

# Corneal lamellar grafting to repair late complications of mitomycin C trabeculectomy

Takeo Fukuchi  
Hidenobu Matsuda  
Jun Ueda  
Akiko Yamada  
Kieko Suda  
Haruki Abe

Division of Ophthalmology and  
Visual Science, Graduated School of  
Medical and Dental Sciences, Niigata  
University, Niigata, Japan

**Purpose:** To report corneal lamellar grafting to repair the late-onset complications after MMC trabeculectomy.

**Methods:** Multiple case reports.

**Results:** A 76-year-old male with primary open-angle glaucoma (POAG) and a 55-year-old male with late developmental glaucoma complicated by bleb leaks from a microhole 10 and eight years after surgery, respectively. Severe ciliochoroidal detachment and a shallow anterior chamber were persistent in one case and bleb-related infection recurred in another. Additionally, a 46-year-old male with POAG had hypotony maculopathy with a giant ischemic bleb 18 months after surgery. Although these patients were quite resistant to medical and surgical treatments, they were successfully treated by corneal lamellar grafting without complications.

**Conclusions:** Tectonic corneal lamellar grafting is a reliable and final surgical method to improve severe cases of hypotony maculopathy or bleb leak after mitomycin C trabeculectomy.

**Keywords:** mitomycin C, trabeculectomy, postoperative complications, hypotony maculopathy, bleb leak, corneal lamellar grafting

## Introduction

Mitomycin C (MMC) trabeculectomy is still used worldwide as a convenient and effective method to reduce intraocular pressure (IOP) in glaucomatous eyes that cannot be controlled with maximum tolerated doses of medications.<sup>1-7</sup> Soon after Chen<sup>1</sup> introduced MMC as an adjunctive agent during trabeculectomy, cases of hypotony associated with a shallow-to-flat anterior chamber or ciliochoroidal detachment were often seen because of the strong antifibroblastic effect of MMC.<sup>8-10</sup> Once such complications occurred, they tended to persist for long periods. MMC trabeculectomy with laser suture lysis<sup>11-13</sup> or non-penetrating filtering surgery<sup>14,15</sup> were recommended to decrease postoperative complications related to hypotony in the early phase. Although these reliable modifications greatly reduced the occurrence of hypotony maculopathy, this complication still occurs. In addition, late-onset hypotony after MMC trabeculectomy often occurs with a bleb leak because of microhole formation.<sup>16-20</sup> While a bleb leak as a result of microhole formation may result in hypotony, a shallow anterior chamber, or ciliochoroidal detachment, it is thought to be related closely to blebitis or endophthalmitis as the most severe complications after MMC trabeculectomy.<sup>21,22</sup>

We treated three patients who had severe complications associated with MMC trabeculectomy with corneal lamellar grafting. Two patients had bleb leaks from a microhole and another had a rare case of slow-onset hypotony maculopathy. We present these cases and discuss corneal lamellar grafting as a reliable and final surgical

Correspondence: Takeo Fukuchi  
Division of Ophthalmology and Visual  
Science, Graduated School of Medical and  
Dental Sciences, Niigata University, I-757  
Asahimachi, Niigata 951-8510, Japan  
Tel +8125 227 2296  
Fax +8125 227 0785  
Email tfuku@med.niigata-u.ac.jp

treatment for severe hypotony or bleb leaks after MMC trabeculectomy.

