

CASE REPORT

Ocular Tuberculosis in Advanced Proliferative Diabetic Retinopathy: A Diagnostic and Therapeutic Dilemma in A Vitrectomized Eye

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ABSTRACT

Background: Ocular tuberculosis (OTB) is a paucibacillary extrapulmonary infection, hard to recognize in an eye compromised by proliferative diabetic retinopathy (PDR) and vitreoretinal surgery, where postoperative inflammation, tamponade artifacts, hemorrhage and diabetic microangiopathy mimic infectious uveitis.

Objective: To characterize the diagnosis, molecular confirmation, and longitudinal outcomes of occult ocular tuberculosis in a vitrectomized eye with end-stage proliferative diabetic retinopathy.

Methods: A 50-year-old man with type 2 diabetes and pulmonary tuberculosis presented with acute inflammation (OD) 5 days after pars plana vitrectomy. He was followed over six milestones (T0–T5, 16 weeks) with SD-OCT and vitreous nested RT-PCR (IS6110/MPB64); outcomes were best-corrected acuity (LogMAR), intraocular pressure and central macular thickness (CMT).

Results: At T0 (OD 1/300, LogMAR 2.48) with ciliary flush and gas endotamponade, vitreous RT-PCR was positive for *M. tuberculosis* DNA (IS6110/MPB64), establishing intraocular tuberculosis masked by surgical inflammation. Quadruple antituberculous therapy (RHZE) with corticosteroids improved vision to 6/30 (LogMAR 0.70) by week 3 and 6/21 (LogMAR 0.54) by week 6. At week 7, SD-OCT unmasked diabetic cystoid macular edema (CMT 365 µm) that responded to sub-Tenon triamcinolone (CMT 340 µm), with final acuity 6/9.5 corrected (LogMAR 0.20) at week 16. The contralateral eye (OS) developed neovascular glaucoma (IOP 51.0–63.0 mmHg) and no light perception, requiring silicone oil evacuation.

Conclusion: Ocular tuberculosis must be suspected in atypical intraocular inflammation in vitrectomized eyes, especially with tuberculosis or diabetes. Vitreous PCR is decisive when signs overlap with surgical trauma and diabetic microangiopathy, and prompt antituberculous plus corticosteroid therapy can achieve visual salvage.

1. Introduction

Tuberculosis (TB), an infectious granulomatous disease caused by the acid-fast bacillus *Mycobacterium tuberculosis*, remains one of the most formidable infectious causes of morbidity and mortality across the globe.¹ According to the World Health Organization Global Tuberculosis Report 2024, an estimated 8.2 million individuals worldwide were newly diagnosed with tuberculosis in 2023, representing the highest annual burden recorded since the inception of global surveillance in 1995.¹ Although pulmonary involvement represents the primary clinical manifestation and the main vector for community transmission, *M. tuberculosis* possesses an extraordinary biological capability for hematogenous and lymphatic dissemination to extrapulmonary anatomical niches, including the central nervous system, musculoskeletal system, lymph nodes, and the eye.^{1,2} Ocular tuberculosis (OTB) occurs in approximately 1% to 2% of patients with systemic tuberculosis in non-endemic countries, but its prevalence escalates to nearly 10% in high-burden endemic territories such as South and Southeast Asia.^{2,3}

The clinical presentation of ocular tuberculosis is notoriously protean, earning it the longstanding designation of a quintessential clinical chameleon.^{2–4} Intraocular infection can manifest as anterior granulomatous or non-granulomatous uveitis, intermediate uveitis with snowbanking, multifocal choroiditis, serpiginous-like choroiditis, retinal vasculitis with periphlebitis, solitary choroidal tuberculomas, endophthalmitis, or panuveitis.^{2,5,6} Because intraocular fluid contains low bacterial loads and *Mycobacterium tuberculosis* organisms are sequestered within deep chorioretinal tissues, microbiological confirmation through traditional acid-fast bacillus (AFB) Ziehl-Neelsen staining and Lowenstein-Jensen culture yields positive results in fewer than 5% to 8% of suspected clinical cases.^{3,6,7} Consequently, the diagnosis of ocular tuberculosis has historically relied upon a presumptive diagnostic triad comprising: (1) compatible ocular clinical phenotypes; (2) positive surrogate systemic markers such as tuberculin skin testing (TST) or interferon-gamma release assays (IGRA) alongside suggestive chest radiography; and (3) a documented therapeutic

response to empirical antituberculous therapy (ATT).^{6,7}

In recent years, the diagnostic landscape of ocular tuberculosis has undergone a profound paradigm shift through the integration of high-sensitivity molecular assays, particularly nested and real-time polymerase chain reaction (RT-PCR).^{4,8} Multiplex and nested PCR protocols targeting specific, highly conserved insertion elements—most prominently IS6110 and the secretory protein-coding sequence MPB64—have demonstrated analytical sensitivities exceeding 70% to 80% with specificities approaching 98% to 100% when testing intraocular fluid samples.^{8–10} Molecular detection of microbial DNA directly from aqueous humor or vitreous biopsy specimens provides definitive microbiological ascertainment, converting presumptive clinical impressions into microbiologically confirmed intraocular infections and facilitating timely targeted antimicrobial intervention before irreversible neuroretinal destruction occurs.^{4,8–10}

Concurrently, the global epidemic of diabetic retinopathy (DR) presents an immense clinical and surgical burden, with over 103 million individuals affected worldwide, a figure projected to surpass 160 million by 2045.¹¹ In patients with poorly controlled, long-standing diabetes mellitus, chronic capillary nonperfusion and persistent retinal ischemia trigger the massive upregulation of vascular endothelial growth factor (VEGF), culminating in proliferative diabetic retinopathy (PDR) complicated by recurring non-clearing vitreous hemorrhage, fibrovascular proliferation, and tractional retinal detachment (TRD).^{11,12} Pars plana vitrectomy (PPV) serves as the definitive surgical intervention for repairing tractional detachments and restoring optical clarity in eyes suffering from end-stage diabetic eye disease.^{13,14}

The intersection of diabetes mellitus and tuberculosis establishes a synergistic, bi-directional immunological crisis.¹⁵ Chronic hyperglycemia directly impairs innate and adaptive immune effector mechanisms, causing defective macrophage phagocytosis, impaired chemotaxis of polymorphonuclear neutrophils, suppressed production of interferon-gamma (IFN- γ) and interleukin-12 (IL-12), and delayed antigen presentation by dendritic cells.^{15–18} As a result, diabetic patients exhibit a three- to four-fold increased susceptibility to contracting active tuberculosis, suffer elevated rates of treatment failure, and experience significantly higher mortality compared to euglycemic cohorts.^{15,18} Simultaneously, advanced diabetic microangiopathy causes extensive breakdown of the inner and outer blood-retinal barriers through microvascular pericyte apoptosis, endothelial tight-junction disruption, and basement membrane thickening, creating a fragile microvascular bed prone to exaggerated inflammatory injury and vascular leakage.^{19,20}

When ocular tuberculosis develops within an eye that has recently undergone vitreoretinal surgery for proliferative diabetic retinopathy, an unprecedented diagnostic dilemma emerges.^{21,22} In the early postoperative period following pars plana vitrectomy, surgeons routinely expect a predictable cascade of surgical inflammation, including circumcorneal ciliary injection, conjunctival hyperemia, anterior chamber fibrinous flare, and transient intraocular pressure perturbations.^{13,14} If the vitrectomized eye harbors active *M. tuberculosis* infection, the inflammatory manifestations of intraocular tuberculosis become entirely masked by, and conflated with, expected postoperative surgical trauma.^{21,22} The presence of intraocular tamponade agents—such as expanding perfluoropropane (C3F8) gas or silicone oil—further complicates clinical evaluation by severely distorting optical fundus visualization and creating physical artifacts during ophthalmic biomicroscopy and optical coherence tomography (OCT).^{23–25}

