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Case report

Excisional goniotomy with Kahook Dual Blade in a patient with glaucoma secondary to Transthyretin Amyloidosis

Natalie Brossard Barbosa[a,*], Tomas M. Grippo[b,c,d]

[a] Universidad de la Republica, Catedra de Oftalmologia, Montevideo, Uruguay
[b] Grippo Glaucoma and Cataract Center, Buenos Aires, Argentina
[c] Hospital Aleman, Buenos Aires, Argentina
[d] Yale University, CT, USA

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ABSTRACT

Purpose: To report for the first time the successful use of the Kahook Dual Blade excisional goniotomy technique in a patient with Transthyretin Amyloidosis.
Patient and methods: The Kahook Dual Blade is a single use ab interno trabeculectomy device that removes the trabecular meshwork reducing aqueous humor outflow resistance. A patient with Transthyretin Amyloidosis underwent this procedure.
Results: Ab interno goniotomy with Kahook Dual Blade was a successful surgical solution to reduce intraocular pressure in a patient with Transthyretin Amyloidosis secondary glaucoma controlling IOP in association with topical hypotensors for at least 6 months.
Conclusions: Ab interno goniotomy with Kahook Dual Blade is a surgical option for this type of glaucoma, that treats the main site of aqueous outflow resistance in this pathology with the advantage of being minimally invasive.

1. Introduction

Familial Amyloid Polyneuropathy (FAP) is a rare and sometimes fatal autosomal dominant disease. Clinical manifestations are consequence of the accumulation of amyloid deposits in the peripheral nerves, the autonomic system, the heart, kidneys and eyes.[1] It shows high phenotypic and genotypic heterogeneity, with incomplete penetrance and variable age of onset.[2]

Transthyretin amyloidosis (ATTR), or type I, is the most common type of Familial Amyloid Polyneuropathy. The different types of FAP are classified based on their amyloid-forming precursor protein.[3] In Type I this protein is transthyretin (TTR) which is involved in the blood transportation of retinol and thyroxine.[4] In its original state it is a stable tetramer, mutations in this protein make it become structurally unstable and dissociate into fibrils with a toxic effect when accumulated.[5] The most frequent causative genetic mutation found worldwide of this type of amyloidosis is the substitution of valine for methionine at position 30 of the TTR gene (Val30Met) in chromosome 18q.[6] This mutation is most prevalent in Portugal, Sweden and Japan.[7] TTR is produced primarily (95%) by the liver but it is also synthesized by the choroid plexus of the brain and the retinal pigment epithelium.[8]

The diagnosis mainly depends on the patients family history of FAP. If negative, a biopsy of the affected organ or salivary gland is mandatory (showing green birefringence with Congo Red of beta pleated amyloid material). The genetic study is confirmatory of the disease and its type.[7]

Liver transplantation has proven to be the most effective treatment for ATTR stopping the neuropathy in 70% of cases.[9] Tafamidis is the only drug approved for ATTR (early stage).[10] However, neither liver transplantation nor tafamidis is capable to halt the progression of ocular involvement given the in situ production of TTR by the retinal pigment epithelium.[8] Retinal panphotocoagulation could damage the RPE and thus stop its progression[11] but this hasn't been sufficiently investigated so far.

The main ocular consequences of ATTR are keratoconjunctivitis sicca, secondary glaucoma and vitreous deposits of amyloid material.[12] The leading cause of irreversible blindness in ATTR patients is open angle glaucoma secondary to amyloid deposition in the trabeculum hindering aqueous humor outflow.[13]

Secondary glaucoma is relatively common with a prevalence reported in a review of 513 patients by Beirao et al. of 20%,[14] and increases with the duration of the disease and time even after liver

* Corresponding author. Grippo Glaucoma Center. Luis Maria Campos 250. Apt 1- O. C1426BON, Buenos Aires, Argentina.
E-mail address: brossardnatalie@gmail.com (N.B. Barbosa).

