CASE REPORT

Managing advanced unilateral pseudoexfoliative glaucoma

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SUMMARY

The only proven therapy for glaucoma is intraocular pressure (IOP) reduction, which can be accomplished by different means. Each should be properly discussed with patients in order to best preserve visual function and quality of life. We report a case of unilateral pseudoexfoliative glaucoma, treated for years with triple topical IOP-lowering drugs. The patient presented with advanced optic neuropathy and important ocular side effects secondary to the treatment. Having discussed his options and prognosis, laser trabeculoplasty was performed while maintaining the remaining therapy considering the advanced stage of glaucoma. His IOP was effectively reduced and no progression was noted after 1-year follow-up. Although medical therapy is the mainstream in glaucoma management, its side effects should not be ignored, especially in unilateral cases. Surgery might have been a better solution, but we chose to perform laser trabeculoplasty, an effective and safer alternative, considering the unlikely but serious risk of the “wipe-out phenomenon” in this case.

BACKGROUND

Glaucomatous optic neuropathy, or simply glaucoma, remains the most commonly acquired optic neuropathy and a leading cause of blindness. Its overall estimated prevalence varies widely across population-based studies: primary open-angle glaucoma (POAG) is believed to affect between 1.1% and 2.1% of whites aged 40 years and older, with a higher prevalence in some ethnic groups such as African Americans (who are 3–4 times more likely to suffer from it and at least four times more likely to become blind by it), while primary angle-closure glaucoma affects around 0.1% of white populations in Europe and the USA.¹ Secondary open-angle or angle-closure glaucoma may be caused by a variety of different pathologies and their overall prevalence is harder to estimate.

Several risk factors contribute to and increase the likelihood of developing glaucoma, but high intraocular pressure (IOP) remains the most important and, notably, one of the few (if not truly the only) we can target for treatment.^{1–4} There are three main strategies for lowering the IOP: medical, laser therapy and surgery. Most patients are treated medically with topical eye drops or gels, with a number of available agents to choose from: β -blockers, prostaglandins analogues, carbonic anhydrase inhibitors and others. Although most drugs are relatively well tolerated, one cannot forget there are some important side effects for each of these medications, not only ocular but possibly also systemic.

In addition, the use of some excipients and the chronicity of glaucoma treatment come as a probably overlooked problem to the ocular surface, with many patients presenting dysfunction of the ocular tear film and the ocular surface integrity and reporting a wide range of ophthalmic symptoms and signs which may include discomfort, burning, ulceration, scarring and possibly vision loss in severe cases.

A relatively common cause of chronic open-angle glaucoma is the pseudoexfoliative (PXF) syndrome, or more correctly, pseudoexfoliative glaucoma (PXG), accounting for approximately 15–20% of all open-angle glaucoma diagnosis.² It tends to be more frequent in women aged over 50 (although male patients appear to be at a higher risk of developing glaucoma),³ with an estimated overall prevalence between 0.6% (age 52–64) and 5% (age 75–85).² Thought to be an ocular manifestation of a systemic disease, in the eye it is characterised by deposition on the trabecular meshwork and other structures of the anterior segment of a grey–white fibrillar extracellular material produced by abnormal basement membranes of ageing epithelial cells.^{1–4} Classically, it leads to unilateral glaucoma, but the ‘uninvolved’ eye most likely has subclinical PXF syndrome, so it may be more adequate to call it an *asymmetrical* disease.² It also tends to present a higher incidence of late medical therapy failure than POAG.^{5–6} with patients having to be submitted to laser therapy or surgery more often. These two particular aspects—unilateral or asymmetric disease and poorer response to medical treatment—mean that PXG may constitute a truly difficult form of glaucoma to manage in some cases, making us weigh the potential side effects of prescribing eye drops only for one eye (often in associations and for a long period of time) versus the risk of disease progression or more invasive treatment modalities, namely surgery. Laser trabeculoplasty may, therefore, be a powerful adjunct in the treatment of many patients with PXG, making it possible in some cases to lower the medical therapy or even avoid the risks of surgery.

CASE PRESENTATION

We report a case of a Caucasian male patient, 64 years old, with no relevant medical history, who presented to our ophthalmology department with a glaucoma diagnosis. He had been followed in a private setting by another doctor for many years who had prescribed two different eye drops for his right eye: a combination of a prostaglandine analogue (latanoprost) with timolol and brinzolamide,

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Figure 1 Hypertrichosis and heterochromia. Hypertrichosis and heterochromia induced by chronic therapy with a prostaglandin analogue (latanoprost). Note the darker iris on the right eye, treated for glaucoma.

a carbonic anhydrase inhibitor. His doctor did no treatment whatsoever in the left eye and did not use any other eye drops, such as lubricants, although the patient experienced some burning and foreign body sensation since he started the medication. He also referred non-complicated cataract surgery by phacoemulsification in the right eye 2 years earlier due to diminished visual acuity (VA).