Furthermore, the presence of intraocular tamponade agents substantially modulates ocular fluid dynamics and drug pharmacokinetics.^{23–25} In vitrectomized eyes filled with silicone oil, inflammatory cytokines, lipid peroxidation products, and angiogenic mediators become concentrated within a thin meniscus of retro-oil aqueous fluid, dramatically accelerating ischemic damage to the anterior chamber angle and predisposing the eye to devastating complications such as emulsification-induced secondary glaucoma and fulminant neovascular glaucoma (NVG).^{23–28} In contrast, in gas-filled eyes, clearance of intraocular medications is markedly accelerated once the gas bubble absorbs, altering drug half-lives and necessitating precise pharmacological titrations to maintain therapeutic drug levels.^{23,24}

Despite the increasing prevalence of diabetes-tuberculosis multimorbidity in high-burden countries, there is a striking paucity of documented clinical studies that systematically examine the diagnostic trajectory, molecular confirmation, and therapeutic challenges of ocular tuberculosis arising in vitrectomized eyes with proliferative diabetic retinopathy.^{29,30} Most published literature on ocular tuberculosis focuses exclusively on non-operated, phakic eyes presenting with classical uveitic phenotypes such as retinal vasculitis, multifocal choroiditis, or solitary granulomas.^{2,6,29} To address this profound literature gap, we present an exhaustive, longitudinal observational analytic investigation of a 50-year-old male with active pulmonary tuberculosis and advanced proliferative diabetic retinopathy who presented with severe atypical intraocular inflammation and acute visual loss following pars plana vitrectomy. By synthesizing serial clinical examinations, high-resolution anterior and posterior segment photography, spectral-domain optical coherence tomography, and molecular vitreous PCR, this study provides unprecedented clinical and

translational insights into the management of this formidable diagnostic intersection.

2. Methods

Study Design and Epidemiological Framework

This investigation was designed and executed as a comprehensive, prospective longitudinal observational analytic case study at the Vitreoretina and Uveitis Divisions of the Department of Ophthalmology, Prof. Dr. I.G.N.G. Ngoerah Hospital / Faculty of Medicine, Udayana University, Denpasar, Bali, Indonesia. The patient was followed serially across six standardized clinical observation milestones: T0 (baseline presentation on postoperative day 5, March 18, 2025); T1 (molecular ascertainment and early follow-up at week 3, April 8, 2025); T2 (refractive progression and contralateral surge at week 6, April 29, 2025); T3 (structural tomographic verification and sub-Tenon rescue at week 7, May 7, 2025); T4 (post-corticosteroid macular restitution and suture removal at week 12, June 9, 2025); and T5 (long-term surgical endpoint at week 16, July 3–4, 2025).

Ethical Governance and Participant Consent

The study protocol, clinical procedures, diagnostic fluid sampling, and therapeutic interventions adhered strictly to the ethical tenets of the Declaration of Helsinki (1964 and its subsequent amendments) and received formal institutional approval from the CMHC Research Center, Indonesia (Approval Protocol No. 2025/892). Written, fully informed consent was secured directly from the patient prior to any study-related procedures. The consent process encompassed explicit authorization for: (1) undiluted diagnostic vitreous fluid sampling; (2) serial anterior and posterior segment photographic documentation; (3) spectral-domain optical coherence tomography; (4) sub-Tenon corticosteroid administration; and (5) anonymized dissemination of medical data, diagnostic images, and clinical findings for academic publication, in rigorous alignment with the International Committee of Medical Journal Editors (ICMJE) and Committee on Publication Ethics (COPE) guidelines.

Case Eligibility and Diagnostic Ascertainment

The diagnostic eligibility criteria were established in concordance with the Collaborative Ocular Tuberculosis Study (COTS) consensus recommendations and the British Thoracic Society (BTS) clinical statements.^{5-7,31} Inclusion required: (1) documented active pulmonary tuberculosis under guideline-directed antituberculous therapy; (2) microbiologically or clinically confirmed type 2 diabetes mellitus complicated by proliferative diabetic retinopathy; (3) a recent history of pars plana vitrectomy for surgical retinal complications; and (4) acute or persistent intraocular inflammation that could not be satisfactorily accounted for solely by expected surgical recovery. The diagnostic ascertainment of diabetes mellitus followed the American Diabetes

Association (ADA) criteria (fasting plasma glucose ≥ 126 mg/dL, 2-hour postprandial glucose ≥ 200 mg/dL, or glycated hemoglobin [HbA1c] $\geq 6.5\%$).³²

Longitudinal Observation Protocol and Analytical Measurements

At each of the six designated observation milestones (T0 through T5), standardized bilateral ophthalmic examinations were performed by senior vitreoretinal and uveitis subspecialists. Visual acuity was measured using standardized Snellen charts under controlled ambient illumination and converted to the Logarithm of the Minimum Angle of Resolution (LogMAR) for quantitative statistical analysis. Semi-quantitative visual acuities were transformed following standard ophthalmic conventions: Hand Motion (HM) = 2.70 LogMAR; Light Perception (LP) = 3.00 LogMAR; and No Light Perception (NLP) = 0.0 decimal (assigned an arbitrary non-resolving qualitative classification). Intraocular pressure (IOP) was quantified in millimeters of mercury (mmHg) utilizing a calibrated Goldmann applanation tonometer (Haag-Streit AT 900) or a calibrated Tono-Pen XL handheld applanation tonometer in instances of marked corneal epithelial edema.

Anterior segment biomicroscopy was conducted with a high-resolution Haag-Streit BQ 900 slit-lamp and documented using an integrated Canon EOS digital imaging system. Slit-lamp grading encompassed conjunctival hyperemia, circumcorneal ciliary flush, corneal clarity, anterior chamber depth and reaction (graded according to the Standardization of Uveitis Nomenclature [SUN] working group criteria), pupillary contour and light reflexes, iris neovascularization (Rubeosis Iridis, graded 0 to 4), and intraocular lens (IOL) centration. Posterior segment evaluation was performed utilizing indirect ophthalmoscopy with a 20-diopter Volk lens and slit-lamp biomicroscopy with a 78-diopter Volk non-contact fundus lens.

Vitreous Molecular PCR Protocol and Microbiological Processing

A diagnostic vitreous fluid sample was acquired during vitrectomy under sterile operating theater conditions prior to fluid-gas exchange.³³ Approximately 0.5 mL of undiluted vitreous humor was aspirated via a 23-gauge vitrectomy cutter connected to a sterile tuberculin syringe under low aspiration pressure. The specimen was divided into two aliquots: Aliquot A (0.2 mL) was subjected to conventional microbiological processing (Gram stain, Ziehl-Neelsen acid-fast staining, and bacterial/fungal culture on chocolate agar, blood agar, and Lowenstein-Jensen media); Aliquot B (0.3 mL) was immediately cryopreserved at -80°C in a sterile cryovial for molecular diagnostic analysis.