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transplantation (LT).[15]

ATTR secondary glaucoma presents several distinct features: amyloid deposits in the anterior chamber (AC) and pupillary edge, anterior capsule of the lens, iridocorneal angle and conjunctival vessels.[16] 49% of patients with vitreous amyloid deposits present with glaucoma.[13] The deposit of amyloid in the pupil edge and a fringed pupil would also be highly associated with the development of glaucoma.[13] The development of severe glaucoma after vitrectomy for amyloid opacities is present in up to 60% of vitrectomized eyes in a study by Latasiewicz et al. and is usually not controllable with topical medications.[17] In a recent report, Beirao et al. describes that glaucoma is more common in vitrectomized eyes, however, the exact mechanism by which the vitrectomy could induce or worsen glaucoma is still unknown.[18] An increase in vitreal opacities that leads to vitrectomy could simply be a reflection of a more advanced stage of the disease, with a resultant concomitant increase in trabecular amyloid material deposition and therefore the association.

2. Case report

The patient is a 56 year old Argentinian man with a family history of ATTR diagnosed in 1995 which required liver transplantation that same year. He also suffers from cardiac involvement. Ever since, the patient remained under immunosuppressive treatment with cyclosporine po 200mg qd and meprednisone 2mg twice a week.

His past ocular history (POH) was remarkable for development of amyloid ocular complications as vitreous opacities that required four previous 25- gauge vitrectomies elsewhere, the first one in 2009 in his left eye when his vision improved from 4/200 to 20/16 and three other vitrectomies in his right eye (two in 2015 and the last one in 2018). Histologic analysis of vitreal opacities confirmed amyloid depositions. He is pseudophakic in his right eye since 2017.

He presented to our consult for the first time in 2018 with a best corrected visual acuity (BCVA) of hand movement (HM) OD and 20/25 OS. A diagnosis of secondary glaucoma had been made after the first vitrectomy in his OS by his retina surgeon, being prescribed topical ocular hypotensors including timolol 1% OU, brimonidine 0,2% OU, bimatoprost 0,03% OU and oral acetazolamide 250mg bid. His IOP was 40 mmHg in his OD and 13 mmHg in his OS. AC angles were wide open with a pigmented trabeculum in both eyes. Other remarkable clinical findings were amyloid material deposition at the pupillary margin and surface of the left lens, and fringed pupil OU (Fig. 1). The vertical cup to disc ratio was 0.9 OU.

Despite our initial surgical recommendation, patient was lost to follow up. He returned to us 7 months later in May 2019. At this time he had undergone an unsuccessful trabeculectomy (we do not know whether mitomycin C was used) in his OD followed by a tube shunt surgery with implantation of an S2 Ahmed glaucoma drainage device (GDD). BCVA at this time was HM OD and 20/30 OS. He presented with an unusually cystic and elevated bleb surrounding the plate, with extrusion of a portion of the tube (Fig. 2A). IOP was 32 mmHg OD and 14 mmHg OS with reinstalled topical hypotensors (timolol 1% OU, brimonidine 0,2%OU, bimatoprost 0,03% OU). Gatifloxacin and prednisolone acetate 1% were indicated qid to reduce inflammation and the risk of infection.

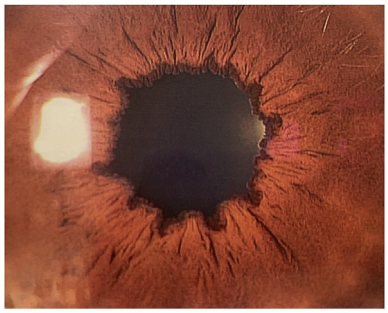

Fig. 1. Fringed pupil with amyloid deposition.

