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Case Report

Reversal of Optic Disc Cupping After Filtering Surgery in Juvenile Glaucoma: A Case Report

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Abstract

Purpose: To report and present imaging of a case of reversal of optic disc cupping following filtering surgery in juvenile glaucoma.

Observation: A 22-year-old woman visited our emergency department complaining of blurred vision for two weeks in her right eye associated with bilateral ocular pain. Her medical history included bilateral juvenile glaucoma treated since 2018, occurring in the context of a significant family history of glaucoma. On the initial examination, intraocular pressure was 43 mmHg in both eyes. Fundus examination showed bilateral optic disc cupping. Humphrey perimetry revealed advanced glaucomatous scotomas surrounding fixation. Filtering surgeries were performed: a deep non-perforating sclerectomy for the right eye followed by a trabeculectomy for the left. Transient decompression retinopathy occurred in both eyes. Intraocular pressure reduction was followed by a reversal of the optic disc cupping. This morphological recovery was not associated with improvement in other structural parameters such as retinal nerve fiber layer or ganglion cell complex thickness or perimetric functional indices.

Conclusion and importance: This is a rare case of reversal of optic disc cupping in an adult. This case highlights the dynamic sclero-laminar movements involved in the pathogenesis of glaucoma and raises the question of the consequences of these kinetics.

Keywords: Juvenile glaucoma; Optic nerve; Lamina cribrosa; Glaucoma imaging; Spectral domain optical coherence tomography; Intraocular pressure lowering

Introduction

Glaucoma is a chronic optic neuropathy characterized by a remodeling of Optic Nerve Head (ONH) tissues. These deformations are the result of the stress exerted by Intraocular Pressure (IOP) on the sclero-laminar region [1].

Currently, IOP reduction remains the main factor identified to slow the progression of optic nerve fiber loss [2]. By reducing the mechanical forces applied to the ONH, this decrease might be associated with reversibility of the deformations initially induced. As early as 1965 in cases of congenital glaucoma, Chandler and Grant reported morphological improvement in optic disc cupping on fundus photography after surgical IOP reduction [3]. These changes are often found in children, but they can also occur in adults [4]. Several mechanisms have been suggested to explain this phenomenon, although the consequences at the functional level remain unclear.

Case Presentation

A 22-year-old woman visited our emergency department complaining of blurred vision for two weeks in her right eye associated with bilateral ocular pain. Her medical history included juvenile glaucoma treated since 2018, occurring in the context of a significant family history of glaucoma.

On first presentation, IOP measured by Goldmann applanation tonometry was 43 mmHg in both eyes, despite good adherence to glaucoma drops (timolol-dorzolamide and timolol-bimatoprost combinations). Central corneal pachymetry was 521 µm in the right eye and 509 µm in the left. Visual acuity was 0.0 logMAR with no optical correction. The iridocorneal angle was open, with an anterior iris insertion close to the scleral spur, numerous iris trabeculae, and a pale trabecular appearance. Aside from gonioscopy, the anterior segment was normal. Fundus exam revealed concentric optic disc cupping without focal defects. There was a slight congested appearance to the retinal vessels, particularly in the right eye (Figure 1A and B). Optical coherence tomography (OCT, Cirrus, Zeiss, Oberkochen, Germany) showed a decrease in Retinal Nerve Fiber Layer (RNFL) and Ganglion Cells Complex (GCC) thickness (Figure 1C and D). Humphrey perimetry (Humphrey field analyser, Zeiss, Oberkochen, Germany) revealed advanced glaucomatous scotomas surrounding fixation (Figure 2).

Due to the advanced stage of glaucoma on presentation and the uncontrolled IOP despite medical therapy, filtering surgeries were performed in both eyes, beginning with the most compromised right eye. A non-perforating sclerectomy was performed to achieve gentle decompression, reducing the risk of optic nerve snuff-out. Oral acetazolamide was prescribed until the procedure could be performed. On the first postoperative day, IOP was 3 mmHg, visual acuity decreased to 1.0 logMAR with a myopic shift to - 4.75. The bleb was diffuse without leakage, and the anterior chamber was

