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Review Article

Fungal Blebitis Caused by *Aspergillus ustus* (Section *Usti*) After Trabeculectomy: Clinical Course, Management Challenges and Literature Review

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Abstract

Purpose: To describe the first reported case of blebitis caused by *Aspergillus ustus* (section *Usti*) after glaucoma filtering surgery and to summarise recent evidence regarding fungal bleb-related infections.

Methods: Case report and updated narrative review. A comprehensive literature search was conducted in PubMed, MEDLINE and EMBASE from database inception through March 2025 using the following terms: "blebitis," "bleb-related infection," "fungal endophthalmitis," "*Aspergillus*," "trabeculectomy," "section *Usti*," "*Aspergillus ustus*," and "*Aspergillus calidoustus*." No language restrictions were applied. Case reports, case series, retrospective studies and review articles were eligible. A total of 10 primary references meeting the inclusion criteria were included in the final narrative synthesis.

Results: A 73-year-old woman developed subacute blebitis five weeks after trabeculectomy with Mitomycin-C (MMC). Despite intensive antibacterial therapy and two anterior vitrectomies, improvement occurred only after intravitreal voriconazole (100 µg/0.1 mL). Vitreous culture ultimately identified *Aspergillus ustus* (section *Usti*). The infection resolved microbiologically but progressed to phthisis bulbi; the eye was subsequently enucleated.

Conclusion: Fungal blebitis remains extremely rare but should be suspected in subacute cases with poor response to antibiotics. Early Pars Plana Vitrectomy (PPV), prompt vitreous sampling and intravitreal voriconazole are key to controlling infection. Section *Usti* species display reduced azole susceptibility, which may influence outcomes and necessitate combination antifungal therapy.

Keywords: Blebitis; Trabeculectomy; *Aspergillus ustus*; Fungal Endophthalmitis; Voriconazole; Glaucoma Surgery

Introduction

Bleb-related infection (blebitis) is an uncommon but vision-threatening complication of glaucoma filtering surgery with a lifelong risk of occurrence. Modern multicentre studies such as the Collaborative Bleb-related Infection Incidence and Treatment Study (CBIITS) report a cumulative incidence of approximately 2% within five years, identifying bleb leakage, young age and use of MMC as major risk factors [1]. Additional contributors include thin or avascular blebs, inferior bleb location and prior ocular surface disease, all of which promote microbial entry through the filtering site [2].

Although bacterial pathogens predominate, fungal blebitis is increasingly recognised. Data from exogenous fungal endophthalmitis suggest a gradual rise in fungal isolates, probably related to the growing number of immunosuppressed patients and improved diagnostic methods [3,4]. Among fungi, *Aspergillus* accounts for approximately one-quarter of exogenous infections and the clinical course is typically subacute and destructive, leading to poor visual outcomes when diagnosis is delayed [5].

Within the genus *Aspergillus*, section *Usti*-which includes *A. ustus* and *A. calidoustus*-represents a clinically significant group because of reduced azole susceptibility and frequent misidentification in older reports [6,7]. Ocular infection by section *Usti* is exceptional: the only published cluster involved nosocomial post-cataract endophthalmitis, with all cases resulting in enucleation [8]. No previous case of blebitis following glaucoma filtering surgery caused by this section has been reported. A summary of published section *Usti* ocular infections is provided in Table 1.

Author, Year	Pathogen	Infection Type	Prior Surgery	Treatment	Outcome
Saracli, et al., 2007 [8]	*A. ustus* (section *Usti*)	Post-operative endophthalmitis (post-cataract; nosocomial cluster)	Cataract surgery	Systemic antifungal (voriconazole / amphotericin B)	Enucleation in all cases
Glampedakis, et al., 2021 [6]	*Aspergillus* section *Usti* (multiple spp.)	Invasive aspergillosis (multicenter; primarily non-ocular)	Immunocompromised states (various)	Voriconazole-based; limited by reduced azole susceptibility	High mortality; poor prognosis in azole-resistant isolates
Bosetti, et al., 2023 [7]	*A. calidoustus* (section *Usti*)	Invasive aspergillosis (ocular involvement described)	Various; prior immunosuppression	Azole therapy; combination antifungals considered	Variable; poor prognosis with azole resistance
Present case, 2025	*A. ustus* (section *Usti*)	Fungal blebitis after trabeculectomy (first reported case)	Trabeculectomy with MMC	Intravitreal voriconazole 100 μg/0.1 mL + PPV	Microbiological resolution; phthisis bulbi; enucleation
MMC: Mitomycin-C; PPV: Pars Plana Vitrectomy; spp.: species.					