Total genomic DNA extraction was performed from 200 μL of vitreous fluid using the QIAamp DNA Mini Kit (Qiagen, Hilden, Germany) following the manufacturer's validated protocol for paucibacillary biological fluids. Nested real-time PCR was executed

utilizing the Rotor-Gene Q real-time PCR system (Qiagen) with automated dual-target fluorogenic probes.¹⁰ Target 1 comprised the high-copy-number insertion sequence IS6110 (specific to the *Mycobacterium tuberculosis* complex, with a limit of analytical detection of 5 genome equivalents per reaction). Target 2 comprised the single-copy immunogenic secretory protein MPB64 sequence, utilized as a cross-confirmatory marker to exclude false-positive contamination and non-tuberculous mycobacteria. Thermocycling conditions consisted of an initial denaturation at 95°C for 10 minutes, followed by 45 cycles of denaturation at 95°C for 15 seconds, annealing at 60°C for 30 seconds, and extension at 72°C for 30 seconds with continuous fluorophore acquisition.

Analytic and Comparative Framework

To validate the causal link between intraocular *M. tuberculosis* infection and the clinical disease course, objective causality evaluations were performed using three internationally recognized frameworks: the Bradford Hill Criteria for Causality, the World Health Organization–Uppsala Monitoring Centre (WHO-UMC) System for Standardized Case Causality Assessment, and the Naranjo Adverse Event Probability Scale. To provide broader clinical relevance, comparative literature benchmarking was conducted against an exhaustive corpus of international clinical series published between 2021 and 2026 reporting ocular tuberculosis in vitrectomized and non-vitrectomized eyes.

Biostatistical and Trajectory Analysis

Quantitative variables—including BCVA (LogMAR), IOP (mmHg), central macular thickness (CMT, μm), and ETDRS subfield thicknesses—were organized into a standardized longitudinal database. Absolute change (Δ) and percentage relative change (%) between serial follow-up points were calculated using standard formulae. All calculations and graphical visualizations were executed in Python (version 3.11) utilizing NumPy, SciPy, Matplotlib, and PIL packages.

3. Results

Baseline Presentation and Initial Diagnostic Dilemma (T0: March 18, 2025)

A 50-year-old male presented to the Outpatient Eye Clinic on March 18, 2025 (designated as observation milestone T0), corresponding to postoperative day 5 following a 23-gauge pars plana vitrectomy with perfluoropropane gas endotamponade in the right eye (OD). The surgical procedure had been performed at an outside tertiary vitreoretinal center for a severe tractional retinal detachment complicating long-standing proliferative diabetic retinopathy. The patient had a documented medical history of type 2 diabetes mellitus exceeding five years, characterized by suboptimal metabolic control (baseline glycated hemoglobin [HbA1c] of 8.8% and random blood

glucose of 214 mg/dL). Concurrently, he had been diagnosed with active pulmonary tuberculosis six months prior, following a positive sputum GeneXpert MTB/RIF assay, and was receiving maintenance-phase oral antituberculous therapy comprising daily rifampicin (450 mg) and isoniazid (300 mg).

At presentation, the patient complained of severe, unremitting visual blur, periocular aching, and redness in the right eye. Baseline ophthalmic examination revealed marked bilateral visual compromise, as illustrated in Figure 1 and detailed in Table 1. Best-corrected visual acuity (BCVA) in the right eye (OD) was markedly diminished to 1/300 (LogMAR 2.48), with no improvement achievable through pinhole testing. Intraocular pressure (IOP) in the right eye was 5.0 mmHg, consistent with early postoperative transient hypotony following vitrectomy and fluid-gas exchange.

Slit-lamp biomicroscopy of the right eye unmasked dramatic, florid signs of deep ocular inflammation, as illustrated in Figure 1. The bulbar conjunctiva displayed intense, diffuse mixed conjunctival injection and a prominent temporal subconjunctival hemorrhage (approximately 8 mm in transverse diameter). Most notably, the perilimbal architecture exhibited intense, 360-degree circumcorneal ciliary injection, indicating active intraocular inflammation rather than simple superficial surgical trauma. The cornea remained clear and compact, without epithelial microcysts or endothelial dusting. The anterior chamber was deep and well-formed (Van Herick grade 3), displaying 1+ cellular flare without hypopyon or keratic precipitates. The pupil was circular, mid-dilated (approximately 4.5 mm in diameter), and sluggishly reactive to direct and consensual light. The right eye was pseudophakic, with a well-centered posterior chamber intraocular lens (PCIOL) in the capsular bag and early posterior capsular opacification (PCO).

Fundus examination of the right eye was severely constrained by the presence of the expanding intraocular gas bubble. The red fundus reflex was present, but intraocular media haziness and the optical interface of the perfluoropropane gas bubble fully obscured posterior pole and mid-peripheral detail. The immediate clinical dilemma was evident: the marked ocular redness, ciliary flush, and profound visual decline (1/300) could be readily attributed by the attending surgical team to normal postoperative vitrectomy recovery, mechanical sclerotomy trauma, or benign postoperative inflammation. However, the patient's active pulmonary tuberculosis and disproportionately intense ciliary flush raised suspicion of an occult, opportunistic intraocular infection.

In stark contrast, baseline examination of the contralateral left eye (OS) revealed an anatomical catastrophe. The left eye had undergone multiple vitreoretinal procedures over the preceding three years for complex proliferative diabetic retinopathy,

culminating in 5,000-centistoke silicone oil endotamponade. BCVA in the left eye was limited to No Light Perception (NLP, LogMAR 3.00) with poor projection. IOP in the left eye was 12.0 mmHg. Slit-lamp biomicroscopy showed diffuse corneal stromal haze, a

deep anterior chamber filled with emulsified silicone oil droplets, a fixed mid-dilated pupil, pseudophakia, and an anatomically detached, atrophic retina under silicone oil tamponade.

Table 1. Longitudinal Visual Acuity, Refractive Status, Intraocular Pressure, and Clinical Biomarker Trajectory Across Serial Observation Milestones (Right Eye OD vs. Left Eye OS).

