Review

Oculoplastic Challenges in Patients with Glaucoma

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Abstract

Glaucoma is typically a disease that occurs in advanced age, requiring lifelong monitoring and treatment with topical medications, laser procedures, or surgery. Patients with glaucoma may also experience oculoplastic issues due to the natural aging process or as a result of glaucoma treatment or surgery. Eyelid surgery in these individuals can lead to complications and undesirable results. Therefore, it is crucial for oculoplastic surgeons to be aware of the incidence and risk factors associated with oculoplastic problems specific to glaucoma patients. Understanding these potential complications is essential for taking necessary precautions and achieving successful surgical outcomes. The purpose of this review is to raise awareness among ophthalmologists specializing in oculoplasty and glaucoma and to contribute to the quality of life of glaucoma patients.

Keywords: Ectropion, eyelid surgery, glaucoma, oculoplastic problems, periorbitopathy, prostaglandin analog, punctum stenosis

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Introduction

Glaucoma is a disease primarily seen in older patients, who also commonly experience age-related (involutional) eyelid changes. This review, however, focuses specifically on iatrogenic oculoplastic problems that arise because of medical or surgical treatment in glaucoma patients, as well as important considerations to keep in mind during their treatment, with the aim of raising awareness of oculoplastic problems unique to glaucoma patients.

A description of oculoplastic problems associated with topical anti-glaucoma treatment was first published in 2004 and included trichiasis and periorbitopathy in patients using prostaglandin analogs (PgA).[1,2] However, the history of reporting oculoplastic problems associated with glaucoma surgery dates back further.[3] Later, cases of orbital cellulitis or exposure were also reported, typically in patients with tube insertion.[4,5,6] These oculoplastic problems are specific to glaucoma patients and require a separate, more careful evaluation compared to other patients with oculoplastic conditions.[7,8] The treatment plan for oculoplastic issues in these patients must be managed according to the glaucoma medications used and the type of glaucoma surgery they have undergone.

Oculoplastic problems specific to glaucoma patients can be categorized into four main headings: (1) oculoplastic problems related to medical treatment, (2) oculoplastic problems related to surgical treatment, (3) acute angle-closure glaucoma after some oculoplastic surgeries, and (4) the appropriate treatment for patients with oculoplastic conditions who also have preexisting glaucoma.

Oculoplastic Problems Related to the Medical Treatment of Glaucoma

The initial treatment for glaucoma typically involves medical therapy. It is important to consider the potential issues that may arise in the eyelid and orbit due to antiglaucoma medical treatment when performing oculoplastic surgery.

Prostaglandin-Associated Periorbitopathy

PgA are often the preferred first-line medical treatment for glaucoma because they effectively reduce intraocular pressure (IOP) and have minimal systemic side effects.[9] However, some patients may experience local side effects such as prostaglandin-associated periorbitopathy (PAP), deepening of the upper eyelid sulcus (DUES), upper eyelid drooping, orbital fat atrophy, enophthalmos, eyelash growth, and hyperpigmentation (Figures 1, 2, 3).[2,9,10,11,12,13,14,15]

DUES was initially observed in patients using bimatoprost and later identified with other PgA drugs as well.[2] Additionally, some periocular changes in the lower eyelid have also been reported.[11,13,14,15] The incidence of DUES was found to be lowest with latanoprost and highest with bimatoprost, ranging from 5.8% to 80%.[11,13,14,15,16] The first sign of PAP during evaluation is loss of the periorbital fat pads, which is particularly common in older patients.[11] In up to 80% of PAP cases, a difference of 2 mm or more between the two eyes can be detected by Hertel exophthalmometer.[11]

Orbital fat volume was quantitatively measured using magnetic resonance imaging and compared between the eyes of 9 patients treated unilaterally with bimatoprost.[9] It was discovered that the orbital fat volume significantly decreased with bimatoprost use, averaging 14.60±2.1 cm^3 in the treated eyes compared to 17.0±4.3 cm^3 in the control eyes, which may

