 51% of all reported cases. This was followed by deep anterior lamellar keratoplasty (18%), Descemet Stripping Endothelial Keratoplasty (8.2%), cataract surgery (8.2%), Argon laser iridoplasty (8.2%), phakic lens implantation (2.7%), trabeculectomy (1.9%), goniotomy (0.9%), C3F8 gas injection (0.9%) [2], TSCPC (28%) [6], and MP-TSCPC (11%) [8].

MicroPulse transscleral cyclophotocoagulation (MP-TSCPC) is a novel procedure for treating refractory advanced glaucoma that uses repetitive micropulses of diode laser in an "on-off" cyclic manner, delivered with the Cyclo G6 Glaucoma Laser System (IRIDEX Corp., Mountain View, CA). MP-TSCPC provides a more consistent and predictable effect in lowering intraocular pressure (IOP) and several IOP-lowering medications with a better safety profile than traditional continuous TSCPC [9]. The mechanism of action of this technique is not yet fully understood. The pulses of light are emitted in the infrared region (810 nm) and are strongly absorbed by the melanin present in the pigmented ciliary epithelium. During the "on cycle," the thermal photocoagulation effect of the laser destroys the ciliary body, and it is proposed that the "off cycles" play a role in reducing heat damage by restricting the accumulation of caloric energy in the adjacent non-ciliary structures, thereby preventing coagulation temperatures from being reached and reducing collateral damage and adverse effects [4]. The decrease in IOP results from the reduction of aqueous secretion due to ciliary body damage, the enhancement of uveoscleral outflow [10], and the enhancement of the trabecular meshwork outflow pathway.

To the best of our knowledge, this is the first reported case of bilateral Urrets Zavalia Syndrome (UZS) after MicroPulse transscleral cyclophotocoagulation (MP-TSCPC) with partial spontaneous resolution. A recent study by Dorairaj et al. [11] found that mydriasis is a common side effect after MP-TSCPC with spontaneous recovery, and they reported that myopic females with brown iris had a higher risk of developing this complication, which is consistent with our case. Another short-term multicenter retrospective study conducted by Radhakrishnan et al. included 143 patients (167 eyes) with various types and stages of glaucoma who underwent MP-TSCPC to assess efficacy

and complications. The success rate of MP-TSCPC was 36.5%, and mydriasis (11%) was the most common complication after MP-TSCPC, followed by persistent punctate keratitis. They also found that the Asian race and phakia were associated with higher odds of developing mydriasis [8]. Egbert et al. studied transscleral diode laser cyclophotocoagulation (TSCPC) as first-line surgical therapy for glaucoma in 92 eyes and observed that 28% of their patients developed an atonic pupil that did not respond to light or accommodation [6]. Spontaneous resolution of UZS after TSCPC has been described by Vieira et al. [12]. In eight eyes of five patients post-TSCPC, one case had complete recovery in one eye, and another case had partial resolution of the fixed dilated pupil with sectoral paralytic iris superiorly after one year from the procedure, which resembles the status of the left eye in our patient. Isac et al. also reported spontaneous pupillary recovery of UZS following Descemet's membrane endothelial keratoplasty [3], and Lifshitz reported accommodative weakness and mydriasis with UZS following laser treatment at the peripheral retina [13]. Our patient also reported UZS with partial spontaneous pupillary recovery and accommodation weakness, requiring a temporary +4.50 add for near vision.

The pathogenesis of Urrets Zavalia Syndrome (UZS) remains unclear, but several theories have been proposed. The original theory by Urrets Zavalia suggests that an elevation in intraocular pressure (IOP) after penetrating keratoplasty in keratoconus patients could cause iris ischemia, leading to permanent damage to the constrictor iris sphincter muscle and resulting in a fixed and dilated pupil [1]. This theory has been extended to other open eye surgeries such as trabeculectomy, cataract surgeries, non-penetrating keratoplasty, and phakic intraocular lens implantation [13]. Evidence supporting this theory includes iris angiography studies showing signs of iris ischemia [5].

Another theory proposes that there is permanent damage to the sympathetic fibers supplying the iris sphincter muscle in the area of the paralytic iris sphincter [14]. This hypothesis may explain cases of UZS that occur after laser procedures such as peripheral retinal photocoagulation [3], argon laser peripheral iridoplasty, and transscleral cyclophotocoagulation (TSCPC) [6, 12]. It is believed that circumferential damage to the ciliary nerves, which run radially from the posterior pole toward the iris sphincter muscle, could be the cause.

A third hypothesis suggests that direct damage to the iris, rather than the ciliary body, may occur during laser delivery. This may be due to the fact that the anatomy and location of the ciliary body is not fixed, particularly in axially myopic eyes, where it can extend up to 2 mm behind the limbus [6].

Further research is needed to fully understand the pathogenesis of UZS and to develop effective prevention and management strategies for this rare but serious complication.

Conclusion

We presented a unique case of bilateral UZS following MP-TSCPC for refractory angle-closure glaucoma, which is a relatively safe technique for treating advanced glaucoma. To our knowledge this is the only case of bilateral simultaneous UZS reported in medical literature, making it a noteworthy occurrence. UZS is a rare but known complication of various ophthalmic procedures, including MP-TSCPC. This case highlights the need for careful monitoring of patients undergoing MP-TSCPC and the importance of considering UZS in the differential diagnosis of patients presenting with fixed and dilated pupils postoperatively. Further research is needed to better understand the pathophysiology of UZS and to identify effective treatment options for this challenging condition.

Statement of Ethics

The patient in this study has given her written informed consent to publish this case, including history elements and images of her eyes. This study was reviewed and the approval was waived by the local Institutional review board at King Khaled Eye Specialist Hospital.

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