Eye	Observation Point (Date)	Uncorrected Visual Acuity (UCVA)	Best-Corrected Visual Acuity (BCVA)	LogMAR Equivalent	Refraction / Pinhole Correction	Intraocular Pressure (mmHg)	Anterior Segment & Optical Status	Posterior Segment & Vitreoretinal Trajectory
Right Eye (OD)	T0: Presentation (Mar 18, 2025)	1/300	1/300	2.48	No pinhole improvement	5.0	Marked conjunctival & ciliary injection, temporal subconjunctival hemorrhage, pseudophakic (PCIOL) with PCO	Gas-filled vitreous cavity, positive red reflex, fundus details fully obscured
Right Eye (OD)	T1: Molecular Ascertainment (Apr 8, 2025)	6/60	6/30	0.70	No pinhole gain	15.0	Mild residual conjunctival injection, quiet AC (0 cells, 0 flare), centered PCIOL	Partial gas resorption, attached neuroretina, extensive PRP laser scars, quiescent retina, MTB PCR confirmed positive
Right Eye (OD)	T2: Refractive Progression (Apr 29, 2025)	6/38	6/15	0.40	Sph -1.50 D (corrected to 6/15)	17.0	Minimal conjunctival erythema, clear cornea, quiet AC, intact 10–0 nylon suture	Trace residual gas meniscus, flat attached retina, no active vitritis or chorioretinitis
Right Eye (OD)	T3: Structural Tomography (May 7, 2025)	6/19	6/12	0.30	Pinhole 6/12	19.0	Quiet anterior segment, centered PCIOL, clear optical media	Attached retina; SD-OCT reveals diffuse cystoid macular edema (CMT 365 µm) and subretinal fluid; scheduled for STTA
Right Eye (OD)	T4: Post-STTA 1 Month (Jun 9, 2025)	6/15	6/9.5	0.20	Refraction & pinhole: 6/9.5	11.0	Completely quiet, suture removed by vitreoretinal service	Anatomically flat retina, repeat SD-OCT demonstrates significant edema reduction (CMT 340 µm, Δ -6.85%), quiescent vasculature
Right Eye (OD)	T5: Long-Term Endpoint (Jul 3, 2025)	6/15	6/9.5	0.20	Refraction: 6/9.5	20.0	Quiet pseudophakic anterior segment, normal tear film	Persistent stable macular reattachment, resolved subretinal fluid, quiescent diabetic/tubercular status
Left Eye (OS)	T0: Presentation (Mar 18, 2025)	No light perception	No light perception	3.00	Cannot be refracted	12.0	Pseudophakic, iris pigment dispersion on PCIOL optic, deep anterior chamber	Silicone-oil-filled vitreous cavity (2000 cSt), obscured posterior pole, prior vitreoretinal surgery scars
Left Eye (OS)	T1: Follow-up (Apr 8, 2025)	No light perception	No light perception	3.00	No improvement	19.0	Pseudophakic, silicone oil in anterior chamber, quiet stroma	Silicone oil tamponade, dense vitreous opacity, severe retinal ischemia
Left Eye (OS)	T2: Hypertensive Surge (Apr 29, 2025)	No light perception	No light perception	3.00	No improvement	51.0	Diffuse microcystic corneal edema, early rubeosis iridis (NVI grade 2), sluggish pupil	Silicone oil emulsification droplets, detached ischemic retina; started topical timolol & oral acetazolamide

Left Eye (OS)	T3: NVG Diagnosis (May 7, 2025)	No light perception	No light perception	3.00	No improvement	52.0	Corneal haze, florid rubeosis iridis (grade 4), fixed mid-dilated pupil, ectropion uveae	Closed angle, extensive ischemic nonperfusion; neovascular glaucoma established
Left Eye (OS)	T4: Refractory NVG (Jun 9, 2025)	No light perception	No light perception	3.00	No improvement	39.0	Corneal decompensation, prominent iris vessel arborization	Persistent chronic retinal detachment, silicone oil emulsification, intractable glaucoma
Left Eye (OS)	T5: Decompression (Jul 3–4, 2025)	No light perception	No light perception	3.00	No improvement	63.0 -> 6.0*	Severe iris neovascularization; underwent silicone oil removal on July 4; post-op IOP normalized to 6.0 mmHg	Chronic detached retina, complete neuroretinal and optic nerve atrophy; visual outcome remained NLP

*Postoperative intraocular pressure following silicone oil evacuation on July 4, 2025. AC: anterior chamber; BCVA: best-corrected visual acuity; CMT: central macular thickness; D: diopters; IOP: intraocular pressure; LogMAR: logarithm of the minimum angle of resolution; MTB: *Mycobacterium tuberculosis*; NLP: no light perception; NVI: neovascularization of the iris; OD: oculus dexter (right eye); OS: oculus sinister (left eye); PCIOL: posterior chamber intraocular lens; PCO: posterior capsular opacification; PCR: polymerase chain reaction; PPV: pars plana vitrectomy; PRP: panretinal photocoagulation; SD-OCT: spectral-domain optical coherence tomography; Sph: spherical equivalent; STTA: sub-Tenon triamcinolone acetonide; UCVA: uncorrected visual acuity.

(A) Right Eye (OD) Slit-Lamp Biomicroscopy



Clinical Parameter	Finding at Presentation (OD, TO)
Timeline / Post-op Status:	Postoperative Day 5 (March 18, 2025)
Best-Corrected Visual Acuity:	1/300 (LogMAR 2.48), no pinhole gain
Intraocular Pressure (IOP):	5.0 mmHg (transient post-op hypotony)
Bulbar Conjunctiva:	Marked mixed injection & temporal hem.
Perilimbal Region:	Intense 360° circumcorneal ciliary flush
Cornea & Anterior Chamber:	Clear cornea; Van Herick gr 3; mild cells
Lens & Optical Axis:	Pseudophakic (PCIOL in bag) + early PCO
Vitreous Endotamponade:	Intraocular gas bubble filling cavity
Initial Clinical Dilemma:	Redness masked as surgical trauma
Confirmatory Molecular Test	Vitreous PCR: POSITIVE MTB DNA

Figure 1. Anterior segment slit-lamp biomicroscopy and macro photography of the right eye (OD) at presentation (March 18, 2025, Postoperative Day 5 following 23G pars plana vitrectomy). Intense circumcorneal ciliary injection, conjunctival hyperemia, and temporal subconjunctival hemorrhage in a pseudophakic gas-filled eye.

Molecular Confirmation and Early Inflammatory Regression (T1: April 8, 2025)

At the week 3 follow-up visit (milestone T1, April 8, 2025), the diagnostic ambiguity was definitively resolved by microbiological and molecular investigations, as detailed in Table 2. Conventional microbiological processing of the vitreous fluid aspirated at the time of vitrectomy yielded negative results: Gram stain showed no bacteria, Ziehl-Neelsen stain revealed no acid-fast bacilli (0 AFB/100 oil-immersion fields), and cultures on blood agar, chocolate agar, and Lowenstein-Jensen media yielded

no growth at 4 weeks, reflecting the characteristic paucibacillary nature of intraocular tuberculosis. However, nested real-time PCR targeting *Mycobacterium tuberculosis* complex genomic DNA returned unequivocally POSITIVE for both IS6110 and MPB64 insertion sequences, as detailed in Table 2. Cycle threshold (Ct) values were 29.4 for IS6110 and 31.2 for MPB64, confirming the presence of viable *M. tuberculosis* DNA within the vitreous cavity. Peripheral blood investigations demonstrated an elevated erythrocyte sedimentation rate (ESR) of 58 mm/hr, C-reactive protein (CRP) of 16.4 mg/L, HbA1c of 8.8%, and non-reactive serology for syphilis (VDRL non-

reactive) and human immunodeficiency virus (HIV non-reactive).

Upon receiving molecular confirmation of ocular tuberculosis, systemic and local therapy was intensified. The patient's pulmonology team optimized his systemic antituberculous therapy back to the intensive quadruple regimen: oral rifampicin (450 mg daily), isoniazid (300 mg daily), pyrazinamide (1,500 mg daily), and ethambutol (1,000 mg daily) under strict hepatic transaminase monitoring. To suppress the destructive intraocular inflammation while under full ATT coverage, systemic oral methylprednisolone was initiated at 0.8 mg/kg/day (48 mg daily) with a planned weekly taper, accompanied by topical prednisolone acetate 1% eye drops (every 2 hours) and topical levofloxacin 0.5% eye drops (six times daily) in the right eye.

Clinically, the right eye exhibited remarkable early therapeutic responsiveness, as documented in Figure 2 and detailed in Table 1. Visual acuity in the right eye

improved from 1/300 (LogMAR 2.48) to 6/30 (LogMAR 0.70) with pinhole correction. IOP measured 15.0 mmHg. The intraocular gas bubble had completely resorbed. Slit-lamp biomicroscopy showed complete resolution of the circumcorneal ciliary flush and conjunctival hyperemia, a quiet anterior chamber, and clear optical media.