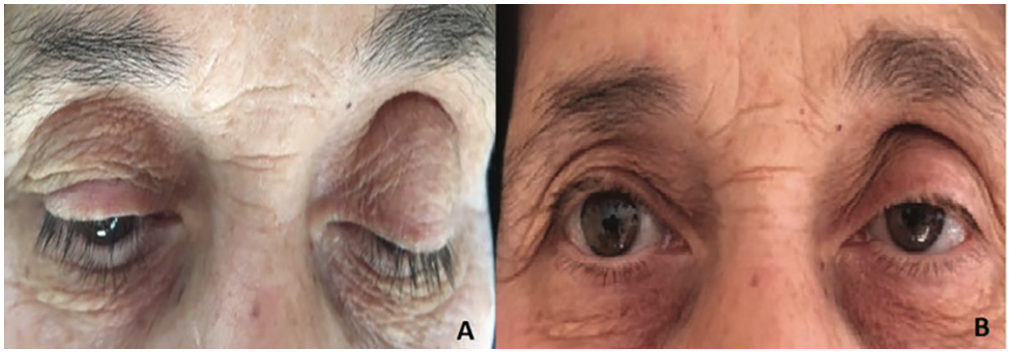

Figure 1. In a 71-year-old female patient using bimatoprost for left pseudoexfoliative glaucoma, deepening of the upper eyelid fold is more prominent when looking downward (A). In the primary position, the same patient shows a deepening of the left upper eyelid fold and ptosis (B)

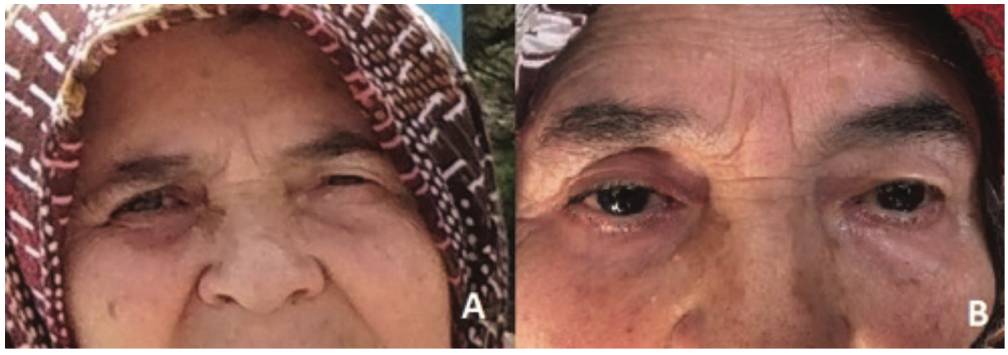

Figure 2. A 74-year-old female patient shows noticeable periorbitopathy (B) that developed after starting travoprost for right pseudoexfoliative glaucoma, when compared to her earlier photographs (A) and medical history

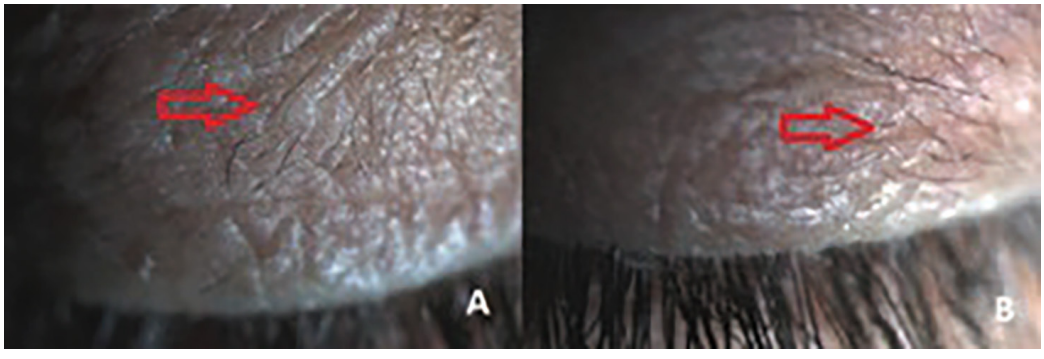

Figure 3. A 60-year-old female patient using travoprost in both eyes for primary open-angle glaucoma presented with bothersome increased eyelid hair growth (red arrows; A: right eye, B: left eye). Her treatment was changed

cause enophthalmos (14.7±2.5 mm in treated eyes and 16.0±2.3 mm in control eyes).[9]

Separation of the levator muscle or degeneration (decrease in collagen) of the Müller muscle has been reported as a cause of DUES and ptosis.[16,17] The decrease in eyelid fat pads is believed to result from apoptosis of orbital fibroblasts, triggered by reorganization of the extracellular matrix.[18,19] The onset time of DUES and orbital atrophy can vary between 1 month and 5 years.[16] Eyelid pigmentation is reported least frequently with latanoprost (5.9%) and most frequently with bimatoprost (25.9%).[20,21] Increased eyelid pigmentation is caused by the stimulation of melanogenesis in melanocytes.[22] Eyelash changes have been reported at rates ranging from 2.9% to 53.8% with bimatoprost, 0.7% to 57.1% with travoprost, and 0% to 77% with latanoprost.[20,23,24,25] In one case, increased hair growth on the cheeks in addition to the eyelashes was observed 3 months after starting travoprost.[26] Hypertrichosis has been linked to the ability of PgA to prolong the anagen phase of hair follicles during their resting period.[27] For example, Figure 3 shows a 60-year-old female patient using travoprost monotherapy for primary open-angle glaucoma who experienced increased eyelid hair growth that led to discomfort, prompting a change in her treatment.

