

# Acute Attack of Glaucoma after Scleral Melting and Iris Blockage of the Surgical Ostium: A Case Report of a Complication Derived from a Mitomycin C Supplemented Trabeculectomy

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## ABSTRACT

**Aim:** To describe a case of an acute attack of glaucoma due to scleral melting in the area where a trabeculectomy was previously done. This condition resulted from the blockage of the surgical opening due to an iris prolapse in an eye that was previously supplemented with mitomycin C (MMC) during a filtering surgery and bleb needling revision.

**Case description:** A 74-year-old Mexican female with a prior glaucoma diagnosis who assisted to an appointment presenting an acute ocular hypertensive crisis after several months of adequately controlled intraocular pressure (IOP). Ocular hypertension had been regulated after undergoing a trabeculectomy and bleb needling revision; both supplemented with MMC. The severe IOP increase occurred due to uveal tissue blockage in the filtering site, related to melting of the sclera in the same area. The patient was successfully treated through the use of a scleral patch graft and the implantation of an Ahmed valve.

**Conclusion:** An acute attack of glaucoma associated with scleromalacia after trabeculectomy and needling has not been previously reported and is currently attributed to MMC supplementation. Nevertheless, the use of a scleral patch graft and further glaucoma surgery seems to be an efficient way to treat this condition.

**Clinical significance:** Even though this complication was appropriately managed with this patient, we want to prevent further cases like this through the judicious and careful use of MMC.

**Keywords:** Bleb, Filtering surgery, Mitomycin C, Sclera, Trabeculectomy.

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## INTRODUCTION

Trabeculectomy is the most common surgical treatment of glaucoma<sup>1,2</sup> since it was first described at the end of the 1960s.<sup>3,4</sup> However, this method has had several technical modifications, one of the most important being the perioperative application of anti-scarring therapy.<sup>5</sup> 5-Fluorouracil and MMC have been used for the last decades to prolong the control of IOP through their antifibrotic actions, which modulate scarring after surgical intervention, mainly in the conjunctiva and the scleral flap.<sup>6–8</sup>

Mitomycin C is an antibiotic with antineoplastic properties, which was obtained through the isolation of the bacteria *Streptomyces caespitosus*, and inhibits DNA synthesis through the generation of oxygen radicals and alkylation. In high concentrations, MMC also inhibits RNA and protein synthesis as it acts upon the entire cellular cycle, mainly in phases G1 and S.<sup>9</sup> Histopathologic studies have demonstrated its antifibrotic effect, which includes the inhibition of fibroblast migration and the reduction of collagen synthesis.<sup>9,10</sup> Further research has addressed ocular surface changes that occur during the application of MMC in a trabeculectomy, such as the development of a slowly increasing filtration of aqueous humor, microcysts, hypocoelularity, avascularity, epithelial thinning, reduction of goblet cell density, and reduction of fibroblast activity.<sup>10</sup>

A 2016 survey reported that antifibrotics were being used in 93–99% of trabeculectomies, and 63–97% of those cases specifically used MMC.<sup>2</sup> Despite the favorable anti-scarring effect