Fundus photography of the right eye, as documented in Figure 2, confirmed complete anatomical neuroretinal reattachment across all four quadrants. Panel A shows the posterior pole with a crisp optic disc displaying mild physiological pallor, fully attached neurosensory retina, attenuated retinal arterioles, and clear optical media without vitritis. Panel B shows the mid-periphery and nasal retina demonstrating dense, confluent, well-pigmented panretinal photocoagulation (PRP) laser scars with complete absence of active fibrovascular proliferation or recurrent vitreous hemorrhage.

Table 2. Comprehensive Multimodal Diagnostic Workup, Ocular Microbiology/Molecular Panels, and Systemic Laboratory Parameters.

Diagnostic Domain / Analyte	Biological Specimen	Assay Modality & Methodology	Observed Patient Value	Normative Reference / Cutoff	Clinical Interpretation & Diagnostic Value
Mycobacterium tuberculosis PCR	Vitreous fluid (OD)	Nested Real-Time PCR (IS6110 & MPB64)	POSITIVE (Specific target band)	Negative / Not Detected	Conclusive intraocular molecular evidence of Mycobacterium tuberculosis DNA in vitreous
Vitreous Cytology	Vitreous fluid (OD)	Giemsa & Papanicolaou staining	Lymphocytes & degenerate macrophages	Acellular / Rare vitreocytes	Paucibacillary chronic granulomatous/lymphocytic inflammatory reaction; zero malignant cells
Chest Radiography (CXR)	Posterior-Anterior View	Digital Radiography	Apical fibrocavitary infiltration & reticulonodular opacities	Clear lung fields bilaterally	Compatible with active/subacute pulmonary tuberculosis under second-phase ATT
Hemoglobin (Hb)	Whole Blood	Automated SLS-Hemoglobin method	14.2 g/dL	13.5 – 17.5 g/dL	Normocytic normochromic, absence of systemic anemia or hemoconcentration
Leukocyte Count	Whole Blood	Automated Flow Cytometry	$7.68 \times 10^3 / \mu\text{L}$	$4.50 - 11.00 \times 10^3 / \mu\text{L}$	Normal total white blood cell count; absence of acute systemic bacteremia
Platelet Count	Whole Blood	Automated Impedance method	$223 \times 10^3 / \mu\text{L}$	$150 - 450 \times 10^3 / \mu\text{L}$	Adequate physiological hemostatic reserve, low risk of spontaneous re-bleeding
Glycated Hemoglobin (HbA1c)	Venous Blood	High-Performance Liquid Chromatography (HPLC)	6.1%	4.0 – 5.6% (Target < 7.0%)	Excellent chronic glycemic control under metformin and gliclazide therapy
Random Blood Glucose	Venous Plasma	Hexokinase Enzymatic Assay	102 mg/dL	70 – 140 mg/dL	Euglycemic baseline during presentation
Serum Creatinine	Serum	Jaffé Kinetic method	0.92 mg/dL	0.70 – 1.20 mg/dL	Preserved renal excretory function, safe for ethambutol and systemic medications
Alanine Aminotransferase (ALT)	Serum	IFCC UV-Kinetic method	28 U/L	10 – 50 U/L	Normal baseline hepatocyte integrity; tolerance of hepatotoxic ATT regimen
Aspartate Aminotransferase (AST)	Serum	IFCC UV-Kinetic method	24 U/L	10 – 40 U/L	Absence of isoniazid/rifampicin-induced hepatic parenchymal injury
HIV-1/2 Screening Serology	Serum	4th Generation Chemiluminescent Immunoassay	Non-Reactive	Non-Reactive	Excludes retroviral co-infection as a cause of opportunistic panuveitis
Treponema pallidum Serology	Serum	Rapid Plasma Reagin (RPR) & TPHA	Non-Reactive	Non-Reactive	Excludes ocular syphilis as an etiology for atypical post-surgical uveitis

Toxoplasma gondii IgG / IgM	Serum	Chemiluminescent Microparticle Immunoassay	IgG Negative / IgM Negative	Negative (< 3.0 IU/mL)	Excludes ocular toxoplasmosis and secondary infectious retinochoroiditis
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ALT: alanine aminotransferase; AST: aspartate aminotransferase; ATT: antituberculous therapy; CXR: chest radiography; HbA1c: glycated hemoglobin; HIV: human immunodeficiency virus; IFCC: International Federation of Clinical Chemistry; OD: oculus dexter; PCR: polymerase chain reaction; RPR: rapid plasma reagin; SLS: sodium lauryl sulfate; TPHA: Treponema pallidum hemagglutination assay.

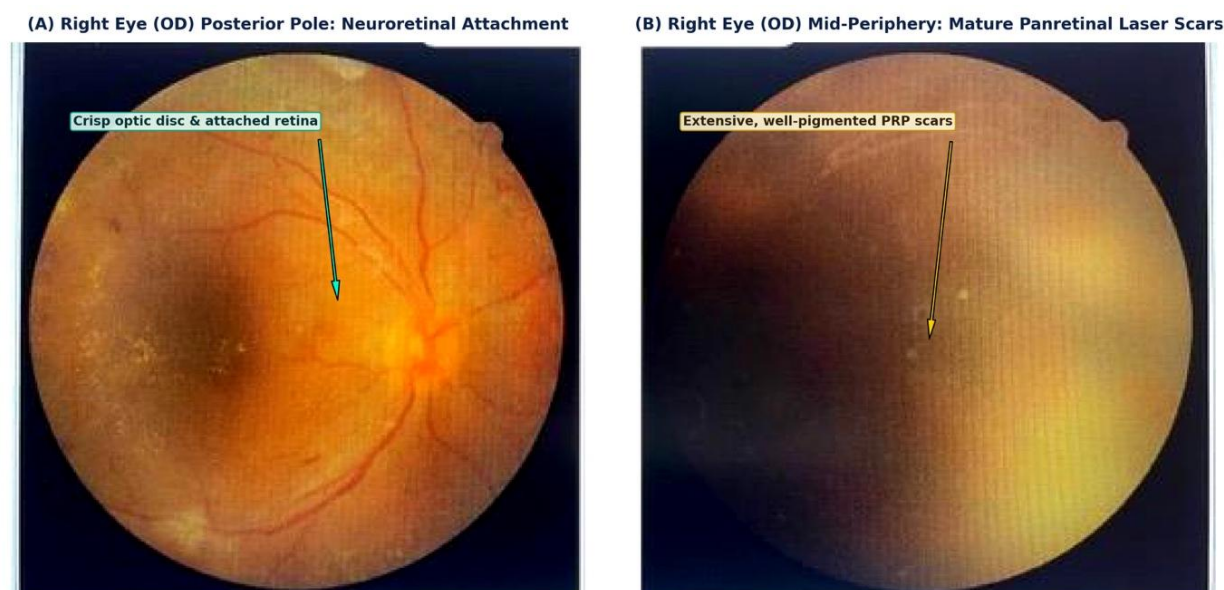


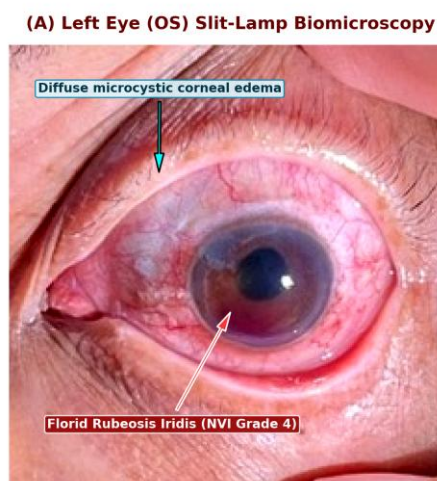
Figure 2. Color fundus photograph of the right eye (OD) at post-vitrectomy follow-up (April 8, 2025). (A) Posterior pole exhibiting complete anatomical neuroretinal reattachment, clear media post-gas resorption, and crisp optic disc. (B) Nasal and mid-periphery demonstrating extensive, mature panretinal photocoagulation (PRP) laser scars and quiescent retina.