PAP is generally reversible within 1 to 6 months after discontinuing the medication.[23,26,27,28,29] Furthermore, two different studies evaluating the transition of patients who developed PAP from conventional prostaglandin F2α analogs to omidenepag isopropyl, a new selective prostaglandin-EP2 agonist, suggested that switching to omidenepag isopropyl improved patient satisfaction. Additionally, it was indicated that this transition could help mitigate DUES and pigmentation of the eyelid and periocular skin.[30,31]

Punctum and Canalicular Problems

This phenomenon was first reported in the literature in 1998 by McNab[32] with timolol maleate. Although a direct causative relationship was not established, it was suggested that punctal stenosis could occur due to cicatricial effects from long-term use. Ulusoy et al.[33] reported that punctal stenosis was observed more frequently in individuals over the age of 65 who were using glaucoma eye drops. However, the study did not specify which antiglaucoma medications were used or their duration, focusing only on whether drops were used or not. Kashkouli et al.[34,35] found that punctal obstruction was more common in patients using dorzolamide/timolol fixed combination (26 of 130 glaucoma patients [20%] vs. 24 of 280 controls [8.57%]) with treatment durations ranging from 2 weeks to 156 months. They also noted a significantly higher incidence of obstruction in the upper canalicular system. Topical antiglaucoma medications can cause inflammatory and fibrotic changes in the conjunctival surface. These changes may be linked to the medications themselves, the preservatives used in commercial formulations, or the length of time the topical treatment is used.[31] It is likely that similar changes could occur in the epithelium and subepithelial tissue of the lacrimal drainage system, leading to stenosis with increased fibrosis and eventual occlusion. Since the upper lacrimal system is closer to the conjunctiva and fornix, it is expected to be more affected by topical medications than the lower lacrimal system.[35] Kashkouli et al.[35] noted that some patients in their series had been using topical medications for many years, suggesting that the effects may be dose-dependent. For those who had been using drops for a shorter period, they suggested the reactions were idiosyncratic.[35] Kashkouli et al.[35] also demonstrated that the timolol/dorzolamide combination therapy had a greater adverse impact on the lacrimal duct system compared to monotherapy. Ortiz-Basso et al.[36] reported that there was no significant difference between the groups in the development of lacrimal obstruction with the use of a single topical antiglaucoma medication. For these reasons, a thorough examination of the upper lacrimal system should be conducted in glaucoma patients who present with tearing and epiphora.[35]

Antiglaucoma Drug-Induced Ectropion

The first cases of drug-induced ectropion were reported with dipivefrin in 1991 and later with Iopidine (apraclonidine) in 1999.[37,38] Subsequent reports identified dorzolamide and brimonidine as topical drops frequently responsible for this condition.[39,40] Skin cicatrization due to chronic hypersensitivity (allergy) to eye drops can cause shortening of the anterior lamella and lead to ectropion.[39,40] In cases where ectropion surgery failed, it was often attributed to the continued use of topical antiglaucoma drops, and improvement was noted when the medication was discontinued.[38] The point that should be kept in mind here is that early diagnosis and early discontinuation of the drug increases the chance of full recovery.[39,40]

When addressing ectropion caused by antiglaucoma topical medication, it is essential to discontinue all topical medications if more than one is used, and then reintroduce them one at a time to identify the responsible agent. Short-term use of topical steroids can be beneficial, and it is important to remember that cicatricial changes are reversible. Preservative-free drugs should be used, and patients should be informed that trabeculectomy may be necessary (Figure 4).[39,40]

Oculoplastic Problems Related to the Surgical Treatment of Glaucoma

Ptosis of the Upper Eyelid

Ptosis can occur months to years after trabeculectomy surgery, with incidence rates reported as high as 19%.[3,41] Şen Malkoç[8] reported that ptosis after trabeculectomy was observed in 35 of 339 eyes (10.3%). Thirty eyes of 30 patients (8.8%) had transient ptosis and 5 eyes of 4 patients (1.5%) had persistent ptosis. Song et al.[3] noted that ptosis can arise regardless of whether the surgery is combined with cataract surgery or is primary or secondary, and does not depend on the type and size of the conjunctival flap. Roddy et al.[42] reported an increased rate of ptosis following glaucoma drainage device (GDD) placement compared to trabeculectomy and cataract surgery.