## Case reports

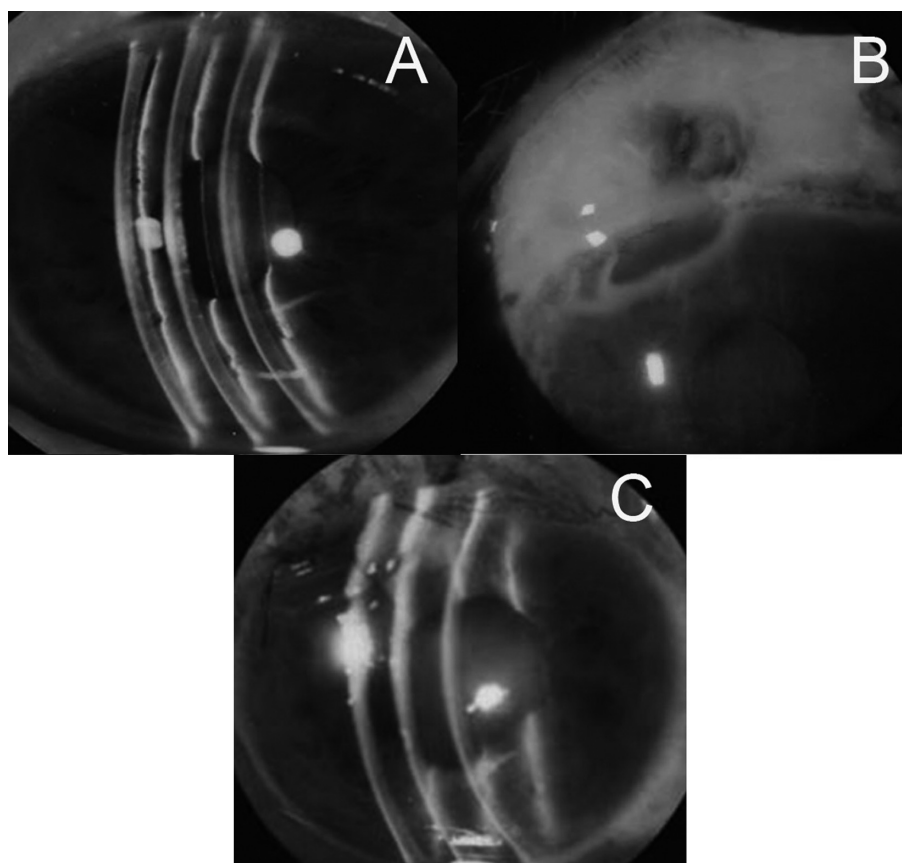
### Case 1

A 76-year-old Japanese male with POAG underwent MMC trabeculectomy in his left eye in July 1994 (at 65 years of age). The surgical method for MMC trabeculectomy was followed as previously reported.<sup>23</sup> MMC was applied at 0.02 mg/mL for five minutes. His postoperative left IOPs were kept between 9 and 12 mmHg. In December 2004, he visited our clinic complaining of left conjunctival infection and blurred vision. His left eye had associated leakage from a microhole of the bleb with Seidel's phenomenon (Figure 1A), a shallow anterior chamber of Grade 1 by Spaeth's classification<sup>24</sup> (Figure 1B), and a marked circumferential ciliochoroidal detachment.

We tried several medical and surgical treatments, including administration of an oral carbonic anhydrase inhibitor, injection of autologous blood into the bleb, and repeated bleb

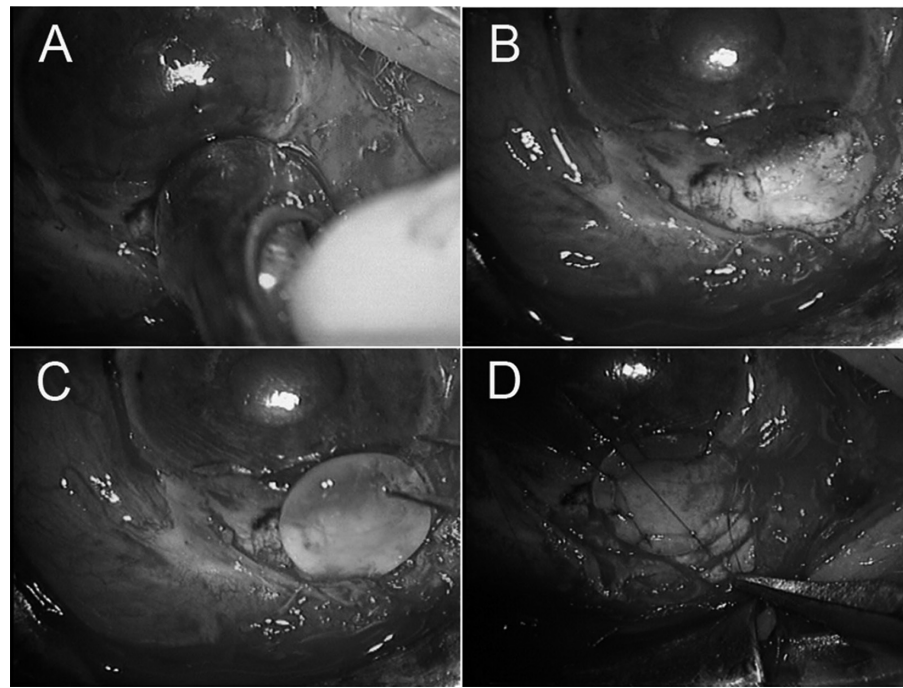
reformation with compression sutures, but they provided only temporal relief. Finally, we decided to perform corneal lamellar grafting.