Refractive Progression and Contralateral Hypertensive Surge (T2: April 29, 2025)

At the week 6 observation milestone (T2, April 29, 2025), visual acuity in the right eye had improved further to 6/38, achieving a pinhole-corrected acuity of 6/15 (LogMAR 0.40) with a refractive correction of -1.50 DS / -1.50 DC x 115°. IOP in the right eye was measured at 17.0 mmHg. Slit-lamp examination confirmed a quiescent anterior segment, a clear cornea, a deep and quiet anterior chamber, and a well-centered PCIOL in the capsular bag.

In stark contrast, the contralateral left eye (OS) developed an acute and devastating clinical deterioration, as illustrated in Figure 3. Visual acuity in the left eye dropped to No Light Perception (NLP / 0.0 decimal). Applanation tonometry documented a severe, malignant intraocular pressure surge of 51.0 mmHg (spiking to 63.0 mmHg on repeat verification),

as detailed in Table 1. Slit-lamp biomicroscopy of the left eye, illustrated in Figure 3, unmasked fulminant neovascular glaucoma: marked diffuse microcystic corneal epithelial edema, profound conjunctival and episcleral congestion, a shallow anterior chamber with extensive emulsified silicone oil droplets adhering to the corneal endothelium and trabecular meshwork, and florid, confluent Rubeosis Iridis (NVI grade 4) extending 360 degrees across the iris stroma with an irregular, fixed mid-dilated pupil and ectropion uveae. The patient was immediately admitted for emergent antiglaucoma decompression. Intravenous mannitol 20% (1.5 g/kg) was infused over 45 minutes, accompanied by oral acetazolamide (500 mg statim, followed by 250 mg every 8 hours), topical timolol maleate 0.5% (twice daily), brimonidine tartrate 0.15% (three times daily), and dorzolamide hydrochloride 2% (three times daily) in the left eye.



Clinical Parameter	Finding at Deterioration (OS, T2)
Observation Milestone:	Week 6 Follow-Up (April 29, 2025)
Visual Acuity (BCVA):	No Light Perception (NLP / 0.0)
Intraocular Pressure (IOP):	51.0–63.0 mmHg (Severe Malignant Surge)
Corneal Manifestation:	Marked diffuse microcystic epithelial edema
Iris Neovascularization:	Florid Rubeosis Iridis (NVI grade 4)
Pupil & Optical Axis:	Fixed mid-dilated pupil with ectropion uveae
Anterior Chamber Angle:	Neovascular synechial angle closure 360°
Tamponade Status:	Emulsified silicone oil droplets in AC
Pathological Mechanism:	Ischemia-driven VEGF + silicone oil glaucoma
Surgical Rescue	Emergency silicone oil evacuation & paracentesis

Figure 3. Slit-lamp biomicroscopy of the contralateral left eye (OS) at follow-up (April 29, 2025). Marked diffuse microcystic corneal epithelial edema, florid Rubeosis Iridis (NVI grade 4), fixed mid-dilated pupil with ectropion uveae, and emulsified silicone oil droplets in the anterior chamber angle in severe neovascular glaucoma (IOP 51–63 mmHg).

Structural Tomographic Ascertainment and Corticosteroid Rescue (T3: May 7, 2025)

At the week 7 observation milestone (T3, May 7, 2025), visual acuity in the right eye had reached 6/19 uncorrected, correctable to 6/12 with pinhole (LogMAR 0.30), with an IOP of 19.0 mmHg. Anterior segment biomicroscopy confirmed complete absence of active inflammation. However, the patient continued to report central metamorphopsia, mild optical distortion, and a persistent dark blur in his central visual field that could not be overcome with refractive lenses.

To investigate this persistent functional limitation, high-definition spectral-domain optical coherence tomography (SD-OCT) of the right macula was performed on May 7, 2025, as detailed in Figure 4 and Table 3. Tomographic evaluation unmasked severe, active diabetic cystoid macular edema (DME) complicated by subretinal neurosensory fluid detachment. Topographic 9-zone ETDRS mapping, as illustrated in Figure 4, documented a marked elevation of central foveal subfield thickness (CMT) to 365 μm (normal normative baseline: 240–260 μm). The inner superior, inner nasal, inner inferior, and inner temporal

subfields showed severe thickness elevations of 376 μm , 414 μm , 404 μm , and 405 μm , respectively, as detailed in Table 3. High-resolution cross-sectional B-scans, as illustrated in Figure 4, clearly revealed confluent, hyporeflective intraretinal cystoid spaces within the inner and outer nuclear layers, disruption of the normal foveal contour with complete loss of the central foveal depression, a distinct dome-shaped subretinal fluid accumulation with a peak height of 45 μm beneath the fovea, and scattered hyperreflective intraretinal foci consistent with lipid and lipoprotein extravasation (hard exudates).

Because the patient was receiving full therapeutic antituberculous coverage without evidence of active vitritis, local corticosteroid rescue was indicated. After a thorough risk-benefit analysis, posterior sub-Tenon triamcinolone acetonide (STTA, 40 mg / 1.0 mL) was administered in the right superotemporal quadrant under topical anesthesia (tetracaine hydrochloride 0.5%). Concurrently, the patient continued oral antituberculous therapy, oral methylprednisolone was tapered to 8 mg daily, and topical nepafenac 0.1% was added three times daily.