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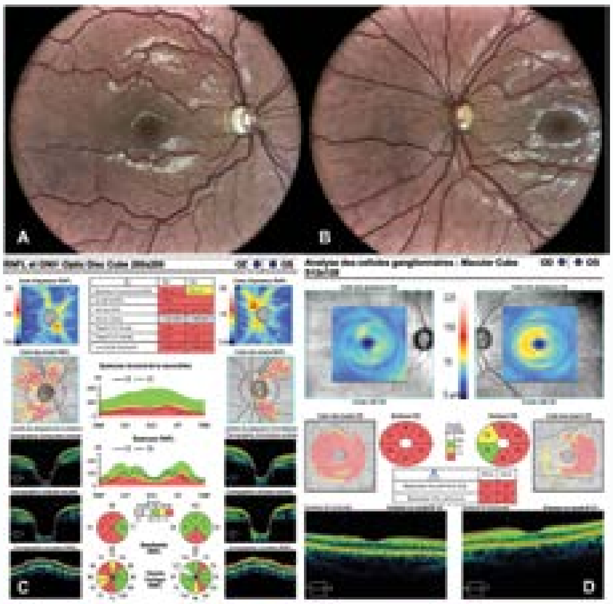

Figure 1: Fundus photography (A = right; B = left) and optical coherence tomography at the initial examination. **(A, B)** In both eyes, fundus photographs showed significant concentric optic disc cupping with a vertical cup disc ratio of approximately 0.9. The neuroretinal rims were generally regular without visible notching. **(C, D)** RNFL and GCC thicknesses were reduced, particularly in the right eye.

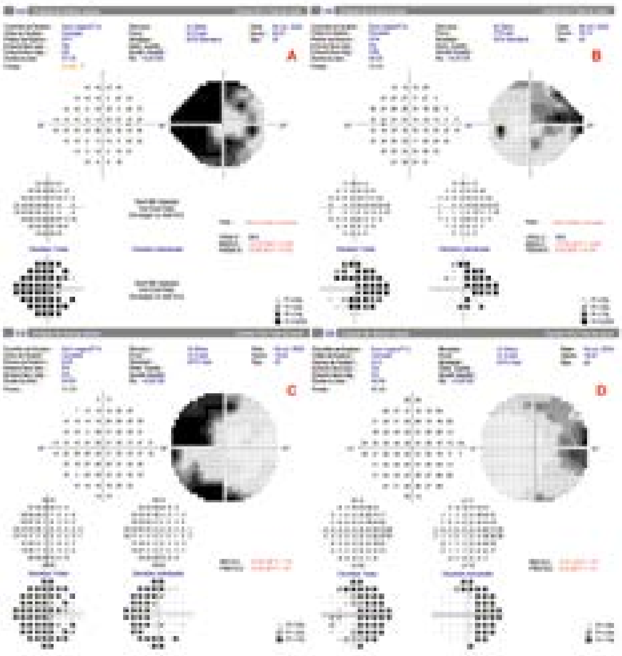

Figure 2: Humphrey automated visual field at the initial examination. **A, C** In the right eye, the 24-2 field (A) was tubular, with a pronounced nasal paracentral scotoma on the 10-2 field (C), explaining the patient's initial visual complaint. **B, D** In the left eye, the 24-2 field (B) showed a profound superior arcuate scotoma associated with an early inferior one, both also reaching the 10-2 nasal hemifield (D).

narrow but formed. Fundus exam revealed low-grade decompression retinopathy with no choroidal detachment (Figure 3A). In the left eye, a trabeculectomy was chosen, attempting to limit the IOP decrease by tightly suturing the scleral flap. Oral acetazolamide was initially discontinued to preserve the filtration in the right eye and then reintroduced 48 hours prior to the trabeculectomy to avoid sudden ocular decompression (preoperative left eye IOP ranged between 20 and 35 mmHg on maximal medical therapy over the month between the two surgeries). The trabeculectomy in the left eye proved challenging due to significant scleral elasticity, with intraoperative retraction of the scleral flap, despite proper thickness and size of 4 × 4 mm. Ultimately, eleven sutures were necessary to secure this flap enough to maintain anterior chamber depth. On the first postoperative day, the choice of a tightly sutured trabeculectomy for this eye did not prevent the development of decompression retinopathy (Figure 3B), despite an IOP measured at 10 mmHg. The visual acuity was preserved with no refractive changes. The bleb was elevated with no leakage, and the anterior chamber was formed.