After the anterior chamber formation with hyalونات and conjunctival incision, surgical debridement was performed on scarred conjunctiva and soft tissues on the sclera. Half-layered corneoscleral tissues, including the area of weakened spongy sclera, were dissected away using a corneal trephine 5.5 mm in diameter (Figure 2A). Clean, healthy edges of the dissection were regularized (Figure 2B). Then, donor corneal tissue was used to repair the corneoscleral defect. A round lamellar preserved corneal piece, 5.5 mm in diameter and 0.8 mm thick, was made using a corneal trephine. The piece was sutured exactly to the patient's cleaned-up corneoscleral area with 10-0 nylon (Figures 2C and 2D). A total of eight sutures were placed and made water tight. The conjunctiva was left free except for both edges, which were grafted and sutured with 10-0 nylon. An antibiotic, ofloxacin, and a steroid, 0.1% betamethasone, were prescribed as postoperative medications to be taken four times a day. Oral prednisolone



**Figure 1** Case 1 was complicated by a shallow anterior chamber (A) because of bleb leakage with Seidel's phenomenon (B). After corneal lamellar grafting, the anterior chamber had kept deep (C) and the IOP had also increased.

**Abbreviation:** IOP, intraocular pressure.



**Figure 2** Using a corneal trephine (5.5 mm diameter), half-layered corneoscleral tissues was dissected away (A). Clean, healthy edges of the dissection were regularized (B). Then a donor's lamellar, round, preserved corneal piece with 5.5 mm diameter and 0.8 mm thickness was placed (C) and was sutured exactly to the patient's corneoscleral area with 10-0 nylon (D).

was prescribed at 30 mg per day and then tapered off at the end of the three-week postoperative period.

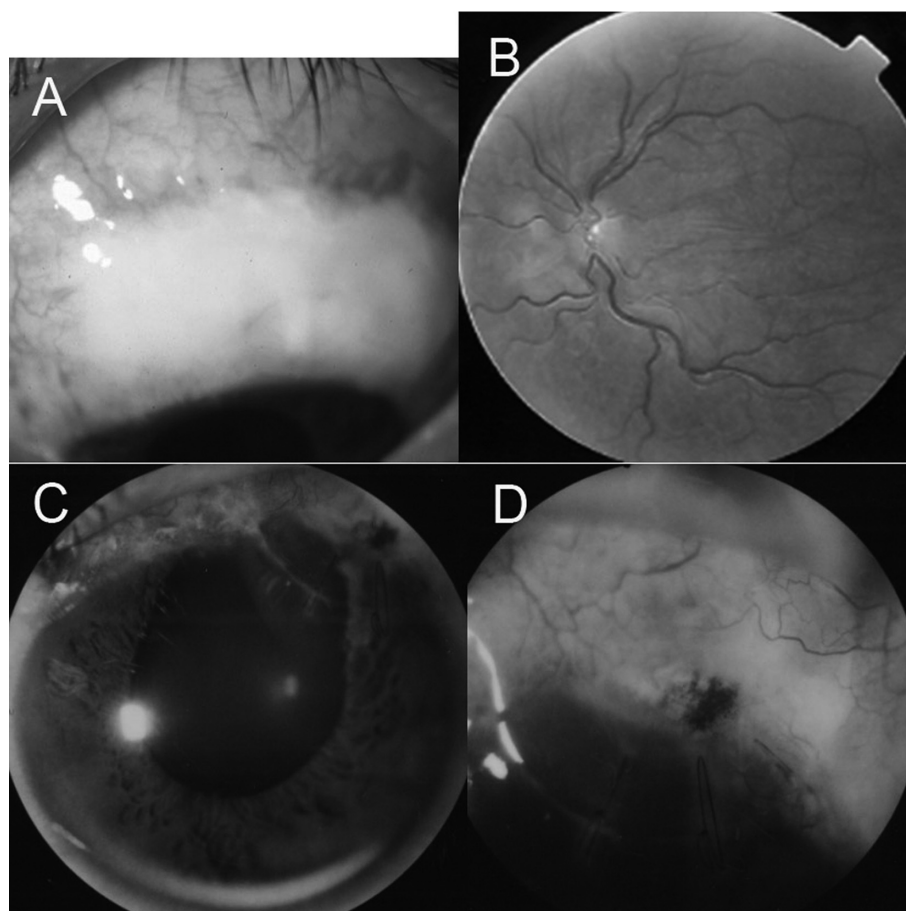
His left IOP increased to 48 mmHg on the second day. The IOPs were controlled between 15 and 18 mmHg with topical medications. The left anterior chamber remained deep without subsequent ciliochoroidal detachment.