During initial examination, his best corrected VA was 20/20 in both eyes. On closer look, there was an obvious difference in his eyelashes' length and width between both eyes, with hypertrichosis on the right side, and heterochromia with the right iris presenting a more brownish hue in comparison to the greyish-blue colour of the left eye (figure 1). The patient and his wife were concerned about the pigmentary changes but decided to continue the prescribed prostaglandin analogue for fear of worsening his sight if he did not do so.

On slit-lamp examination, a decrease in tear meniscus height as well as in break-up time (<5 sec) was noticed, on his right eye, upon fluorescein instillation, which also revealed a punctate keratitis on the cornea's lower one-third (figure 2). Pseudophakic status was confirmed on the right, with a posterior chamber intraocular lens well centred and with no posterior capsular opacification. A careful look at the pupillary margin (figure 3) revealed "moth-eaten" transillumination defects and deposition of a greyish material, non-existent on his left eye, suggestive of PSX. His IOP was 22 mm Hg on the right and 16 mm Hg on the left. According to the Spaeth grading system,

Figure 2 Punctate keratitis. Slit-lamp examination with fluorescein showing punctate keratitis on the cornea's lower one-third in the right eye.

Figure 3 Transillumination defects and deposition of pseudoexfoliative material in the pupillary margin. Slit-lamp examination showing transillumination defects and deposition of pseudoexfoliative material in the pupillary margin (right eye). Note pseudophakic status.

gonioscopy (figure 4) revealed, in his right eye, an open anterior chamber angle (approximately 45°), with a deep iris insertion and a clearly visible ciliary body, a regular peripheral iris and moderate pigmentation of the trabecular meshwork (most marked inferiorly) with an accompanying Sampaulesi line; gonioscopy findings were similar in his left eye, although the angle was somewhat narrower (due to phakic status) and less pigmented. Fundus examination confirmed a generalised compromise of the neuroretinal rim in his right eye, with a diffuse concentric enlargement of the cup (estimated cup-disk ratio of 0.9), suggestive of advanced glaucoma (figure 5); his left eye was unremarkable, with a healthy-looking optic nerve head.

Figure 4 Gonioscopy using Goldmann three-mirror lens. Gonioscopic appearance of the anterior chamber angle (right eye): open anterior chamber angle (approximately 45°), with a deep iris insertion with the ciliary body clearly visible, a regular peripheral iris and moderate pigmentation (+3) of the trabecular meshwork, with an accompanying Sampaulesi line.

Figure 5 Optic nerve head appearance. Retinography detailing the optic discs. Right eye: diffuse compromise of the neuroretinal rim with a cup-disc ratio of 0.9. Left eye: normal, non-suspicious looking disc.

INVESTIGATIONS

Time-domain optical coherence tomography, to assess disc morphology and peripapillary retinal nerve fibre layer (RNFL) thickness, and automated static perimetry (using Octopus Perimeter), for visual field (VF) testing, were requested to evaluate glaucoma severity. In the right eye, OCT revealed a

generalised decrease in the RNFL thickness and a disc morphology compatible with the fundoscopic findings (figure 6). Perimetry showed severe changes of the VF with a mean deviation of -20.6 dB compatible with end-stage unilateral glaucoma with a small island of central vision accompanied by a temporal island (figure 7).

Figure 6 Retinal nerve fibre (RNF) evaluation by optical coherence tomography (OCT). OCT revealed in the right eye an important diffuse reduction of the RNF thickness compared to the left eye, with an average thickness of 39.48 and 78.41 μm , respectively.

Figure 7 Visual field (VF) assessment by the Octopus Perimeter (right eye). VF of the right eye, showing severe changes with a mean deviation of -20.6 dB compatible with end-stage glaucoma with only a small island of central vision accompanied by a temporal island remaining.

DIFFERENTIAL DIAGNOSIS

In summary, the patient presented with unilateral PXG in an advanced stage, for which he was being treated with three different topical IOP-lowering agents. Despite this approach, his IOP was far from being controlled (22 mm Hg) and he also presented with some important side effects, namely hypertrichosis, heterochromia and keratitis.

TREATMENT

After discussing his treatment options, and fearing losing his remaining vision with surgery, we decided to perform double-frequency Nd:YAG laser trabeculoplasty in the right eye, around 50 spots (with a spot size of $50\ \mu\text{m}$, 0.1 s duration and power ranging from 950 to 1100 mW) aimed at the junction of the pigmented and non-pigmented lower 180° trabecular meshwork. No complications were registered; prophylactic apraclonidine 1% was instilled before and after the procedure to avoid early postlaser IOP rise and a short course of topical fluormetholone was also prescribed to treat laser-induced inflammation.

OUTCOME AND FOLLOW-UP

Owing to the glaucoma severity, we decided to maintain the current medical therapy. Lubricants were added, however, to treat the keratitis which resolved with success, leading to a

significant symptomatic improvement. His postlaser IOP ranged from 10 to 12 mm Hg and no deterioration was seen in his OCTs and VF after a follow-up of 1 year.