Table 1: Summary of previously reported *Aspergillus* section *Usti* ocular infections and related reports.

Case Report

A 73-year-old woman with hypertension, dyslipidemia, hyperuricemia, hypothyroidism and bilateral glaucoma under maximal topical therapy (Best-Corrected Visual Acuity [BCVA] 20/20) underwent trabeculectomy with MMC (0.5 mg/mL for 2 minutes) in the right eye. The early postoperative course was uneventful; topical tobramycin/dexamethasone and tropicamide were prescribed and a therapeutic contact lens was applied for a transient bleb leak (Seidel positive).

Thirty-six days later, she presented with a mildly painful red eye and discharge. Slit-lamp examination revealed a whitish, elevated filtering bleb with conjunctival hyperemia and mild corneal edema. Close-up examination of the superior bulbar conjunctiva showed marked vascular congestion and inflammatory changes of the filtering area consistent with early-stage blebitis. Intraocular Pressure (IOP) was 24 mmHg. A diagnosis of stage I-II blebitis was made and the patient was admitted for intensive topical vancomycin and ceftazidime with oral ciprofloxacin-standard empirical coverage for bacterial blebitis per published guidelines (Fig. 1,2) [2].

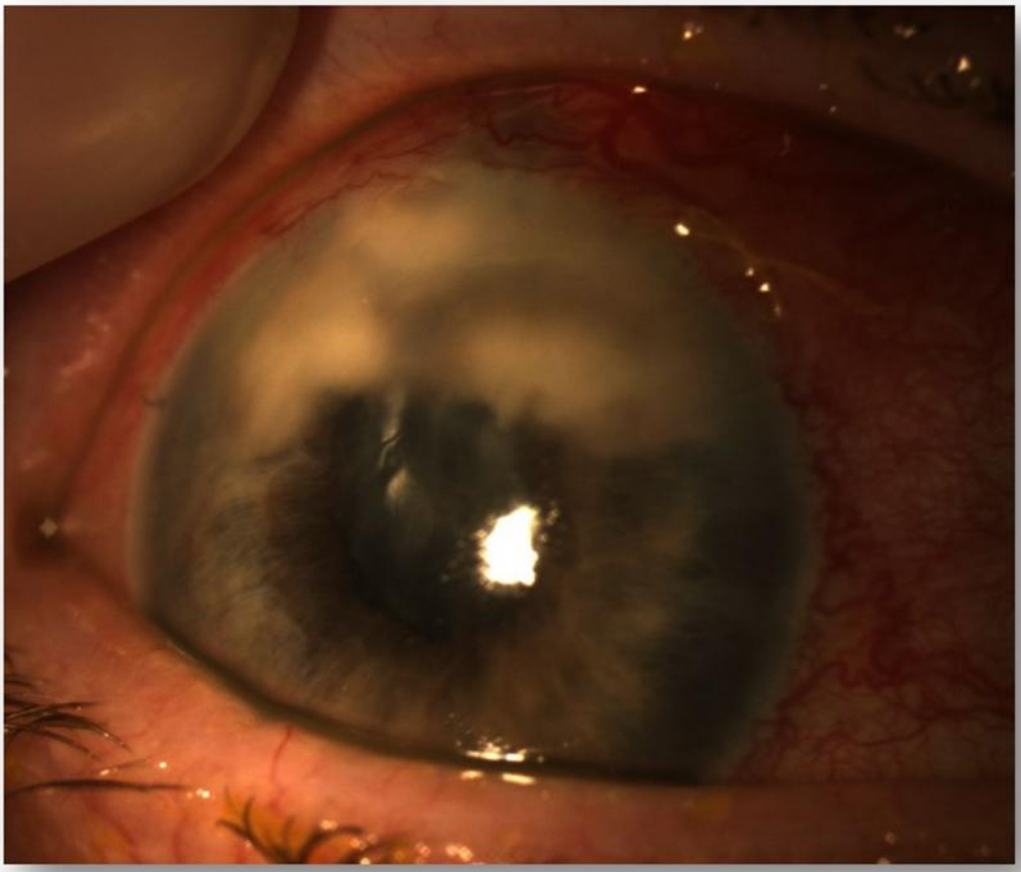

Figure 1: Slit-lamp photograph showing a hyperemic eye with a whitish, elevated filtering bleb and mild corneal edema five weeks after trabeculectomy with MMC.