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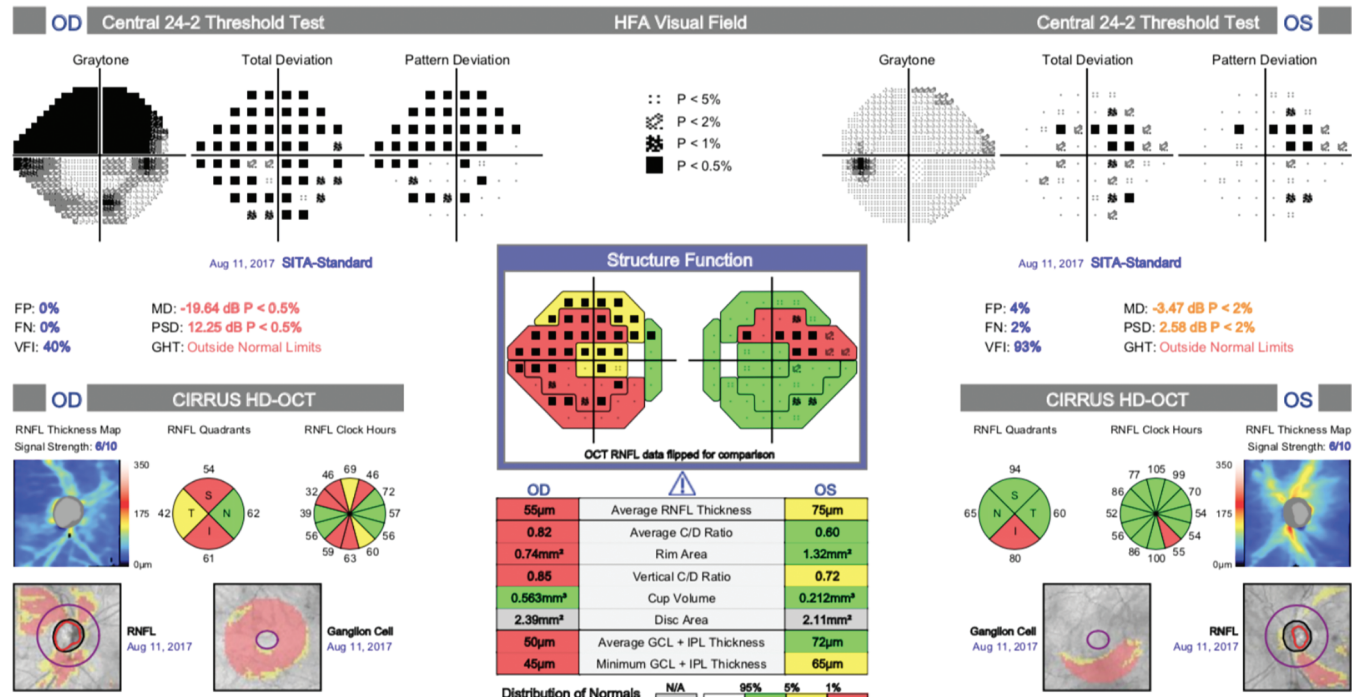
of MMC in glaucoma surgery, a variety of complications have been described;<sup>11–13</sup> however, scleral thinning is rarely reported<sup>14–16</sup> and no report of an acute attack of glaucoma associated with a melted sclera has been found.

In the following section, a case of scleromalacia associated with the use of MMC in a trabeculectomy and bleb needling is described. These procedures later evolved into a hypertensive IOP crisis due to a prolapse of the iris, which in turn blocked the surgical ostium.