During follow-up, we observed a progressive improvement in visual acuity in the right eye, with a return to its initial refraction one month after surgery, along with IOP increasing progressively to 10 mmHg. Six months after the procedure, the IOP continued to gradually increase to 18 mmHg, with a tendency for the visual field to deteriorate, leading to the reintroduction of monotherapy (latanoprost). This choice was ineffective in reducing the IOP to less than 15 mmHg. Finally, a goniopuncture was performed in the seventh month; the IOP immediately dropped to 11 mmHg with no visual acuity loss. Sixteen months after the initial surgery, the bleb was formed, and the IOP was stable at 13 mmHg with no additional glaucoma medications. In the left eye, the IOP remained around 10 mmHg fourteen months after the surgery, with a positive IOP response to digital ocular massage, without performing any laser suture lysis.

One month after the surgeries, persistent morphological changes in the discs were observed. Analysis of the fundus photographs revealed a partial reversal of the cupping (Figure 4), reflected especially by changes in the vascular pathway (yellow arrow), more distinct and lasting in the left eye.

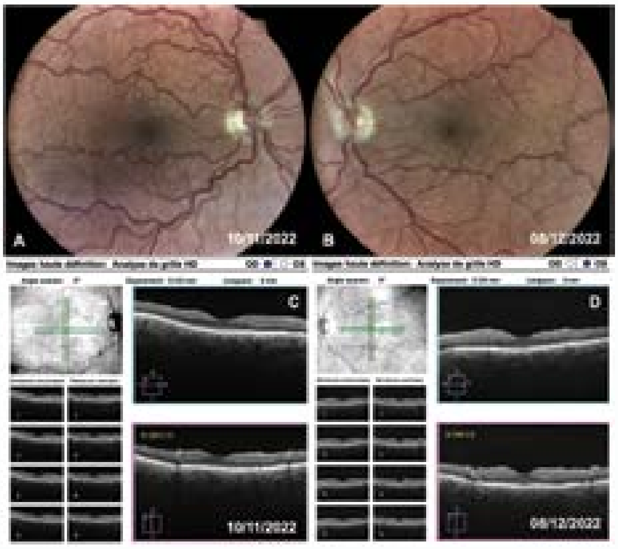

Figure 3: Fundus photography and macular OCT of the patient's right (A, C) and left (B, D) eye on the first postoperative day. **A, B** Fundus photographs showed disc edema, a few intraretinal hemorrhages, and short radial retinal folds extending from the fovea. **C, D** Retinal folds are visible on the macular OCT sections, without macular edema.

A more detailed analysis performed by tomography provides a better understanding of this filling-in of the optic cups. In the left eye, there was an anterior displacement of the Lamina Cribrosa (LC) as well as thickening of the overlying prelaminar tissue (Figure 5B). The more physiologic position regained by the anterior surface of the LC was stable over time. Due to the initial management of our patient in the emergency department, preoperative images of the right eye were not obtained. The postoperative OCT sections of this eye revealed a new posterior displacement of the LC after the fourth month (Figure 5A), consistent with the IOP increase to 18 mmHg, leading to the performance of goniopuncture. The OCT-sections taken substantially after this intervention showed a new anterior displacement of the LC associated with the IOP reduction (13 mmHg).

The possible narrowing of the scleral canal postoperatively was not confirmed by the measurement of Bruch's membrane opening diameter on these OCT sections.

This partial morphological recovery was not associated with an improvement in other anatomical parameters. On the contrary, RNFL and GCC thickness decreased with floor levels being reached (Figure 6). In the left eye, new Humphrey visual fields revealed significant deterioration of the scotomas after surgery (Figure 7). In the right eye, Glaucoma Progression Analysis (GPA) showed stable damage over time. On the most recent field performed, over one year after the surgery, we noted a 2-decibel (dB) improvement in the Mean Deviation (MD) compared with the preoperative field, while maintaining a stable Pattern Standard Deviation (PSD).

More than one year after the surgeries, with stable IOP on no glaucoma medications, a corneal biomechanics measurement was performed using the Ocular Response Analyzer (ORA) (Figure 8). For the left eye, the best Waveform Score (WS) was 8.7, and Corneal Hysteresis (CH) and Corneal Hysteresis Factor (CRF) values were low.