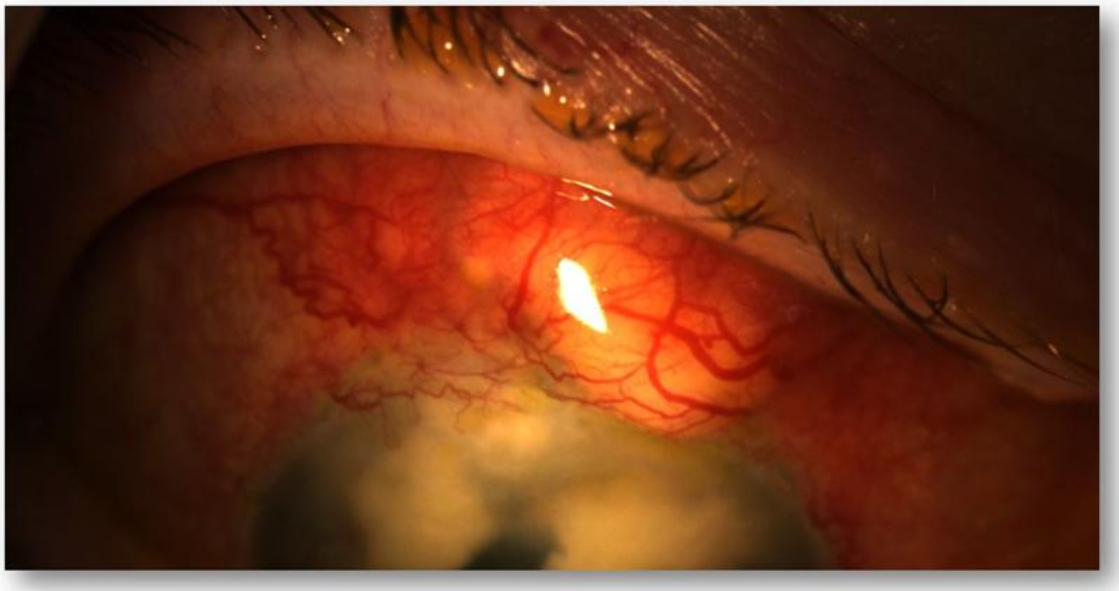

Figure 2: Close-up of the filtering bleb showing marked vascular congestion and inflammatory changes consistent with early-stage blebitis.

Microbiological investigations were initiated at admission: conjunctival swabs and bleb tap samples were plated on blood agar, chocolate agar and Sabouraud dextrose agar and incubated at 35°C and 25°C for up to four weeks to allow detection of fastidious and slow-growing organisms. All initial cultures returned negative at 48 hours and at 14 days.

During hospitalisation, the patient developed a pupillary membrane and endothelial infiltration. Slit-lamp examination revealed cotton-like fibrin masses in the anterior chamber extending through the pupillary axis. A YAG membranotomy and anterior vitrectomy were performed with sampling of aqueous humor; intravitreal vancomycin (1 mg/0.1 mL) was administered. Systemic corticosteroids were given for 24 hours and the patient was discharged after transient improvement (Fig. 3).

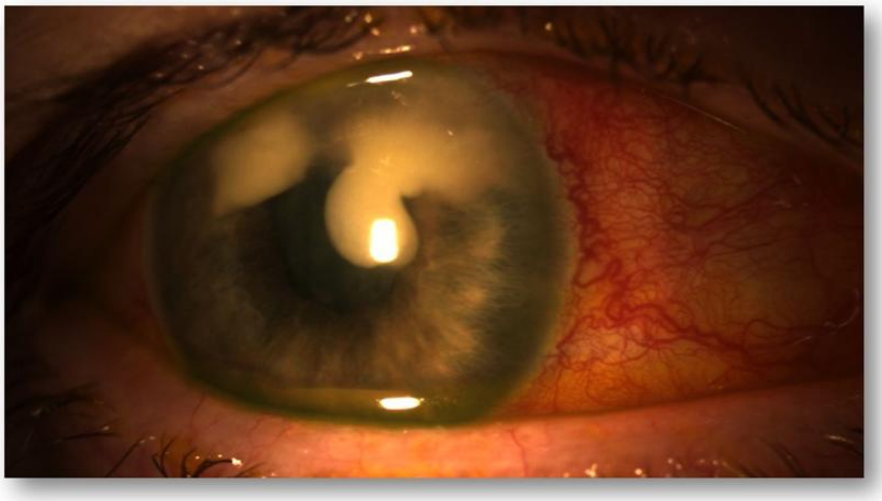

Figure 3: Slit-lamp image showing cotton-like fibrin masses in the anterior chamber extending through the pupillary axis.