Ptosis after glaucoma surgery may be temporary or permanent.[8] If it persists for more than 6 months after surgery,

permanent ptosis should be considered. Transient postoperative ptosis can be caused by factors such as eyelid edema, hematoma in the eyelid or orbit, ocular inflammation, neurogenic factors, and anesthetic infiltration of the third cranial nerve terminal endings or the levator complex. For example, in Figure 5, an Ahmed glaucoma valve was implanted in an 18-year-old female patient, and ptosis in her left eye was observed during the early postoperative period but resolved spontaneously by the 6-month follow-up appointment.

Fukushima et al.[17] reported that preoperative DUES may be an important predictor of ptosis following trabeculectomy. They also found no significant differences between the ptosis and non-ptosis groups regarding glaucoma types, number of antiglaucoma medications or frequency of postoperative needling. In contrast, Malkoç Şen and Serbest Ceylanoğlu[43] emphasized that needling and a history of eye itching due to antiglaucoma drug-associated allergy may increase the risk of ptosis.

Permanent ptosis can result from several factors, including detachment of the levator aponeurosis, age-related fat and soft tissue atrophy, and upper rectus plication suture (although the latter is now less common as plication sutures are no longer placed in the upper rectus). In patients with permanent ptosis, applanation can be challenging, and monitoring visual field defects is complicated by the effect of the eyelid on the visual field.[3,17,41,43,44] For example, if a patient lifts their upper eyelid manually while measuring IOP, they may inadvertently cause a high IOP reading by applying pressure on the eyeball. Additionally, if a patient with a defect in the lower half of the visual field also has ptosis causing an upper visual field defect, their overall visual field will be further narrowed, negatively impacting their quality of life.[43] In such cases, if lifting the upper eyelid without pressing on the eyeball corrects the defect when the visual field is reassessed, ptosis surgery could improve the patient's quality of life (Figure 6). Correcting permanent ptosis in these patients is crucial. Key considerations include:[7]

- A thin, avascular bleb may be more common after trabeculectomy with antimetabolite, increasing susceptibility to bleb infections and ocular surface disease. The risk of blebitis and endophthalmitis due to bleb exposure (lagophthalmos) may be higher.
- In glaucoma patients with a thin, avascular bleb and ptosis, it is important to avoid overcorrection and perform ptosis correction less than the traditional amount.
- When performing Müller muscle surgery via a posterior approach, it is essential to be cautious about flipping the eyelid and the potential mechanical trauma to or drying of the bleb during surgery, which can disrupt bleb function. Song et al.[45] reported similar results between Müller muscle conjunctival resection (MMCR) via the conjunctival approach and levator surgery using the anterior approach. Another retrospective study found that MMCR had a lower revision rate and better cosmetic outcomes.[46] However, in patients who have undergone glaucoma surgery with a filtration bleb, the primary goal should be functional improvement (enhancing vision) without compromising bleb function.[7] In their retrospective study, Putthirangsiwong et al.[47] reported a 10.3% rate of bleb failure following MMCR in patients with ptosis after glaucoma filtration surgery.

Eyelid Retraction

Upper eyelid retraction is less common than blepharoptosis after trabeculectomy.[48,49,50] Thyroid orbitopathy should be ruled

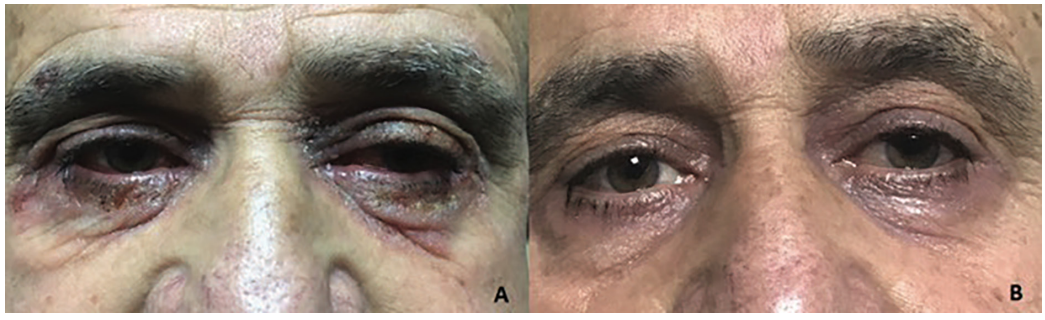

Figure 4. A patient referred from another center who had tried nearly all available topical drops and had drug allergies and minimal ectropion (A) showed improvement in allergic conjunctivitis, ectropion, and contact dermatitis after discontinuing the medications (B). Trabeculectomy was performed on both eyes of this patient