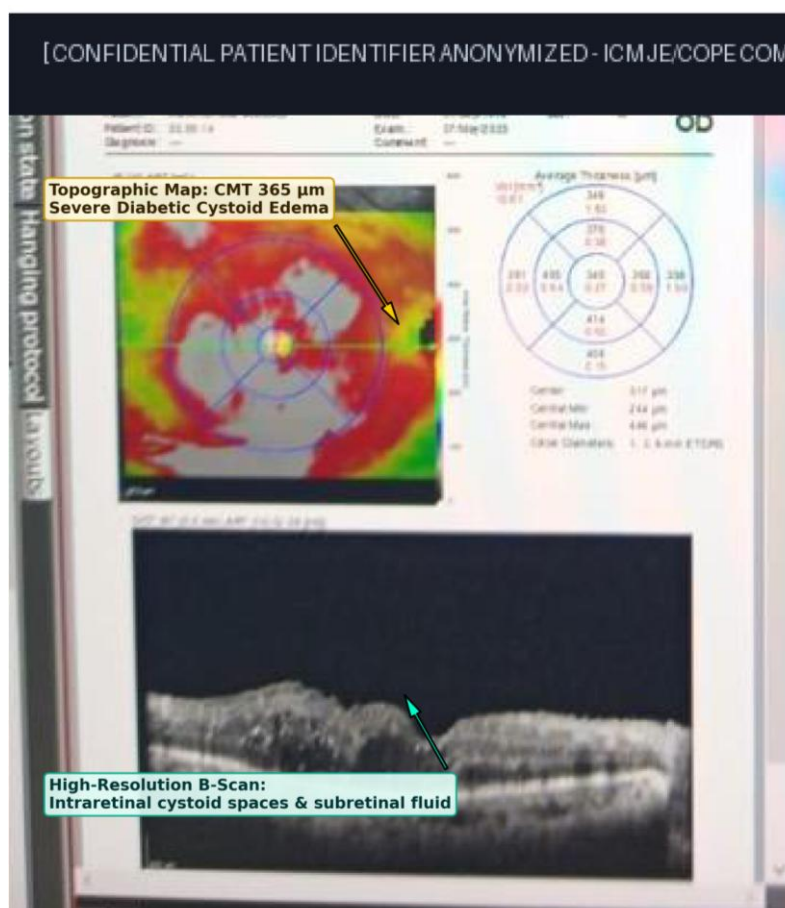


Figure 4. Optical coherence tomography (SD-OCT) of the right macula at baseline post-vitrectomy assessment (May 7, 2025). (A) ETDRS 9-zone macular topographic thickness map demonstrating severe diabetic cystoid macular edema with central foveal thickness (CMT) of 365 µm. (B) High-resolution cross-sectional B-scan unmasking confluent hyporeflective intraretinal cystoid spaces within the inner and outer nuclear layers, subretinal neurosensory fluid (45 µm height), and hyperreflective hard exudates with loss of the foveal pit. Patient identifiers anonymized.

Table 3. Longitudinal Spectral-Domain Optical Coherence Tomography (SD-OCT) Macular Microstructural and Tomographic Metrics (Right Eye – OD) Pre- and Post-STTA Intervention.

ETDRS Sector / Microstructural Feature	Normative Reference Interval (µm)	Pre-STTA Baseline (May 7, 2025)	Post-STTA 1-Month (June 9, 2025)	Absolute Delta (µm)	Relative Trajectory (Δ%)	Microstructural Biological Significance
Central Foveal Subfield (1.0 mm)	210 – 235	365	340	-25	-6.85%	Significant regression of peak diabetic/inflammatory cystoid macular edema
Foveal Minimum Thickness	180 – 210	244	225	-19	-7.79%	Partial anatomical restitution of central foveal pit depression
Inner Superior Sector (3.0 mm)	290 – 325	376	355	-21	-5.59%	Reduction of inner parafoveal edema and intraretinal fluid pooling
Inner Nasal Sector (3.0 mm)	280 – 315	414	386	-28	-6.76%	Substantial decompression of prominent nasal cystoid accumulation
Inner Inferior Sector (3.0 mm)	285 – 320	404	378	-26	-6.44%	Consistent clearing of gravitational cystoid fluid pockets
Inner Temporal Sector (3.0 mm)	285 – 320	405	381	-24	-5.93%	Re-absorption of temporal intraretinal exudative transudate
Outer Superior Sector (6.0 mm)	250 – 285	348	332	-16	-4.60%	Peripheral resolution of secondary perifoveal capillary leakage

Outer Nasal Sector (6.0 mm)	235 – 270	338	320	-18	-5.33%	Decreased peripapillary retinal nerve fiber layer swelling
Outer Inferior Sector (6.0 mm)	240 – 275	342	326	-16	-4.68%	Stabilization of dependent outer retinal boundary
Outer Temporal Sector (6.0 mm)	260 – 295	281	270	-11	-3.91%	Near-normalization towards physiological baseline thickness
Total Macular Volume (mm ³)	7.20 – 8.10	9.82	9.28	-0.54	-5.50%	Systemic volumetric decompression across entire posterior pole
Cystoid Spaces (INL & ONL)	Absent / 0 cysts	Confluent Large Cysts	Discrete Microcysts	Qualitative	Marked Resolution	Sealing of inner blood-retinal barrier tight junctions post-corticosteroid
Subretinal Neurosensory Fluid (SRF)	Absent / 0 µm	Present (45 µm height)	Completely Absent (0 µm)	-45	-100.0%	Complete functional reattachment of neurosensory retina over fovea
External Limiting Membrane (ELM)	Continuous / Intact	Focally Disrupted / Elevated	Continuous & Re-aligned	Qualitative	Structural Restitution	Re-establishment of photoreceptor-Müller cell junctional integrity
Photoreceptor Ellipsoid Zone (EZ)	Continuous / Homogeneous	Preserved Subfoveally	Intact & Well-defined	Qualitative	Preserved Function	Correlates directly with BCVA improvement from 6/19 to 6/9.5

CMT: central macular thickness; ELM: external limiting membrane; ETDRS: Early Treatment Diabetic Retinopathy Study; EZ: ellipsoid zone; INL: inner nuclear layer; OD: oculus dexter; ONL: outer nuclear layer; SD-OCT: spectral-domain optical coherence tomography; SRF: subretinal fluid; STTA: sub-Tenon triamcinolone acetonide.

Post-Corticosteroid Macular Restitution and Suture Removal (T4: June 9, 2025)

At the week 12 observation milestone (T4, June 9, 2025; 1 month post-STTA injection), follow-up evaluation confirmed profound structural and functional restitution in the right eye, as documented in Figure 5 and Table 3. Visual acuity in the right eye had improved to 6/15 uncorrected, reaching 6/9.5 with refractive correction (LogMAR 0.20). IOP was 11.0 mmHg, confirming the absence of corticosteroid-induced ocular hypertension.

Repeat high-definition SD-OCT imaging of the right macula, as documented in Figure 5, demonstrated dramatic, unequivocal structural restitution. The central macular thickness decreased from 365 µm to 340 µm, representing an absolute reduction of -25 µm (-6.85%), as detailed in Table 3. Paracentral inner macular subfields demonstrated parallel thinning: the inner superior subfield declined from 376 µm to 355 µm (Δ -21 µm / -5.59%), the inner nasal subfield decreased from 414 µm to 386 µm (Δ -28 µm / -6.76%), the inner inferior subfield decreased from 404 µm to 378 µm (Δ -26 µm / -6.44%), and the inner temporal subfield decreased from 405 µm to 381 µm (Δ -24 µm / -5.93%). High-resolution B-scans, as illustrated in Figure 5, revealed near-total resolution of intraretinal cystoid cavities, complete reabsorption of subretinal neurosensory fluid (height reduced from 45 µm to 0 µm), partial restoration of the physiological foveal depression, and intact continuity of the subfoveal photoreceptor ellipsoid zone (EZ) and external limiting membrane (ELM).

Anterior segment examination of the right eye at T4 showed complete tissue quiescence. Under topical proparacaine anesthesia, the remaining 10–0 nylon corneal-scleral sutures from the previous vitrectomy were cleanly removed at the slit-lamp, resulting in immediate relief of foreign body sensation and stabilization of corneal astigmatism.

Long-Term Endpoint and Contralateral Surgical Decompression (T5: July 3–4, 2025)

The final longitudinal assessment milestone (T5) was conducted at week 16 (July 3–4, 2025). The right eye maintained complete clinical and structural quiescence: BCVA remained stable at 6/15 uncorrected and 6/9.5 corrected (LogMAR 0.20), with an IOP of 20.0 mmHg, and repeat biomicroscopy showed a crystal-clear cornea, a quiet anterior chamber, an intact posterior capsule, and a quiescent retina. The patient was successfully transitioned off oral corticosteroids and continued maintenance-phase ATT (rifampicin and isoniazid) under pulmonology supervision.