Three weeks later she returned with pain, redness and blurred vision. Examination showed progression of the intraocular inflammatory process with dense white infiltrates occupying the anterior chamber and pupillary area. Given the poor response to prolonged antibacterial therapy and the subacute, indolent clinical course, fungal infection was suspected and oral fluconazole (400 mg loading dose, then 200 mg/day) was initiated empirically. Five days later, a second anterior vitrectomy with vitreous sampling and intravitreal voriconazole injection (100 μg/0.1 mL) was performed. The voriconazole dose was selected based on published pharmacokinetic and safety data demonstrating adequate intraocular penetration and a favourable toxicity profile compared with amphotericin B (Fig. 4) [5,10].

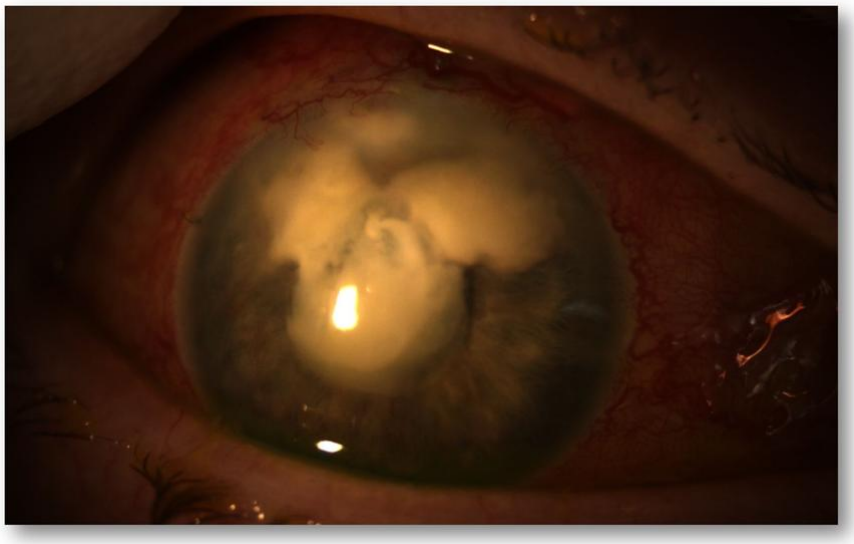

Figure 4: Progression of infection with dense white infiltrates occupying the anterior chamber and pupillary area despite prolonged antibacterial therapy.

Twelve weeks after trabeculectomy, vitreous culture grew *Aspergillus ustus* (section *Usti*), confirmed by characteristic macroscopic colony morphology (velvety, grayish-white growth on Sabouraud agar) and microscopic biseriate conidial heads with rough-walled conidia. Antifungal susceptibility testing demonstrated elevated Minimum Inhibitory Concentrations (MICs) for itraconazole (MIC ≥4 mg/L) and fluconazole (resistant), with borderline susceptibility to voriconazole (MIC 2 mg/L), consistent with the reduced azole susceptibility characteristic of section *Usti* [6,7]. Amphotericin B MIC was 1 mg/L (Fig. 5).

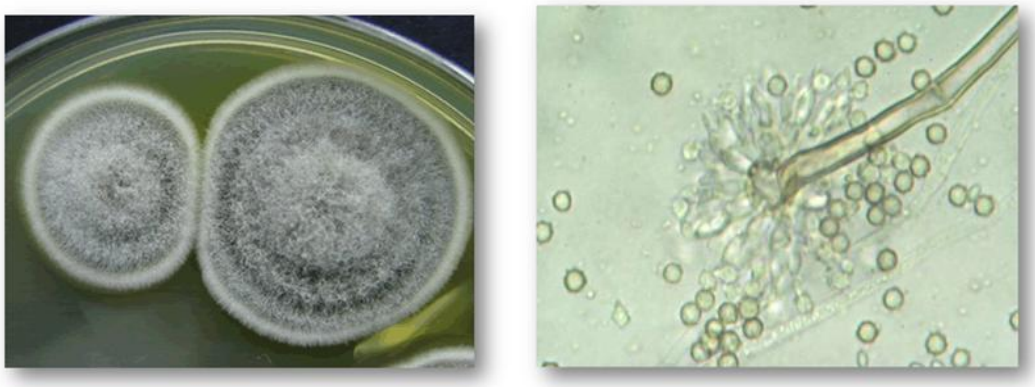

Figure 5: a:(left). Velvety, grayish-white colony of *Aspergillus ustus* on Sabouraud agar; b: (right). Biseriate conidial heads with rough-walled conidia (Lactophenol Cotton Blue, ×400).

At discharge, the bleb was quiet and the cornea mildly edematous. After one year of follow-up, the eye had evolved to phthisis bulbi with light perception but no pain; enucleation was subsequently performed.