**CASE DESCRIPTION**

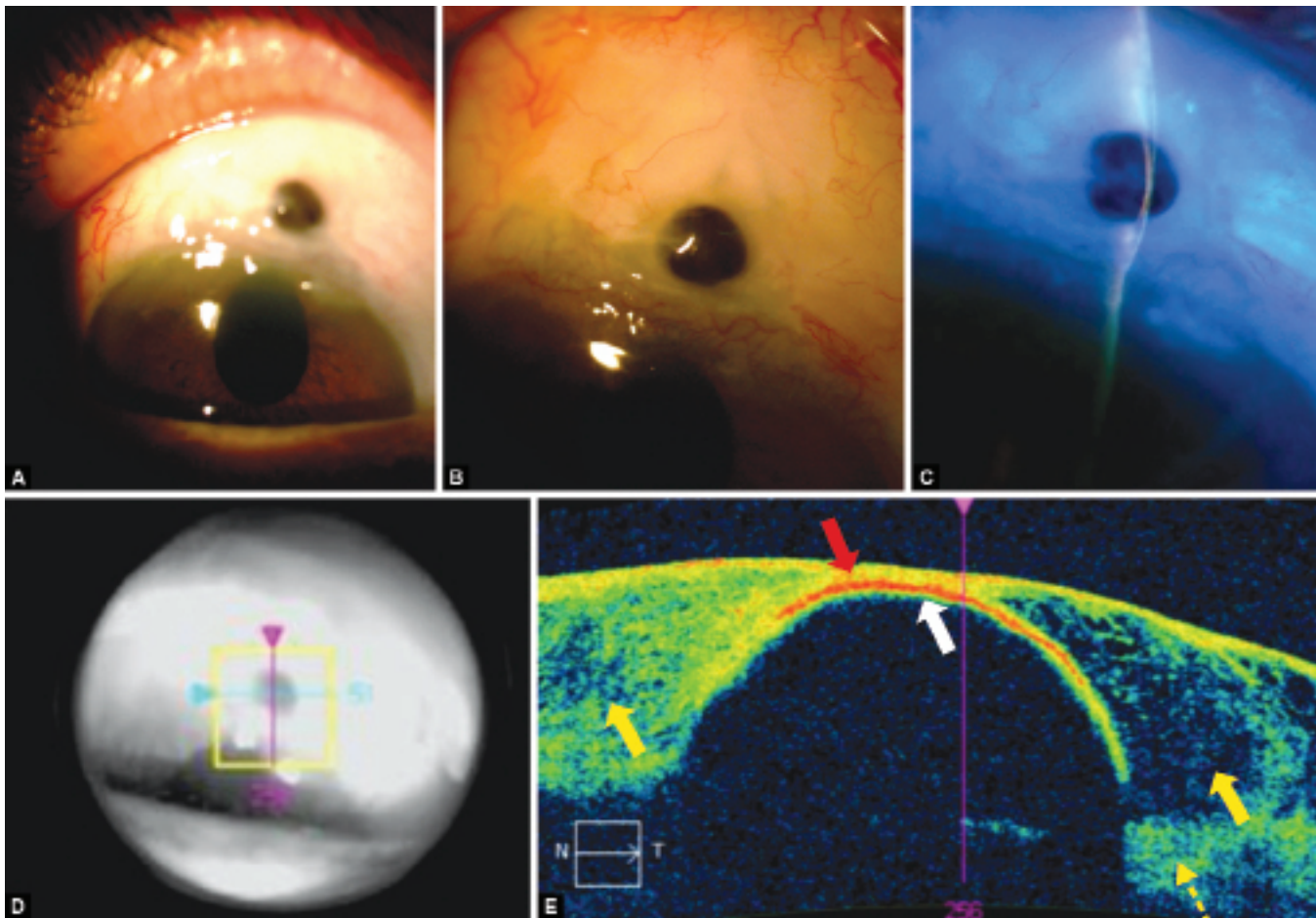
The personal information of the patient was kept confidential, and a written authorization was obtained from her for this case report in which we adhered to the CARE guidelines.<sup>17</sup> A 74-year-old Mexican female with no associated systemic diseases and with an asymmetric primary angle-closure glaucoma diagnosis (Fig. 1) had received topical antiglaucomatous treatment for at least 4 years and was evaluated and medically treated in a glaucoma clinic. Her best corrected visual acuity (BCVA) was 20/20 in both eyes. Her left eye was pseudophakic, and IOP was controlled (<15 mm Hg) without antiglaucoma treatment, having minor damage due to glaucoma. When the patient developed a nonspecific allergy to topical ocular hypotensive agents that were used in the right eye (OD), she required a phaco-trabeculectomy (with a fornix-based conjunctival dissection) with intraocular lens implantation (eye with severe damage due to glaucoma). During the surgery, MMC was supplemented through a subtenonian injection of 0.12 mL that consisted of a mixed formulation of lidocaine with epinephrine and MMC (0.25 mg/mL as a final dose of MMC). This injection was done 8–10 mm from the surgical limbus before the conjunctival peritomy. In addition, a dose of MMC was administered through cellulose sponges soaked with MMC (prepared at 0.25 mg/mL), which were kept in the subconjunctival space for 3 minutes. There were no postoperative complications with an adequate-looking filtering bleb until it started failing due to scarring after 8 months of the surgery. Due to this issue, the patient had to further undergo bleb needling supplemented with MMC (0.12 mL of MMC prepared at 0.25 mg/mL after a dilution in lidocaine with epinephrine) after the trabeculectomy. Following this procedure, IOP was adequately controlled, and the filtering bleb had a satisfactory aspect, classifying it with a score of 10/12 on the Würzburg scale.