DISCUSSION

The reported case is a clear example of how glaucoma (or any other) treatment must be thoroughly planned and balanced. Although the patient's complete previous medical and ocular history was unavailable, making it impossible to have a clear idea of the disease progression, it is fair to say that it was not under good control despite triple therapy, prescribed for some years now. In fact, it was severely advanced with almost total cupping of the disc and only a small island of central vision with accompanying temporal island remaining.

It is well known that PXG has a worse prognosis than POAG, often showing rapid progression and poor response to medical therapy.¹⁻⁶ In most patients, this makes using more than one IOP-lowering drug avoidable. Many cases of PXG are also unilateral, at least at the time of diagnosis (although 25% of patients develop PXF signs in the fellow eye within 10 years)² such as in the reported case, which makes therapy decisions even harder. So how should we treat these patients?

β -Blockers are an excellent first-line therapy option, although most need to be used twice a day and have potential systemic side effects that have to be taken into account (this, however,

was not a major issue with this patient, who was otherwise healthy with no heart problems, asthma or other relevant illnesses). Prostaglandin analogues are another good choice, with a once-daily dosing regimen that may be easier for patients to follow and fewer systemic adverse events, but with important potential secondary ocular changes^{1–4 7 8} such as eyelash lengthening, thickening and hyperpigmentation, and irreversible iris hyperpigmentation (in 11–23% of patients in 6 months)³ which can obviously lead to heterochromia when one eye is not under treatment. Both drug classes (and their associated excipients) can also lead to ocular surface dysfunction, decreasing aqueous tear secretion (β -blockers), causing corneal staining,⁹ inducing inflammation¹⁰ and causing symptoms such as foreign body or burning sensation and hyperaemia, all of which can be a concern to patients' compliance. α -2 Agonists (such as brimonidine), topical carbonic anhydrase inhibitors (such as brinzolamide, also prescribed to our patient) and other now less commonly used drugs (namely miotics—which are, however, associated with an increased risk of induced angle-closure and development of posterior synechiae in PXG²) are also available, but are usually used as second-line therapy options.

Another problem which needs to be taken into account when discussing glaucoma therapy is the surgery failure related to chronic exposure to preservatives present in many of these eye drops. In fact, considering surgery as an “if all else fails” option may not be the wisest choice; earlier, better IOP control may possibly be achieved with trabeculectomy (and probably other surgical approaches), preventing glaucoma progression while avoiding years of ocular exposure to eye drops, which can ultimately make the surgery harder and reduce its success rate.^{1–4 11 12} This is even more worrying in patients with end-stage glaucoma whose options are running out and who cannot afford having uncontrolled IOP for much longer and be submitted to repeated invasive procedures in an attempt to lower it. Only by knowing our patient's full previous history could we discuss the possible best course of action; maybe an earlier surgery could have delayed the disease progression and avoided most mentioned side effects thus decreasing risk of failure if surgery became clearly necessary.

Although recent data seem not to support the traditional idea of “wipe-out phenomenon” with sudden visual loss following surgery in end-stage glaucoma (which can occur in approximately 6% of these cases),^{13–15} due to the patient's concern of losing his remaining vision we decided to perform laser trabeculoplasty hoping to lower his IOP to more acceptable values and slow down his progression. We appear to have been successful in doing so (at least with a 1-year follow-up), although only time will tell if the laser effect is long-lasting and sufficient enough or not. Published data,^{1–4} unfortunately, tells us that in resemblance to what happens with topical therapy, laser trabeculoplasty also presents higher failure rates in PXG than in POAG. Retreatment is, nevertheless, an option (especially since we only treated the lower 180°), and a safe one.

In conclusion, glaucoma remains one of the most important and usually preventable or more easily manageable causes of blindness worldwide. Thankfully, every day new advances in its therapy are registered, contributing to the healthcare and quality of life of these patients. Topical IOP-lowering agents are still the mainstay of glaucoma treatment and efficient in most cases in preventing its progression, and are usually well tolerated. One must not forget, however, that this is a chronic therapy and although probably surpassed by their benefits, all of these drugs have some side effects which should not be disregarded. Ocular surface integrity is essential to the eye's normal

physiology and health and its compromise is a well-known cause of potential serious diseases and many discomforting symptoms, which in turn may lead to poor patient compliance and ultimately glaucoma progression. Hence our responsibility in choosing the best treatment options for our patients and not overlooking what may seem “minor” and “acceptable” adverse effects. Laser treatments such as trabeculoplasty, available and easily performed by most ophthalmologists, stand as good adjunct therapies, in some cases making it possible to avoid multiple topical agents while also being safer than surgery.

Learning points

- ▶ Chronic therapy with topical intraocular pressure-lowering drugs can have a serious impact on ocular surface integrity, affecting patients' quality of life and potentially their treatment compliance.
- ▶ Surgery may be a better alternative when dealing with unilateral glaucoma, especially in cases which tend to respond poorly to medical therapy such as pseudoexfoliative glaucoma.
- ▶ In addition to being an easy and fast procedure, laser trabeculoplasty remains an effective and safe alternative or adjunctive therapy option when treating open-angle glaucoma.

Competing interests None.

Patient consent Obtained.

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