## Case 2

A 55-year-old Japanese male diagnosed with late developmental glaucoma received MMC trabeculectomy by a procedure similar to that used in case 1 in 1992 (at 42 years of age). His left IOP was kept between 5 and 8 mmHg without medication. When blebitis with bleb leak from a microhole occurred in his left eye in December 2000, medical treatments were effective. After blebitis recurred in March 2001, the bleb resection and autologous free conjunctival patch grafting were performed after administration of an oral carbonic anhydrase inhibitor and injection of autologous blood into the bleb. In 2004, bleb leak from a microhole recurred and the IOP decreased to 5 mmHg. We performed corneal lamellar grafting using the same procedure as in case 1. After increasing to 27 mmHg on the next day, the IOPs were maintained between 10 to 13 mmHg with topical medications, and no leakage or blebitis occurred again after the surgery.

## Case 3

A 46-year-old Japanese male with POAG underwent MMC trabeculectomy in both eyes in April 1996 (at 42 years of age). The postoperative IOP decreased to 11 mmHg at three months, 7 mmHg at six months and 4 mmHg at 12 months. Finally, his left IOP was 3 mmHg with a giant ischemic bleb (Figure 3A) and typical hypotony maculopathy (Figure 3B) at 18 months post surgery. The corrected visual acuity was 20/20 at three months and 4/20 at 18 months. Although we tried several medical and surgical treatments, including oral carbonic anhydrase inhibitors, conservative injection of autologous blood, surgical compression sutures, and direct conjunctival cover, his hypotony maculopathy never improved. Finally, we performed corneal lamellar grafting following the same procedure as described for case 1 (Figures 3C and 3D) at 40 months after the initial MMC trabeculectomy. Similarly the IOP increased up to 46 mmHg on the next day, but decreased to 22 mmHg within a week with oral and topical medications. The hypotony maculopathy improved within two weeks. The corrected visual acuity increased to 10/20 at 12 months and 18/20 at 60 months after the corneal grafting. His left IOP has remained between 14 and 18 mmHg only with topical medications, and his left visual field defect has shown no notable progression.



**Figure 3** Case 3 had a giant ischemic bleb (A) and hypotony after MMC trabeculectomy. His left fundus showed typical hypotony maculopathy (B). After corneal lamellar grafting, the anterior chamber had remained deep (C) and the IOP had increased because of complete closure of the scleral cleft (D).

**Abbreviations:** IOP, intraocular pressure; MMC, mitomycin C.

## Discussion

Cases 1 and 2 had complicated bleb leaks from a microhole. Case 1 had combined hypotony with the shallow anterior chamber and circumferential ciliochoroidal detachment while bleb-related infections recurred in case 2. The occurrence of bleb leaks had been increasing because of the use of antifibrotic agents, 5-fluorouracil, or MMC, and to time progress after filtering surgeries.<sup>20</sup> Bleb-related infections, blebitis, or endophthalmitis, are reported to be the most severe complications after MMC trabeculectomy and are closely related to bleb leaks.<sup>21,22</sup> Microholes can supply a route for bacteria from the ocular surface into the bleb and eye. Case 3 was a rare case of slow-onset hypotony maculopathy with a large ischemic bleb. Generally, hypotony maculopathy after MMC trabeculectomy results from persistent overfiltration, ciliochoroidal detachment, hyposcretion of aqueous humor or leakage from an epithelial defect, a microhole, or insufficient sutures from the early postoperative periods.<sup>8–10</sup> The IOPs were over 10 mmHg in the early postoperative phase,

but both the IOPs and visual acuity decreased slowly over 18 months in case 3. An experiment has shown that the anti-fibrotic effects of MMC can continue for the long term.<sup>25</sup>