22 months after the surgery, the patient had an abrupt episode of intense ocular pain in the OD without any relevant cause. The patient had an IOP of 62 mm Hg in the OD, which decreased to 48 mm Hg in the following 8 hours with the use of acetazolamide (125 mg TID, orally). This eye presented a moderately formed, hypovascular filtering bleb, thinning of the scleral flap, and iris tissue prolapse in the limbus (Fig. 2). The anterior chamber was found to be wide, with extensive synechial angle-closure, and without any sign of inflammation, while the posterior chamber had a previously implanted intraocular lens. The eye fundus did not present any other pathology besides the corresponding glaucomatous one observed in the optic nerve. It was identified that the patient had an acute ocular hypertension crisis in the OD due to blockage of the filtering ostium by iridian tissue, which was associated with melting of the sclera. This complication was attributed to the perioperative use of MMC. The hypotensive therapy was reinforced with a topical combination of timolol, dorzolamide, and brimonidine, BID. Furthermore, the dosage of acetazolamide was increased to 250 mg QID per mouth. The day after establishing this regimen, the IOP was 11 mm Hg; however, the patient started showing clinical manifestations of allergy. Therefore, the topical antiglaucoma treatment was interrupted, and she was immediately scheduled for surgery. The patient underwent a combined surgical procedure, which consisted of the removal of the conjunctiva that formed the filtering bleb, as well as the uveal tissue trapped in the melted sclera. This was followed by the placement of a scleral patch graft (Fig. 3) and a conjunctivoplasty to cover the scleral patch. In order to prevent deregulation of the IOP, there was implantation of an Ahmed valve supplemented with MMC in the temporal-inferior quadrant. The surgery proceeded without complications. Twenty-four hours after the surgery, the patient had a pinhole visual acuity of 20/400 in the operated eye,



**Fig. 1:** In the combined report of functional and structural tests, a severe perimetric condition predominantly affecting the superior region of the OD is identified. In addition, there is a scotoma of relatively smaller size in the superior hemifield of the left eye (OS). The tomographic findings highlight severe and generalized thinning of the nerve fiber layer of the OD retina, as well as moderate thinning of the inferior region of the OS. Moreover, there is an asymmetrical alteration of the ganglion cell layer





**Figs 2A to E:** OD anterior segment photographs. (A) Formed anterior chamber, pupil dyscoria with an iridian tissue protrusion along the dissolved region of the scleral flap; (B) Zoomed image of the defect in the limbus region of the scleral flap and the iridian tissue protrusion; (C) Slit lamp photograph showing the uveal tissue covered by the conjunctiva without aqueous humor drainage; (D and E) High resolution OCT image of the filtering bleb in the conjunctival wall (red arrow) and in contact with the iridian tissue (white arrow). This image also shows multiple subconjunctival cystic spaces of the filtering bleb with leftover aqueous humor (yellow arrow) and the sclera adjacent to the melted area (yellow dashed arrow)

and the IOP was 16 mm Hg. There was a gradual amelioration of the visual function in the following visits, with an adequately controlled IOP (10–14 mm Hg) and an improved aspect of the ocular surface tissues. Six months after the surgery, the BCVA was 20/20 in both eyes, and IOP was 12 mm Hg in the OD and 14 mm Hg in the OS. The scleral patch graft was correctly integrated and covered by a slightly hyperemic conjunctiva. In addition, the valve plate was well covered, the bleb was moderately formed, and the valve tube was well positioned without touching the cornea or the iris (Fig. 4). Currently, after 10 months of the aforementioned complication, the patient is under observation, meeting the target IOP in both eyes, without the need for hypotensive topical treatment and without showing any further damage due to glaucoma despite the described ocular hypertensive crisis (Fig. 1).