Figure 5. An 18-year-old female patient with secondary glaucoma due to aphakia had an Ahmed glaucoma valve implanted and exhibited ptosis in her left eye during the early postoperative period (A). In these patients, it is necessary to wait at least 6 months before considering ptosis surgery. At the patient's 6-month postoperative follow-up, the ptosis was observed to have resolved (B)

out as a potential cause. Müller muscle surgery via a posterior approach is generally not preferred after trabeculectomy, because it can compromise bleb function. Therefore, Shue et al.[49] and Awwad et al.[50] have recommended preserving the conjunctiva during levator and Müller muscle surgery to minimize bleb-related risks. Eyelid retraction can occur over diffuse and large blebs (Figure 7). Treatment options for upper eyelid retraction include:

• Manual eyelid adjustment: relaxing the eyelid by pulling it down over the bleb.[48]

• Surgical approaches: performing levator and Müller muscle surgery using either an anterior or posterior approach.[48,51]

• Hyaluronic acid gel: filling the upper eyelid to provide temporary relief.[48]

• Botulinum toxin A injection: to induce therapeutic ptosis.[51]

Glaucoma Drainage Device-Related Lacrimal Gland Changes

In cases where a GDD is placed in the upper temporal region, the lacrimal gland is often near the device. This proximity was reported to cause posterior displacement of the lacrimal gland in 69% of patients (9 out of 13) and flattening of the gland in 57.1% of patients (7 out of 13).[52] However, no significant correlation has been found between changes in the lacrimal gland and clinical symptoms of dry eye.

Gobeka et al.[53] observed that the lacrimal gland volume in the eye with a GDD was lower compared to the other eye, whereas trabeculectomy-treated eyes exhibited higher lacrimal gland volume.

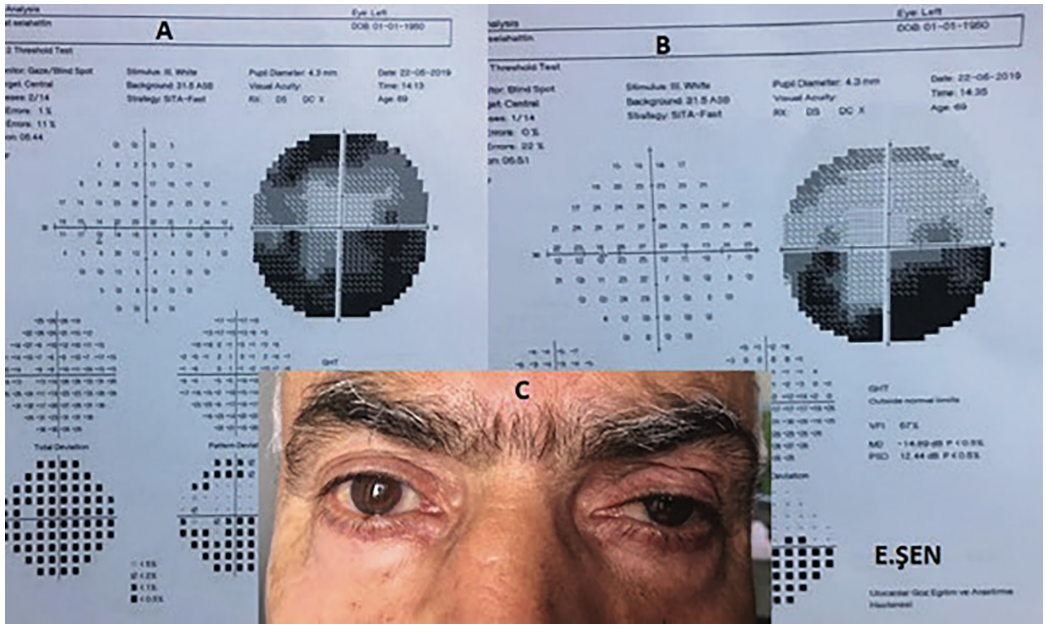

Figure 6. In a glaucoma case with a visual field defect in the inferior hemifield, if there is a defect in the upper visual field due to ptosis (A) and lifting the upper eyelid without pressing on the eyeball corrects the defect when the visual field is retested (B), the patient would benefit from ptosis surgery. The preoperative image of the patient can be seen in panel (C)