Discussion & Conclusion

Juvenile Glaucoma is a rare disease, occurring between the ages of 5 to 18 years and sometimes later. It represents 6% of primary glaucoma, with an incidence of 0.32/100,000 subjects under the age of 20 years [5]. The majority of cases are familial with autosomal dominant transmission and high penetrance: the myocilin gene mutation (MYOC) leading to trabecular dysfunction is the most frequent, present in up to one-third of cases [6]. Identifying families at risk permits earlier diagnosis, as these are very hypertensive glaucoma which can progress rapidly and quietly. These patients should be automatically referred for genetic consultation as soon as the diagnosis is made, as our patient was advised to do.

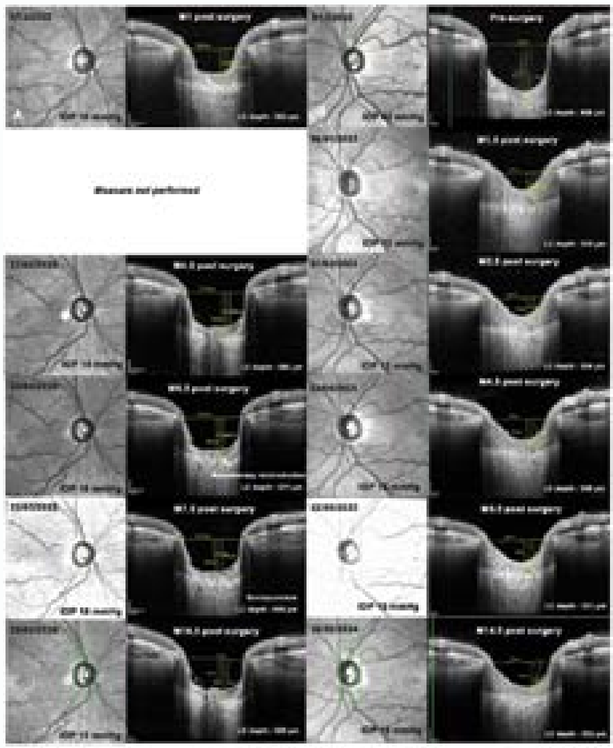

Figure 5: Right (A) and left (B) optic disc spectral domain OCT (SD-OCT) with enhanced deep imaging (EDI) mode pre- and post-operatively, with corresponding IOP values (M = month). The size of the neural canal opening was determined by connecting a line between the two terminations of Bruch's membrane. The distance between this reference line and the anterior border of the LC was measured at 3 points: the deepest and 2 additional points (equidistant by 100 µm from the deepest point). The mean of the 3 measurements (from the 3 points) was considered the LC depth of the selected B-scan. A. In the right eye, a posterior displacement of the LC anterior surface was noted after the fourth postoperative month. The introduction of monotherapy (latanoprost) did not result in any IOP or positional changes. The IOP reduction finally achieved by goniopuncture was followed by a new LC anterior displacement. B. In the left eye, one month after the surgery, we noted an anterior displacement of the LC (red arrows), horizontalization of its anterior surface with a reduction in concavity, and a thickening of the overlying prelaminar tissue. The diameter of the Bruch's membrane opening was unchanged. Over the months, the prelaminar tissue appeared slightly thinned.

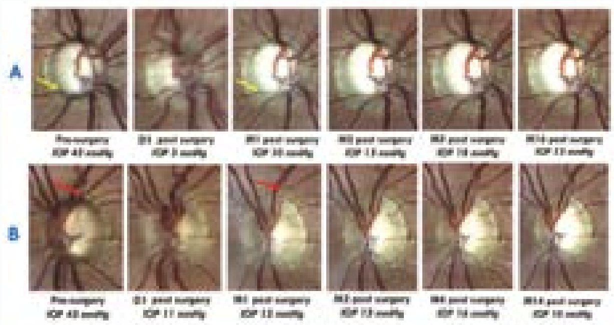

Figure 4: Optic disc photographs of the patient's right **(A)** and left **(B)** eyes at various time points pre- and post-operatively, with corresponding IOP values (D = day, M = month). At one month, there was partial reversal of cupping, with the cup filling in as evidenced by the horizontalization of the bayonet-shaped vessel paths (yellow arrows). There was possible narrowing of the scleral canal (red arrows, using an arterial bifurcation as a reference point). The appearance of disc edema on the first postoperative day was linked to initial hypotony, resolving in the first month following IOP reduction. In addition, both eyes showed a reduction in arterial and venous diameter postoperatively.