Discussion

Bleb-related infections remain a major cause of late visual loss after filtering surgery, despite their declining incidence in contemporary practice [1,2]. Our patient exhibited several well-known risk factors: use of MMC, a thin avascular bleb and postoperative leakage.

Diagnostic considerations and delayed antifungal initiation. Fungal blebitis is rare and frequently misdiagnosed because of its indolent, subacute presentation and poor response to antibacterial therapy [3-5]. In this case, the initial clinical picture-subacute onset, mild pain and absence of hypopyon-was consistent with bacterial blebitis, justifying empirical vancomycin and ceftazidime as first-line therapy. Antifungal coverage was withheld initially because bacterial infection remained the most probable diagnosis and routine culture results were repeatedly negative. The decision to introduce oral fluconazole was ultimately driven by three weeks of clinical deterioration without microbiological confirmation. Retrospectively, earlier consideration of fungal aetiology-prompted by the subacute timeline, the history of MMC use and the absence of a bacterial isolate-might have shortened the diagnostic interval and reduced irreversible structural damage.

Microbiological challenges and species identification. Among *Aspergillus* species, section *Usti* (including *A. ustus* and *A. calidoustus*) is particularly challenging because of reduced susceptibility to azoles, notably fluconazole and sometimes voriconazole [6,7]. Correct species identification is crucial, as many historical *A. ustus* isolates have been reclassified within the *A. calidoustus* complex using molecular methods [7]. The elevated fluconazole MIC observed in this case explains the limited response to initial oral fluconazole and supports the use of voriconazole or combination therapy in confirmed or suspected section *Usti* infections. Vitreous sampling and role of molecular diagnostics. The diagnostic yield of aqueous humor samples is low in fungal endophthalmitis; vitreous sampling-preferably obtained during early PPV-offers higher sensitivity [5]. Emerging molecular techniques such as metagenomic Next-Generation Sequencing (mNGS) and microfluidic real-time PCR panels can detect bacterial and fungal DNA within hours and may substantially shorten the time to targeted therapy [9]. In the present case, mNGS was not available at the time of management; had it been routinely employed, fungal aetiology might have been identified earlier, potentially allowing timely antifungal escalation before further structural deterioration. The integration of these molecular tools into clinical protocols for poorly responsive blebitis should be strongly considered.

Therapeutic approach. PPV combined with intravitreal voriconazole (50-100 μg/0.1 mL) is currently considered the most effective approach for *Aspergillus endophthalmitis* because of its intraocular penetration and lower retinal toxicity compared with amphotericin B, despite its shorter intravitreal half-life [5,10]. Clinical improvement in this case occurred only after intravitreal voriconazole, consistent with published series associating early PPV and intravitreal antifungal therapy with better outcomes. Given the reduced azole susceptibility of section *Usti*, close monitoring and combination therapy-voriconazole plus intermittent intravitreal amphotericin B-should be considered if the initial response is inadequate.

Interpretation of the final outcome. The progression to phthisis bulbi despite microbiological resolution warrants careful analysis. Several factors likely contributed: (1) delayed antifungal initiation-introduced only after three weeks of inadequate antibacterial therapy-allowed cumulative structural damage to uveal and retinal tissues; (2) the inherent tissue-invasive virulence of section *Usti* species, amplified by reduced azole susceptibility, may have perpetuated intraocular destruction even during active treatment; and (3) repeated surgical interventions combined with MMC-related avascular bleb tissue may have further impaired the eye's capacity for structural recovery. This dissociation between microbiological cure and anatomical preservation underscores the importance of early clinical suspicion and prompt antifungal coverage.

Environmental sampling is advisable when *A. ustus* is identified, as previous clusters have been linked to hospital construction or ventilation systems [8].

Conclusion

Fungal blebitis should be considered in any subacute bleb infection that fails to respond to conventional antibacterial therapy. Early vitreous sampling and prompt PPV increase the likelihood of identifying the causative organism and allow timely administration of targeted intravitreal therapy. Intravitreal voriconazole remains the treatment of choice for *Aspergillus blebitis*; however, species within section *Usti* may exhibit reduced azole susceptibility, requiring close monitoring and, in refractory cases, combination antifungal therapy. Rapid molecular tools such as real-time PCR and mNGS can substantially shorten the diagnostic interval and should be integrated into clinical protocols for poorly responsive cases. Environmental investigation should always be considered to exclude nosocomial or construction-related contamination sources.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Acknowledgement

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Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore was exempt.

Informed Consent Statement

Informed consent was obtained from all participants included in the study.

Authors' Contributions

All authors contributed equally to this paper.

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