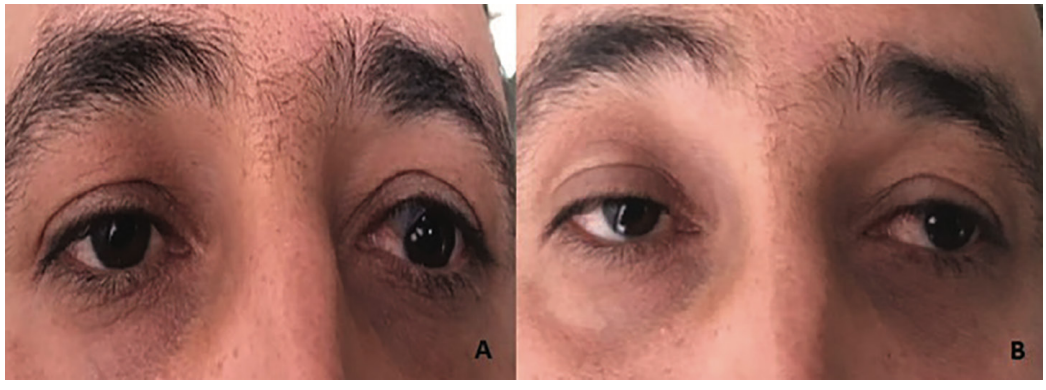

Figure 7. A 45-year-old male patient who underwent trabeculectomy in the left eye exhibits eyelid retraction that is more pronounced when looking down and to the left (A). A diffuse, large, cystic bleb located in the upper nasal area of the left eye is causing mechanical eyelid retraction (B). Surgical correction was not considered because the patient did not have dry eye or lagophthalmos

Glaucoma Drainage Device Exposure

One of the most important complications of GDDs is the erosion of conjunctival tissue over the tube or device plate, often due to insufficient or improper coverage, which leads to exposure over time.[4,5] Examples are shown in Figure 8 and Figure 9. This extrusion can occur immediately after surgery and may lead to serious complications, such as orbital cellulitis and endophthalmitis.[5,6] The Tenon advancement and duplication technique described by Tamçelik et al.[54] was developed to prevent GDD exposure. When used in combination with either a short scleral tunnel (as initially described by the authors[54]) or a long scleral tunnel[55] or scleral flap,[56] the risk of exposure can be reduced. The scleral tunnel technique has been reported to result in a lower risk of exposure compared to the scleral flap in patients with implanted GDDs.[57] Additionally, a variety of graft materials such as pericardium, fascia lata, lyophilized sclera, dura mater, amniotic membrane, and cornea are being used to avoid GDD exposure.[5]

Phthisis Bulbi/Enophthalmos

During glaucoma treatment, complications that occur after cataract or glaucoma surgery can lead to vision loss and phthisis development (Figure 10).

Evisceration and Prosthesis Requirement

Despite trying all available treatments, if high IOP cannot be controlled and in cases of painful blind eye, evisceration and the use of a mobile prosthesis may be necessary (Figure 11). In these patients, the priority is often to alleviate pain rather than address aesthetic concerns.

Acute Angle-Closure Glaucoma After Some Oculoplastic Surgeries

Another point that should be emphasized is the glaucomatous conditions that develop after some oculoplastic surgeries. Acute angle closure has been reported in the literature after blepharoplasty and fascial lifting surgery.[58,59,60] Koçer and Sen[61] reported that static and dynamic pupil measurements may change following blepharoplasty and the risk factors of angle closure should be monitored before and after oculoplastic surgeries. Although the specific factor responsible for pupil dilation -be it anxiety, pain, or pharmacological influences- remains unclear, their study has conclusively shown that pupil dilation increases following blepharoplasty. This dilation is recognized as a significant risk factor for angle closure after oculoplastic surgeries. While subconjunctival and intraocular adrenaline are well-known for their mydriatic effects, temporary unilateral mydriasis can also occur following local lidocaine

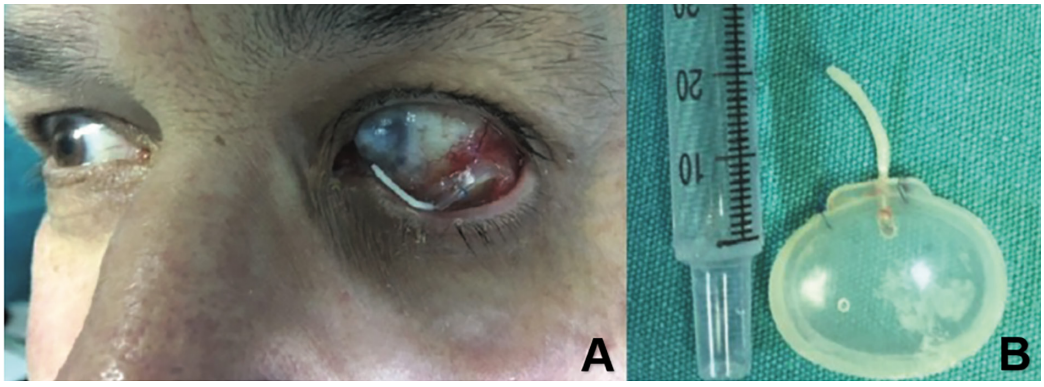

Figure 8. Exposure of a Molteno implant placed at another center (A). The implant was surgically removed (B) and the conjunctiva was primarily closed