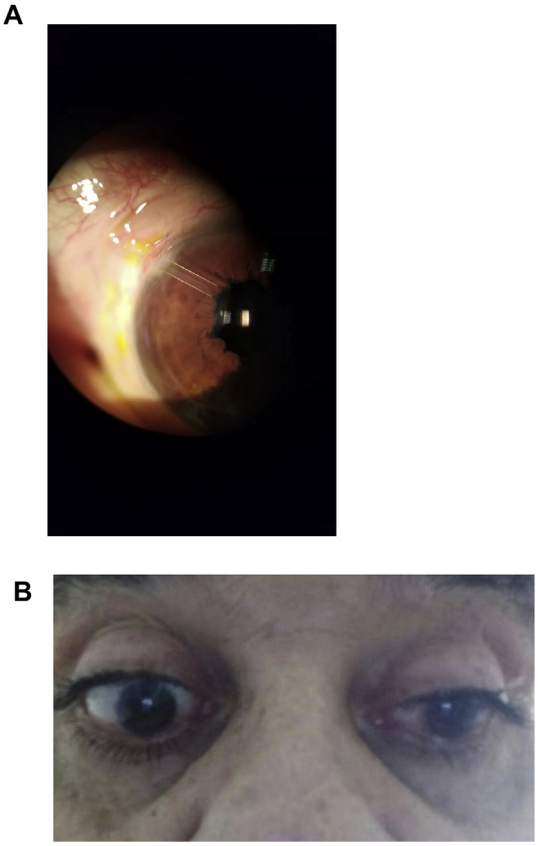

Fig. 2. A. Extruded shunt tube in right eye. Fringed pupil with amyloid deposits. B. Patient's proptotic eyes.

Initial surgical approaches were to cover the exposed tube with a donor scleral patch firstly and secondly with an autologous conjunctival flap rotation. Both surgeries failed to maintain the tube covered for more than a few weeks before erosion of the tissue occurred.

At this point in time, with a recurrent exposed tube, the concern about infection in this chronically immunosuppressed patient raised. Removal of the GDD appeared to be unavoidable but the patient had presented IOPs above 50 mmHg prior to the its insertion causing severe headaches, nausea and vomiting. His prior history of failed glaucoma surgeries plus the lack of a healthy conjunctiva and proptotic eyes (Fig. 2B) made him a poor candidate for a repeat trabeculectomy or GDD. Remaining options contemplated at this point included a combined or possible two stage approach; an ab interno trabeculotomy with Kahook Dual Blade (KDB, New World Medical, Rancho Cucamonga, CA), or a cyclodestructive procedure followed by removal of the valve. Considering the cause of this type of glaucoma we deemed KDB could address this more directly.

The decision not to move forward with a single stage surgical approach with removal of the valve and KDB in the same surgical act was founded in the patient's POH of highly symptomatic IOPs over 50 mmHg before the GDD insertion which could resume if the KDB goniotomy proved unsuccessful. The patient had a very high cardiovascular risk and an emergency glaucoma surgery without the necessary preparation was an unwanted scenario since an external pacemaker was considered needed in the operating room by the anesthesiologist. The procedure is performed in September 2019 in the following manner: a 1.0 mm paracentesis is created, cohesive viscoelastic is injected to fill and pressurize the AC and a 2.2 mm clear cornea temporal incision is used to introduce the KDB into the AC. Under

gonioscopic visualization 120° of nasal trabecular meshwork (TM) and inner wall of the Schlemm's canal are successfully excised. Blood reflux is noted and viscoelastic is then flushed out with balanced salt solution (BSS) and the eye pressurized to 20–30 mmHg. Interrupted sutures are then placed with 10–0 Nylon at incision sites. Following this procedure IOP decreased and the eye became spontaneous Seidel positive. The Ahmed valve is removed in a second instance without any complications and the area of Seidel at the tube entry site fixed. At 6 months follow up, the patient remains with controlled IOPs under 14 mmHg OU, without Seidel and maintaining his baseline HM vision in his right eye with timolol 1% OU, brimonidine 0,2%OU, bimatoprost 0,03% OU. No further complications occurred during follow up.

3. Discussion

There are only a few reports in the literature describing the types of glaucoma procedures performed in FAP patients. The most frequently mentioned procedure is trabeculectomy. Kimura and colleagues[13] reported 15 eyes that required surgery: 11 eyes underwent trabeculectomy, 2 combined ab-externo trabeculotomies and sinusotomies, 1 a cyclodestructive procedure, and 1 an unsuccessful nonpenetrating trabeculectomy. Later, Latasiewcz et al.,[17] presented a small series of three successfully controlled FAP glaucoma patients with nonpenetrating deep sclerectomy with mitomycin C. The only trabeculotomies reported in literature were in the Kimura series, where two ab externo trabeculotomies and associated sinustotomies resulted in one patient successfully controlled in the four month follow up and one failed result.[13] To the best of our knowledge there are no reports of any ab interno excisional goniotomy performed in a FAP secondary glaucoma patient.