Optic disc cupping is a key characteristic of glaucomatous neuropathy. It reflects posterior displacement of the LC associated with neural rim loss secondary to elevated intraocular pressure. Often considered irreversible in adults, the morphological changes illustrated in this case reflect the dynamic nature of the Optic Nerve (ON) tissues. Several mechanisms have been suggested to explain this reversal: narrowing of the scleral canal [7], anterior displacement and thickening of the LC [8] and an increase in overlying prelaminar tissue (expansion of blood [9] and axonal [10] volume, proliferation and hypertrophy of prelaminar glial cells [11]). Although changes of this magnitude remain rare in adults, they may still occur to a smaller degree, detectable with advances in in vivo tomographic imaging [12].

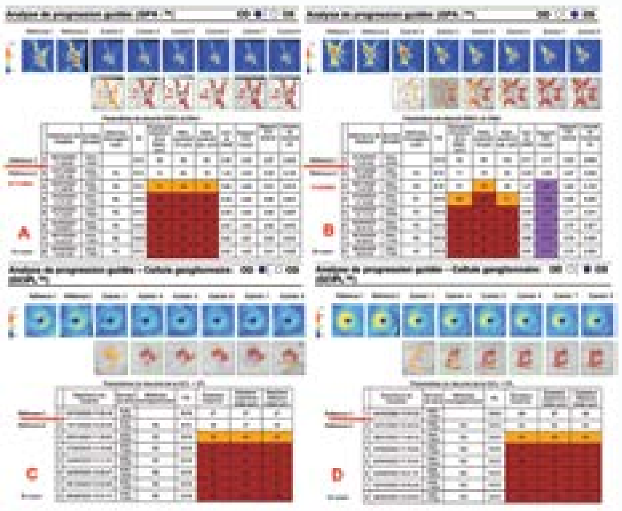

Figure 6: GPA of RNFL and GCC thickness of the patient's right (A, C) and left (B, D) eyes. The respective surgical dates for each eye are indicated by a red line coinciding with the onset of a decrease in the thickness of these parameters.

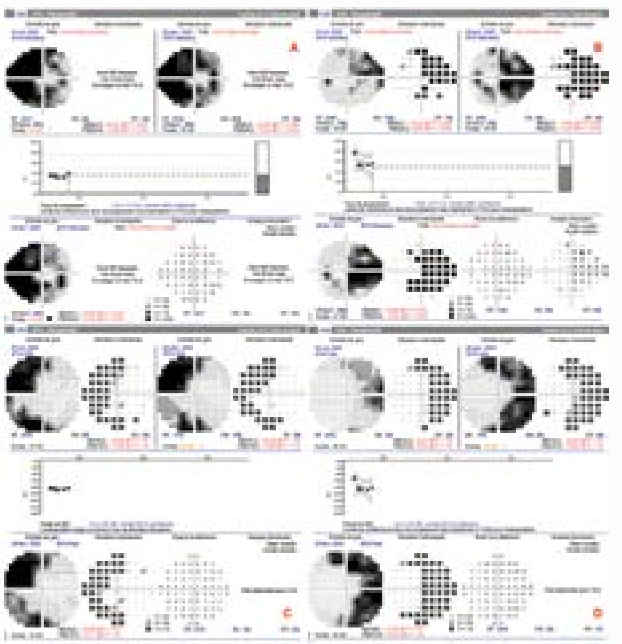

Figure 7: GPA of Humphrey automated visual field 24-2 and 10-2 MD of the patient's right and left eye pre- and post-operatively. A, C For the right eye, undergoing surgery first on November 9, glaucomatous scotomas were stable on GPA. B, D In the left eye, undergoing surgery on December 7, we found a significant deterioration in the visual field one month after surgery compared with the tests performed two months prior to the procedure. Subsequent fields appeared to be stable on GPA.