The treatments for hypotony with overfiltration or bleb leak are summarized in Table 1<sup>24,26</sup> which was modified slightly from Azuara-Blanco.<sup>26</sup> These therapies give a range of choices, ranging from conservative to surgical treatments. For initial conservative methods, a pressure eye patch and an oral carbonic anhydrase inhibitor are often recommended. Bleb injection of autologous blood,<sup>27</sup> bandage contact lenses, and topical application of a chemical irritant,<sup>28</sup> may be the next corrective steps. symblepharon rings or Simmons shell, laser therapy with argon or Nd:YAG laser,<sup>29</sup> cryotherapy, and diathermy have also been reported as treatment methods before surgical procedures. We tried a pressure eye patch, oral carbonic anhydrase administration and bleb injection of autologous blood in all cases, but with minimal effects. As a next step, we should consider relatively conservative surgical methods, such as compression sutures



**Table I** Treatments for hypotony with hyperfiltration or a leaking bleb after MMC trabeculectomy

1. Conservative methods
1) Pressure eye patching
2) Oral carbonic anhydrase inhibitor
3) Topical autologous serum
2. Bandage contact lens, Simmons shell, symblepharon rings
3. Injection of autologous blood
4. Cyanoacrylate glue, fibrin tissue glue
5. Chemical irritants (trichloroacetic acid, sodium nitrate)
5. Cryopexy, diathermy
6. Argon laser, thermal Nd:YAG laser
7. Surgical revision
1) Needling revision, bleb reformation, compression sutures
2) Direct sutures of the scleral flap
3) Removal of the ischemic bleb and patch grafting
(1) Autologous conjunctiva
(2) Autologous or preserved sclera
(3) Preserved cornea
(4) Amniotic membrane

**Abbreviation:** MMC, mitomycin C.

over the bleb, direct resuture, or scleroconjunctival suture of the scleral flap. In particular, the bleb leak from a microhole generally requires surgical treatment<sup>30,31</sup> as in cases 1 and 2. Microholes are made repeatedly because of the very thin and weak ischemic bleb wall. Compression sutures had no notable effects in cases 1 and 3. We tried direct sutures of the sclera flaps but the MMC-treated sclera was too weak to suture in cases 2 and 3. Therefore, we considered performing patch grafting. The materials for patch grafting include the autologous conjunctiva<sup>32</sup> or amniotic membranes.<sup>33</sup> The autologous conjunctiva is the most common and easiest to handle of the materials for patch grafting. It is recommended for primary surgery but not for more resistant and more complicated cases. Although almost two-third of cases with conjunctival grafting have maintained a low IOP, the effect is imperfect and bleb leakage often recurs.<sup>32</sup> More recently, amniotic membranes have been used as patch grafts to reduce stromal melting and promote re-epithelialization in extensive infectious scleral and corneoscleral ulcers.<sup>34</sup> Amniotic membranes are not yet commercially available and several procedures are necessary to use this membrane clinically in Japan. The other common materials for anterior segment reconstruction are preserved sclera,<sup>35,36</sup> pericardium,<sup>37</sup> and dura matter.<sup>38</sup> Scleral tissue is not readily available in Japan and caution must be taken to avoid immunogenicity. For the cases presented here, a preserved cornea is the most suitable grafting tissue<sup>39–41</sup> because we had to close the scleral cleft completely and enable their IOPs to increase for recovery

from long-term treatments. Similar to our report, Ti and Tan<sup>41</sup> reported 20 cases with severe scleral melting after pterygium surgery that were treated with lamellar corneal grafting, and noted that corneal tissue has some constructive advantages over scleral tissue and allows lamellar dissection for a better graft-host fit. For these types of cases, Kosmin and Wishart<sup>36</sup> treated with full thickness scleral grafting and Mistlberger et al<sup>40</sup> with dissection by an Excimer laser and lamellar corneal grafting. Mistlberger noted that a corneal graft is better than the scleral graft because there is less vascularization and scar formation after corneal grafting than after scleral grafting. Our method slightly differed from those reported previously because the corneal graft completely covered the filtering site when placed over the cornea and sclera.

Although a corneal or sclera patch must be used to close the scleral cleft and to free these cases from long-term complications, the biggest issue was the loss of the IOP-lowering effect of trabeculectomy. Fortunately, IOPs in all cases were maintained with topical medications, despite a temporary rise just after the surgery. When elevated postoperative IOPs cannot be controlled with medications, repeated MMC trabeculectomy may be difficult because of conjunctival conditions and other problems. A Seton shunt operation in the other operative area or cyclophotocoagulation can be considered in this condition.

Corneal lamellar grafting is a reliable and final surgical method to improve severe cases of hypotony maculopathy or bleb leak after MMC trabeculectomy.

## Disclosures

The authors report no conflicts of interest in this work.

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