The Kahook Dual Blade (KDB, New World Medical, Rancho Cucamonga, CA) goniotomy is an ab interno trabeculotomy technique that consists of removing the affected TM using a curette with two blades.[19] Compared to traditional ab externo trabeculotomies, KDB excisional goniotomy does a complete excision removing the inner wall of Schlemm's canal and the TM. Traditional ab externo trabeculotomies cut the tissue in a more traumatic fashion leaving leaflets that could occlude collector channels and facilitate fibrosis.

Given the pathophysiology of secondary glaucoma in FAP, where the deposition of amyloid material in the TM would play a preponderant role,[16,20] a surgical technique that removes the affected TM seemed a logical strategy. A similar rationale exists behind a much more frequent type of glaucoma, the pseudoexfoliative glaucoma with fibrillar material in the TM, where the KDB goniotomy or similar surgical ab interno approaches have shown particular success (79,1% and 84,6% success by reducing of IOP in at least 20% or reduction in at least 1 drop with the trabectome[21] or Dual Blade Kahook[22] respectively). It should also be noted the benefit of keeping the conjunctiva untouched for possible future filtrating surgeries.

It is important to have present that the KDB is generally indicated for mild and moderate glaucoma. Like our patient, KDB in patients with advanced glaucoma usually requires topical hypotensors or may require further glaucoma surgeries. Combination of other minimally invasive glaucoma surgeries (MIGS) such as trabecular stents with cyclophotocoagulation presents as an alternative to reduce the use of medications or to achieve target pressures.[23] However, we decided against it in the early postoperative period to avoid further inflammation and the increased probability of sinequiae and failure of our goniotomy procedure. This remains an option in the future as an add on procedure if needed. Successful combinations of MIGS including trabecular or suprachoroidal stents have been reported in the literature for advanced glaucoma[24,25] and remain a possibility for the future. The high cost of istents® and the lack of availability of suprachoroidal stents in our local medium make them less attractive in our case.

We have previously underlined the fact that the development of severe glaucoma after vitrectomy for amyloid opacities is present in a high percentage of eyes, likely as a consequence of amyloid material produced in the RPE cells ending up in the TM instead of accumulating in the vitreous humor in these vitrectomized eyes, but it also should be observed that this surgical procedure is needed in most patients after so many years of ocular ATTR involvement. It is of note that the glaucoma diagnosis was performed before undergoing vitrectomy in his OD, and in this way the confounding effect of this surgical procedure is excluded from the diagnosis of glaucoma in this eye. Also, we believe the prolonged corticosteroid use could potentially have also played a role in the disfunction of the patient's TM. Thus, even though the pathology behind the exact genesis of the patient's glaucoma and severity may be influenced by the above mentioned factors, he represents the typical complexity of ATTR glaucoma cases. Moreover, excisional goniotomies also address the malfunctioning TM of corticoid induced glaucoma. Judging by this rationale and our result so far, the KDB procedure was an appropriate choice, which controlled the IOP in our patient for at least six months and could represent a viable surgical alternative for this type of secondary glaucoma.

4. Conclusions

This case report constitutes the first ab interno excisional goniotomy with KDB ever performed in a patient with FAP secondary glaucoma with good results. This surgical approach targets a main cause of IOP increase in this type of pathology with the benefit of being minimally invasive.

Funding

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Précis

Transthyretin amyloidosis frequently causes secondary glaucoma mainly due to the accumulation of amyloid material in the trabecular meshwork, this is the first report showing a successful approach to this pathology performing an Ab interno goniotomy with the Kahook Dual Blade.

Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Declaration of competing interest

Dr. Grippo, trainer Kahook Dual Blade New World Medical.

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