Changes correlate with the amount of pressure reduction as well as age and severity of the glaucomatous neuropathy [13]. The compliance and load-bearing properties of the ONH may change with age and more advanced disease, explaining the reduction in LC mobility in response to IOP changes [14]. Studies indicate that reversal of disc cupping following surgical IOP reduction can be present up to 2 years after the procedure. It has yet to be determined whether these changes in the appearance of the ONH have any clinical significance [15].

In glaucoma, a visual field defect generally correlates strongly with an abnormal optic disc [16]. This statement may suggest that an improvement in disc anatomy might be accompanied by perimetric improvement. Several case reports have found this possible association [17]. The question of possible reversibility of glaucomatous damage remains delicate, given the limitation of axonal regeneration in humans. Recent studies show an improvement in neuroretinal electrophysiological parameters following IOP reduction, particularly when the visual field is normal or slightly altered [18]. These data might reflect the hypothesis that there are two types of changes that might consecutively occur in retinal ganglion cells: reversible functional changes and irreversible anatomic ones [19].

In our patient's case, RNFL and GCC thickness tended to worsen. Several hypotheses might be advanced to explain this thinning. First, the venous stasis initially induced by the high IOP could cause interstitial tissue edema, distorting the preoperative measurements [20]. Second, hypotony following surgery could lead to an obstruction of axoplasmic transport: the swelling which occurs may be due to the enlargement of axonal elements [21]. Third, these ganglion cells could just be following through with their apoptosis cascade initiated before surgery [22]. Fourth, secondary to IOP reduction, we might imagine an ischemia-reperfusion phenomenon with the release of free radical's toxic to the axons [23]. However, the reduction in arteriovenous caliber noted after surgery, found in cases of IOP reduction in hypertensive glaucoma [24], does not support this last hypothesis.

Functionally, the significant perimetric worsening after surgery in left eye is likely to be related to the period of uncontrolled IOP (20 to 35 mmHg on maximal medical therapy) between the first visual field and the surgical procedure (two months), including one month without oral acetazolamide, so as to preserve filtration in the right eye. However, we cannot exclude the hypothesis that this degradation could also be linked to the sudden decompression upon opening the eye during trabeculectomy. In contrast to a non-perforating sclerectomy, this direct opening of the anterior chamber could lead to sudden shearing movements at the level of the LC. The high tissue elasticity in young patients, reflected in our patient by the difficulty in closing the scleral flap, and the impressive movements of the LC after surgery probably also explain why, despite our precautions, the patient developed decompression retinopathy in both eyes. Currently, the kinetics of laminar displacement are difficult to analyze without the availability of intraoperative *in vivo* imaging. It has been shown that these changes are visible as early as one hour after medical IOP reduction [25] and are possibly visible even sooner after surgical reduction.

In the right eye, the glaucomatous scotoma remained stable on the GPA report. More than one year after the surgeries, we observed a slight improvement in MD in both eyes which could have been due to a learning effect [26] or delayed reversibility of damage. Further tests are required to answer this question.

Finally, this clinical case reminds us that the ONH remains a dynamic tissue even in adults. The LC is a mobile structure whose movements might constitute an interesting parameter to track in glaucoma patients. Its displacement may have a direct impact on the axons and capillary pathways within the laminar pores. It is becoming possible to image these pathways *in vivo* with three-dimensional tomographic reconstruction models [27]. Changes in the LC following IOP reduction could decrease the mechanical shearing of axonal fibers and laminar capillaries, which is probably a key mechanism