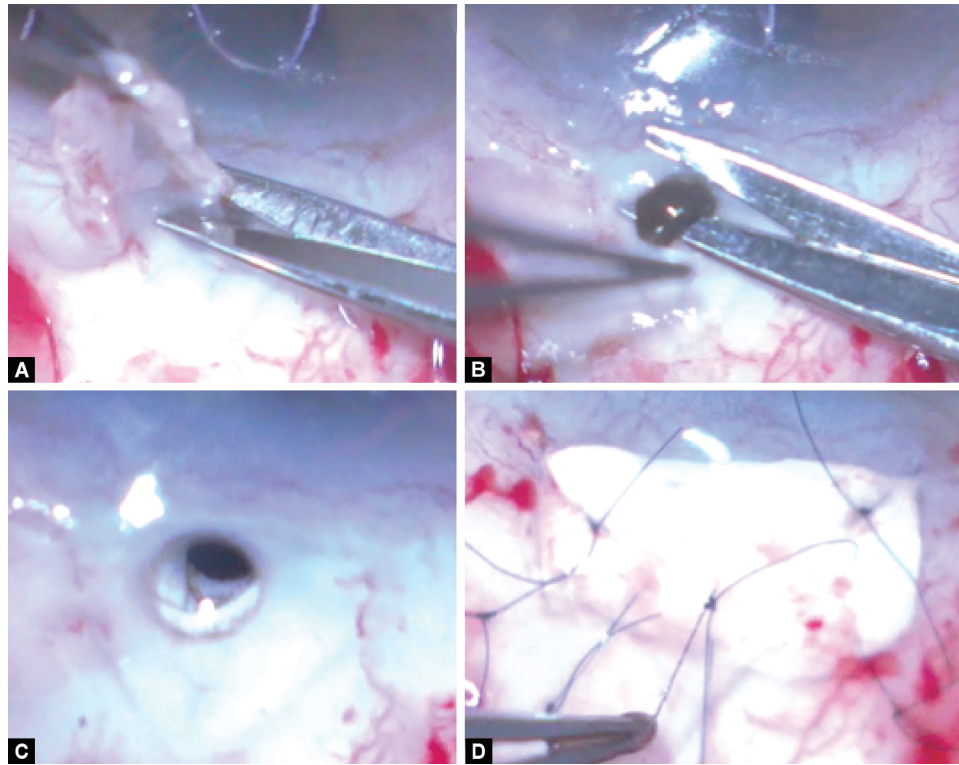
## DISCUSSION

Although the use of MMC has been part of the success of trabeculectomy as a surgical procedure, its use has involved complications such as hypotony, blebitis, escape of aqueous humor through the filtering bleb, endophthalmitis, chronic discomfort, and more.<sup>11–13</sup> And although the complete spectrum of scleral thinning that results from the use of MMC have been widely described in relation to pterygium surgery,<sup>18–25</sup> there are only two reported

cases of scleromalacia resulting from filtering surgery,<sup>15,16</sup> and one more case in a cohort of patients undergoing trabeculectomy to treat refractory glaucoma.<sup>14</sup> These three cases coincide with the intraoperative use of MMC.

The first clinical report of scleral thinning caused by an MMC-supplemented trabeculectomy was published by Mermoud et al.<sup>14</sup> This was a prospective, comparative, and nonrandomized study of 60 eyes of black individuals with refractory glaucoma. All of the included eyes underwent trabeculectomy with limbal-based conjunctival dissection. Thirty of these eyes received a transoperative dosage of MMC in subconjunctival sponges at 0.2 mg for 5 minutes, while there was no antimetabolite used in the other thirty eyes. One of the eyes that received MMC developed scleral thinning 6 months after the surgery; no further demographic information, description of a concurrent visual condition or any other issues were included. In another study, Akova et al.<sup>15</sup> described two pediatric cases that presented significant scleral thinning in one eye, 12 and 15 months after trabeculectomy supplemented with MMC. Both individuals had aphakic eyes that had suffered intense ocular trauma before glaucoma surgery and had a history of limbus-based conjunctival dissection. During surgery, MMC was used at a dosage of 0.4 mg/mL with an exposure time of 5 minutes. Both patients showed constant scleral thinning in the 6 and 24 months follow-ups and required





**Figs 3A to D:** Transoperative photographs. (A) Resection of the avascular filtering bleb; (B) Resection of the iridian tissue; (C) Circular scleral defect with protrusion caused by the viscoelastic used to maintain the shape of the anterior chamber; (D) Scleral patch graft sutured with nylon 10-0 (before trimming sutures)

subsequent glaucoma surgery due to the failure of the previous trabeculectomy. In another report, Coutinho et al.<sup>16</sup> published a case of scleromalacia of the scleral flap of a 22-year-old patient with juvenile glaucoma. The patient presented ocular hypotony 2 years after undergoing trabeculectomy with MMC (0.4 mg/mL for 3 minutes) and fornix-based conjunctival dissection. They documented the melting of the scleral flap 24 months after the surgery, which led to the development of hypotonous maculopathy related to the leakage of aqueous humor. This issue was repaired with a bovine pericardial patch that occluded the fistula, therefore normalizing the IOP and visual function.