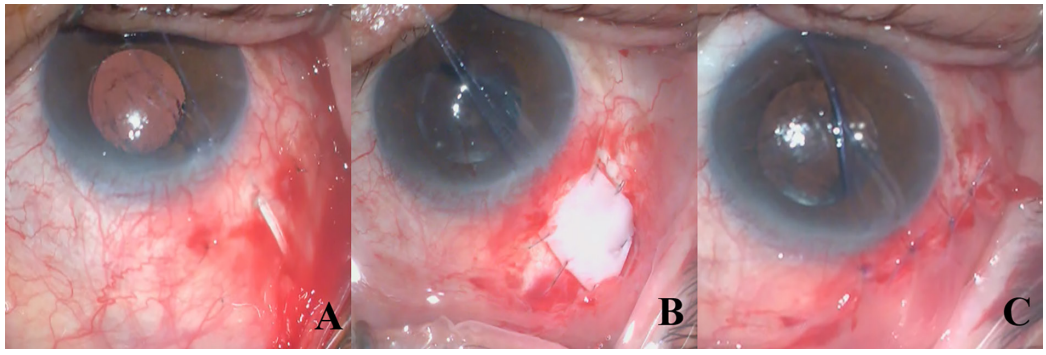

Figure 9. Ahmed glaucoma valve tube exposure through the conjunctiva (A). Lyophilized bovine pericardium was sutured to the sclera with 10/0 nylon sutures as a covering for the exposed area (B). The conjunctiva was primarily closed (C)

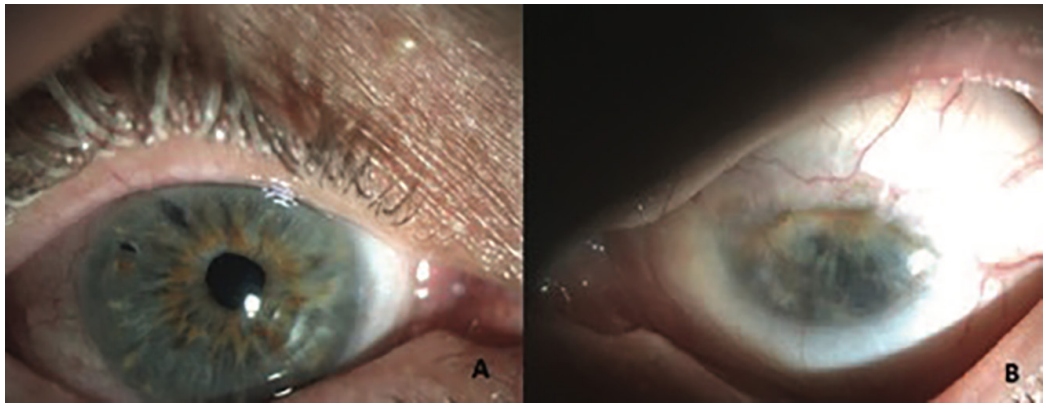

Figure 10. A 72-year-old male patient with angle-closure glaucoma developed phthisis bulbi in the left eye following cataract surgery complicated by expulsive hemorrhage (B). He underwent phacoemulsification with intraocular lens implantation in the right eye (A)

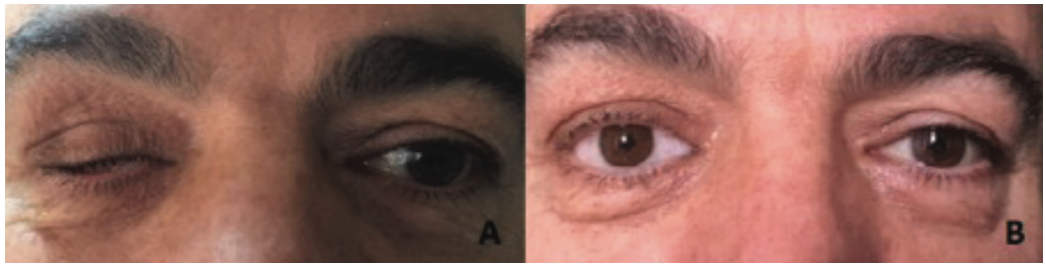

Figure 11. A 59-year-old male patient experienced a right glaucoma crisis, central retinal vein occlusion, and neovascular glaucoma in 2002 and underwent evisceration due to a painful blind eye in 2010. The photo following evisceration (A) shows the right eye prosthesis and the left eye with primary open-angle glaucoma (B)

and adrenaline injections into the eyelid. Furthermore, surgical factors such as emotional stress during the procedure and postoperative eye closure may also contribute to the induction of mydriasis.[61]