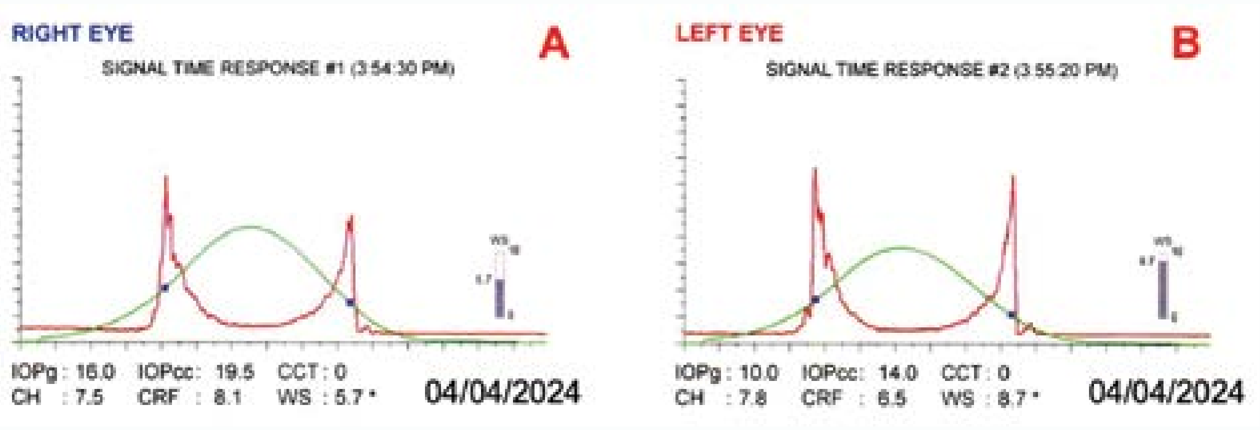

Figure 8: ORA of the patient's right (A) and left (B) eyes after surgery. **A**, For the right eye, the best WS was low, making corneal biomechanics measurements unreliable. **B**, In the left eye, CH was measured at 7.8 mmHg and CRF at 6.5 mmHg, with a corneal compensated IOP (IOPcc) of 14 mmHg.

behind axonal loss in hypertensive glaucoma. The surgical procedure chosen and preoperative IOP control might also have an important role in the kinetics of LC displacement. Indeed, preventing the sudden nature of these movements, especially in young subjects with more elastic tissue, might protect the axons from damaging mechanical shearing forces. These dynamic changes also depend on the stage of the neuropathy, reflecting structural plasticity of the lamina cribrosa. For the right eye, despite the absence of preoperative OCT sections, the LC appears deeper than the left eye postoperatively. Thus, is this persistent posterior displacement a negative prognostic factor linked to a more rigid LC secondary to a more severe glaucomatous neuropathy, or is it a sign of gentler ocular decompression provided by the choice of a sclerectomy? The decompression retinopathy noted in both eyes after surgery seems to support the first hypothesis, with a lamina cribrosa that is not entirely fibrotic either, as evidenced by its post-goniopuncture movement. Studying lamina cribrosa thickness and microarchitecture might also provide some answers. In fact, these parameters might also be improved after IOP reduction without necessarily requiring a corresponding movement of the anterior surface. Unfortunately, access to reliable measurements of these parameters is still limited by current imaging techniques.

The cornea, sclera, peripapillary ring and LC are essentially composed of extracellular matrix encoded by the same genes, explaining why their biomechanical characteristics may be similar. According to this hypothesis, the tissue elasticity observed in our case intraoperatively with the scleral flap and postoperatively with sclero-laminar movements could be reflected in corneal parameters [28]. In addition to corneal thickness, Corneal Hysteresis (CH) is likely to be associated with ON surface deformation in response to IOP changes [28]. Hysteresis reflects the viscoelastic damping capacity of a physical system exposed to a force. In our patient's case, we measured corneal biomechanical parameters with the ORA at a substantial time after the surgeries to rule out changes linked to the initial high IOP [29]. The low values found in the left eye could reflect innate elasticity of the LC, consistent with the scleral elasticity found intraoperatively, reducing the ability of posterior ocular structures to absorb IOP peaks or fluctuations [30]. Conversely to our findings, some studies have found a positive correlation between high CH and greater LC displacement upon increasing [28] or reducing IOP [13]. The mean age of their patients was higher, reminding us that glaucoma is a chronic condition that subjects the LC to IOP forces over a long time. In these patients, low hysteresis could reflect an irreversible rigidity acquired through aging and prolonged elevated pressure [31], in contrast to our young patient's innate elasticity and reversibility. However, other studies have found no such correlation [32].

Preoperative corneal assessment might help to identify patients at risk for mechanical shearing, but currently, the presence of confounding factors makes this difficult to interpret. However, our case illustrates that, despite the precautions taken, we cannot prevent the sudden nature of these movements, even with non-perforating sclerectomy, which should theoretically allow a gentler decompression.

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