In comparison to the cases that have been previously described, our patient had advanced glaucoma and showed signs of allergy to several antiglaucoma medications and long-term ocular hypotonics. Based on these allergic reactions, we decided to do a double supplementation of MMC. Application of the antifibrotic consisted of sponges with a relatively low dosage (0.25 mg/mL) and a moderate exposure time (3 minutes). However, the coadjuvant subtenonian injection of 0.12 mL of MMC (0.25 mg/mL), in addition to the bleb needling that was also supplemented with MMC, could have increased the risk of a potentially ischemic effect (even though the bleb was hypervascular instead of avascular) and MMC-induced apoptosis.<sup>26</sup> It is possible that led to another local inflammatory phenomenon since the patient is not a carrier of any systemic diseases, as well as further focal thinning and melting of the scleral tissue in the limbus portion of the flap. Interestingly, a decade ago, Errico et al.<sup>27</sup> reported a double dosage of MMC in a study that included 43 cases, which received the first administration of MMC at 0.1% in the subtenonian space with an exposure time of 3 minutes, and 1–2 minutes under the scleral flap. They had a 93% success rate after a 2 years follow-up. This justifies the exploration of

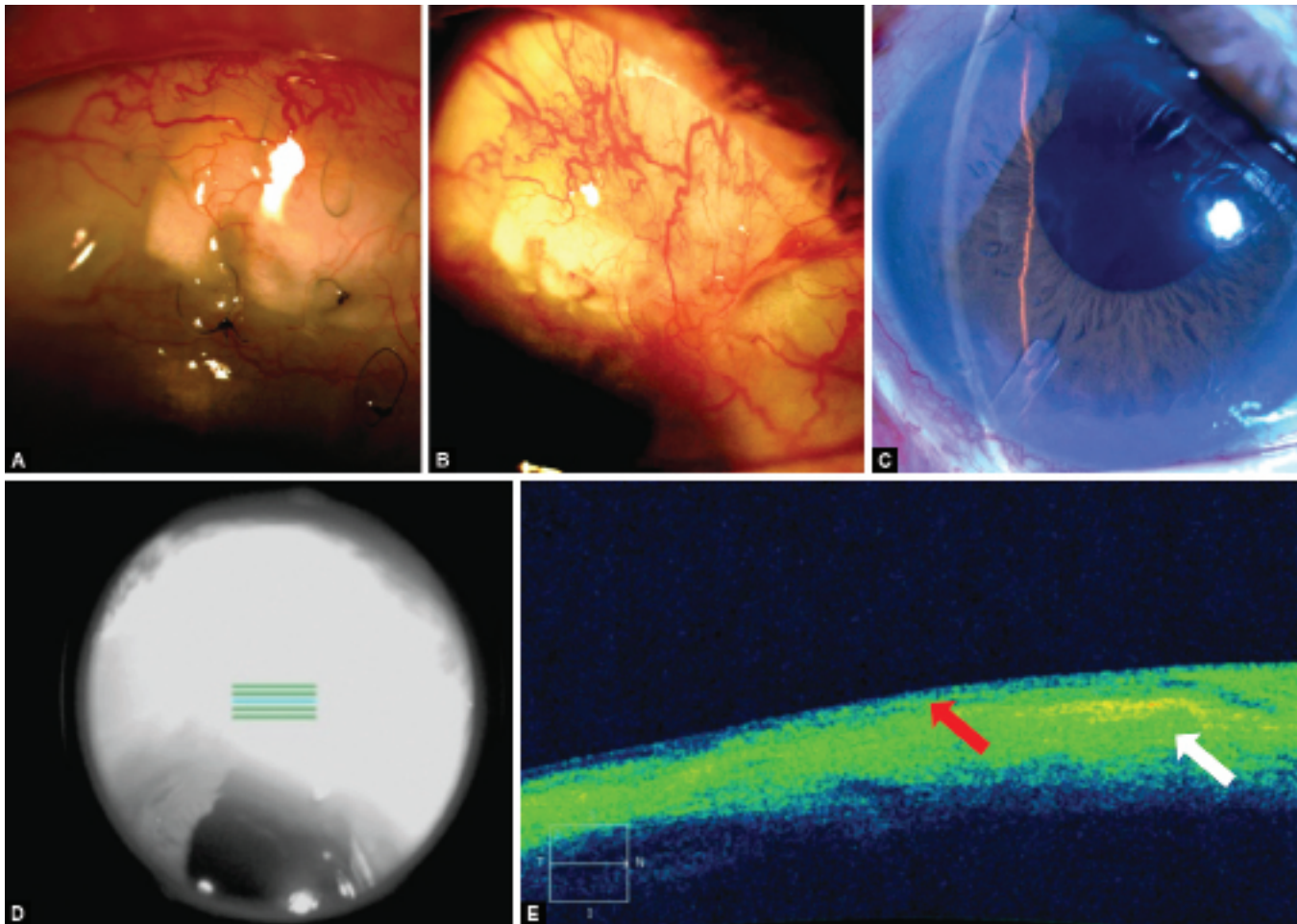
additional supplementations of MMC to potentiate the anti-scarring effect in cases of high risk of failure. Nevertheless, confirmation of its efficacy and valoration through prospective and controlled studies is required. Similarly, MMC supplementation in bleb needling, as in our case report, is a technique that has had empirical and scientific evidence in relations to its efficiency and safety.<sup>28</sup>