Appropriate Treatment for Glaucoma Patients with Preexisting Oculoplastic Conditions

Apart from oculoplastic complications arising from glaucoma treatment, the meticulous selection of appropriate treatment for patients with preexisting oculoplastic conditions is equally important. For instance, when planning blepharoplasty or ptosis surgery, it is essential to determine whether the patient is using PgA. Detecting PAP may be easier in patients using PgA in only one eye, but close monitoring is necessary in those using PgA bilaterally.[8] Age-related periorbital volume loss and PgA-associated lipoatrophy should also be considered when planning blepharoplasty. As orbital lipoatrophy may progress with continued PgA treatment, preserving the fat pads and adopting a conservative approach with minimal skin excision is advised to reduce the risk of postoperative lid retraction and lagophthalmos. Otherwise, the eyes may appear deep-set.[7,8]

Another important consideration for oculoplastic surgeons is the presence of coexisting glaucoma in cases of eyelid malposition. The frequency of glaucoma and eyelid malpositions such as entropion and ectropion increase with aging. Therefore, distinguishing whether lid changes in these patients are due to age-related involutional mechanisms or the medications they are using is crucial in managing the patient's treatment.[39] Additionally, in these patients, the mechanical effect of chronic eye drop use can further exacerbate horizontal and vertical lid laxity, in addition to the involutional changes in the eyelid. Another side effect that may develop is epiphora, which can lead to skin disorders from constant wiping of the eyelid and, over time, to skin scarring. Raising awareness of these side effects in lid malposition allows for early discontinuation of medications. However, if glaucoma coexists with ectropion, an oculoplastic surgeon may overlook this effect, and if surgery is performed while continuing the topical drops, surgical failure and recurrence are inevitable.[8] Topical antiglaucoma medications should be discontinued, inflammation should be controlled with low-potency steroid drops, and IOP should be managed with oral acetazolamide. In patients with significant allergic symptoms and itching, oral antihistamines may need to be added. It should also be kept in mind that trabeculectomy may be required in these patients.[8] In patients with entropion accompanied by glaucoma, particularly with the use of preservative-containing eye drops, corneal exposure may increase. This necessitates prompt and appropriate entropion surgery to prevent potential issues with adherence to glaucoma treatment.

Punctal obstruction was found to be more common in patients using dorzolamide/timolol fixed combination, as discussed in the relevant section.[34,35] Conversely, it would be reasonable to recommend avoiding these medications in patients

who develop punctal obstruction for any reason and undergo surgery. Additionally, the presence of a cystic avascular bleb resulting from previous trabeculectomy surgery with the use of antimetabolites in a patient with nasolacrimal duct obstruction and/or lacrimal sac abscess increases the risk of blebitis and endophthalmitis.

Conclusion

Oculoplastic issues in glaucoma patients can arise as secondary problems related to both medical and surgical treatments. These include:

Medical treatment issues: PAP, punctum and canaliculus problems, and ectropion from topical antiglaucoma medications.

Surgical treatment issues: Ptosis of the upper eyelid, eyelid retraction, GDD-related lacrimal gland changes, GDD exposure, enophthalmos, and secondary evisceration.

These complications require a more specific and careful evaluation compared to other patients. Awareness of these iatrogenic oculoplastic problems and careful management considering their risk factors is crucial. Understanding that glaucoma patients face unique and significant surgical challenges compared to other oculoplastic patients can lead to better functional and aesthetic outcomes. In this special patient group, it is essential to perform surgery without compromising the function of a trabeculectomy bleb and to be mindful of the risks of blebitis and endophthalmitis in the presence of a cystic bleb. When an oculoplastic problem arises in a glaucoma patient, it is important to remember that from the perspective of the glaucoma specialist, it may be necessary to revise the patient's treatment by discontinuing or changing their current medication. From the oculoplastic specialist's perspective, it is essential to approach the patient with this awareness before proceeding with surgical treatment.

Ethics

Informed Consent: Obtained.

Declarations

Authorship Contributions

Surgical and Medical Practices: E.Ş., S.B., Concept: E.Ş., S.B., Design: S.B., K.S.C., Data Collection or Processing: E.Ş., S.B., Analysis or Interpretation: E.Ş., S.B., K.S.C., Literature Search: S.B., K.S.C., Writing: S.B., K.S.C.

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