In the context of MMC applied during the transoperative period, it has been difficult to establish an optimal balance between the dosage and exposure time of sponges with MMC.<sup>29,30</sup> There is a constant development of issues despite the administration of lower doses of MMC (0.1 mg/mL) or the way in which the antimetabolite is administered.<sup>31,32</sup>

Furthermore, for cases such as the one we presented in this report, the tissues that have been used for the scleromalacia reconstruction are cornea, sclera, cartilage, bone, and dura mater.<sup>25</sup> It was also defined that the patient presented a unique complication, an ocular hypertensive crisis due to the mechanical blockage of the surgical ostium, which required the removal of iris tissue to prevent a recurrent blockage. As mentioned above, the melted area was reconstructed with donated scleral tissue, which is usually adhered to corneal tissue for transplant, therefore making it commonly available. In addition, the patch was a compatible solution for this case because of its human origin and its adequate tensile strength that maintains the anatomy and functionality of the region.<sup>33</sup>

The decision to implant an Ahmed valve during the same surgery in which the scleral patch was placed was based on glaucoma-related effects occurring on the OD, as well as the possibility of completely eliminating the filtrating function with the scleral patch. In general, we prefer to use MMC through a subtenonian injection, combined with supplementation through subconjunctival sponges, while





**Figs 4A to E:** OD anterior segment images taken 6 months after the surgical procedure. (A) Scleral patch covered by conjunctiva with remaining sutures; (B) A certain degree of conjunctival hyperemia is observed after removal of sutures; (C) Inferotemporal valve tube in the anterior chamber, far from the cornea; (D and E) OCT image of the scleral patch with high definition horizontal imaging sections showing the conjunctival wall (red arrow) and the already-incorporated scleral patch (white arrow)

preparing the drainage device to be collocated. Despite the scientific evidence that supports this method,<sup>34</sup> there have been another two clinical randomized studies that used low dosages and low exposure time to MMC,<sup>35,36</sup> demonstrating no noticeable effect when MMC was supplemented in that specific manner, and an Ahmed valve was also inserted. Similarly, our routine MMC supplementation in glaucoma surgeries leads to encouraging results in terms of IOP stability and safety parameters. And in this specific case, although we considered that there was not a formal contraindication for the use of MMC due to the lack of systemic diseases and active local inflammation, as well as the fact that the application of MMC for the implantation of the Ahmed valve would have been in the opposite location of the region where the focal scleral alteration occurred, it is possible that the double supplementation of this antimetabolite played a role in the development of scleromalacia.

## CONCLUSION

It can be said that scleromalacia is a rare complication despite the extended use of antimetabolites, in particular, MMC. In this manuscript, we report the first case of scleral melting and iridian blockage of the surgical ostium, presented as an acute

attack of glaucoma as an intermediate-term complication of MMC-supplemented trabeculectomy and subsequent MMC-supplemented bleb needling. Even though this complication was appropriately managed with this patient, we want to prevent further cases like this through the judicious and careful use of MMC, especially in cases that could be susceptible to inflammation or scleral weakening. It is recommended to have periodic and systematic postoperative monitoring of an MMC-supplemented trabeculectomy, and it is crucial to pay special attention to the tissues adjacent to the filtering bleb.

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