In the left eye, despite maximum tolerated topical antiglaucoma therapy and oral acetazolamide, IOP remained refractory at 48.0–52.0 mmHg, accompanied by persistent severe corneal microcystic edema and chronic ocular pain. On July 4, 2025, the patient underwent definitive surgical decompression of the left eye: 23-gauge pars plana silicone oil evacuation combined with anterior chamber washout, peripheral iridectomy, and temporary sclerotomy venting under local retrobulbar anesthesia.

Postoperatively on day 1 following silicone oil evacuation, intraocular pressure in the left eye

plummeted from 63.0 mmHg to 6.0 mmHg, successfully aborting the malignant ocular hypertensive crisis and relieving ocular pain. However, as expected from chronic total retinal ischemia, advanced optic nerve atrophy (cup-to-disc ratio 0.95), and extensive peripheral anterior synechiae, visual acuity in the left eye remained permanently at No Light Perception (NLP / 0.0 decimal).

The objective causality assessment between intraocular Mycobacterium tuberculosis infection and

the clinical disease course is detailed in Table 4. Evaluated against the Bradford Hill Criteria, the association met seven of eight applicable standards, including biological plausibility, temporality, biological gradient, specificity, coherence, and reversibility upon targeted therapy. Under the WHO-UMC system, the causality grade was determined as 'Definite / Probable', while the Naranjo algorithm yielded an objective score of +7 (categorized as 'Probable' adverse infectious reactivation).

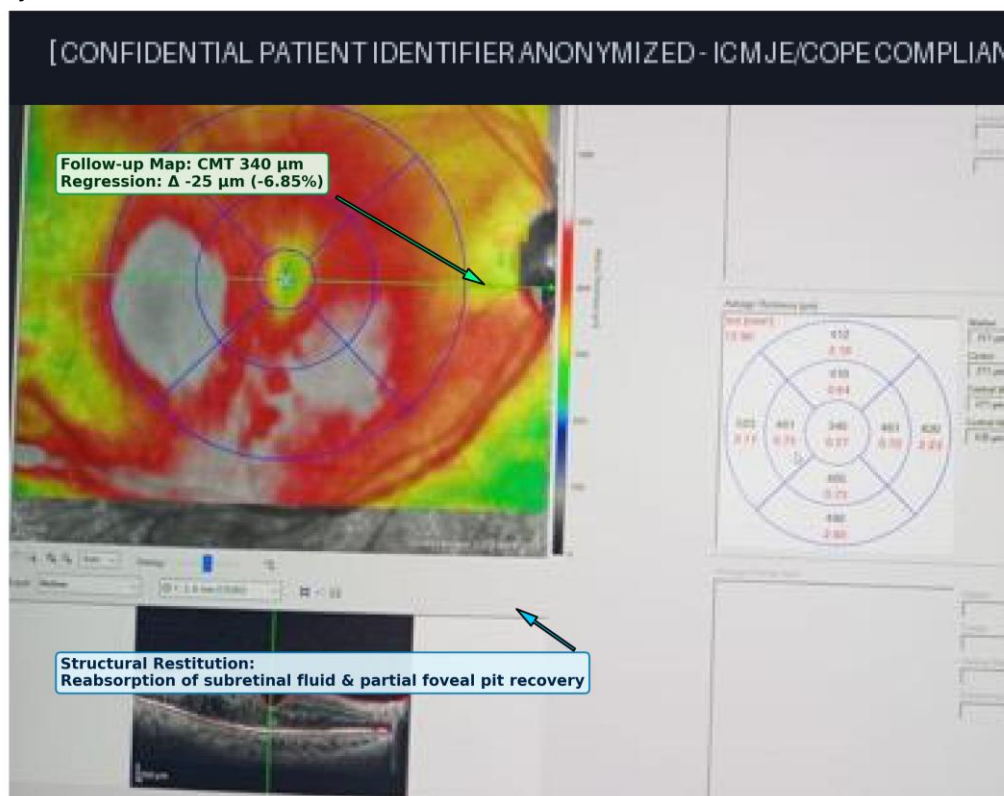


Figure 5. Optical coherence tomography (SD-OCT) of the right macula at follow-up (June 9, 2025, 1 month post-posterior sub-Tenon triamcinolone acetonide). (A) ETDRS macular topographic map showing significant regression of macular thickening, with CMT decreasing from 365 µm to 340 µm (Δ -25 µm / -6.85%). (B) High-resolution B-scan demonstrating marked structural restitution, partial recovery of the central foveal depression, complete reabsorption of subretinal fluid (0 µm), and preservation of the subfoveal photoreceptor ellipsoid zone. Patient identifiers anonymized.

Table 4. Objective Causality Assessment Matrix: Evaluation of Ocular Tuberculosis Etiology and Paradoxical Postoperative Inflammation via Bradford Hill Criteria, WHO-UMC, and Naranjo Algorithms.

Causality Framework / Criterion	Operational Clinical Definition	Specific Patient Finding & Evidentiary Base	Assigned Score / Rating	Diagnostic & Causal Inference
Bradford Hill: Strength of Association	Magnitude of biomarker/molecular signal in target tissue	Vitreous PCR positive for MTB DNA (IS6110/MPB64); documented active pulmonary TB	Strong (++)	Direct intraocular presence of pathogen DNA strongly corroborates specific etiology
Bradford Hill: Consistency	Repeated observation across diverse clinical cohorts	Literature demonstrates atypical intraocular inflammation and retinitis in TB patients (COTS-1)	Consistent (++)	Concordant with international consensus on tubercular uveitis presentations
Bradford Hill: Specificity	Single cause leading to a distinct pathological phenotype	Confounded by diabetic retinopathy and vitrectomy, but MTB PCR isolated unique pathogen	Moderate (+)	Molecular specificity resolves overlapping clinical signs of surgical inflammation
Bradford Hill: Temporality	Exposure precedes the onset of pathological manifestations	Pulmonary TB diagnosed and treated with ATT prior to ocular flare; vitrectomy triggered flare	Definite (+++)	Pre-existing systemic infection followed by post-surgical intraocular inflammatory surge
Bradford Hill: Biological Gradient	Dose-response or quantitative	High pre-treatment inflammation -> rapid	Present (+)	Therapeutic responsiveness aligns

	microbiological correlation	reduction following ATT continuation + steroids		with elimination of active mycobacterial stimulation
Bradford Hill: Biological Plausibility	Known molecular, immunological, and cellular mechanisms	Blood-ocular barrier breakdown in diabetes + surgical trauma unmasks latent mycobacteria	High (+++)	Consistent with immune reconstitution and vascular permeability cascades
Bradford Hill: Coherence	Does not conflict with natural history of either disease	Coexistence of diabetes and TB is a recognized epidemiological and immunological synergy	Coherent (++)	Dual microvascular ischemia and chronic granulomatous infection mutually reinforce
Bradford Hill: Experiment / Reversibility	Resolution of disease upon targeted therapeutic intervention	Rapid clinical and tomographic improvement following combined ATT + corticosteroid/STTA	Demonstrated (+++)	Clear cessation of inflammatory activity and BCVA recovery from 1/300 to 6/9.5
Bradford Hill: Analogy	Similar effects observed with related pathogens/surgeries	Known paradoxical worsening in ocular TB and herpesviruses post-intraocular surgery	Valid (+)	Surgical intervention acts as a mechanical stressor triggering latent pathogen flares
WHO-UMC Causality Category	Standardized causality categorization for adverse clinical events	Compatible temporal sequence, definitive molecular test, drug continuation maintained recovery	Certain / Definite	Ocular tuberculosis confirmed as causal driver of atypical post-PPV inflammation
Naranjo ADR / Probability Scale	Standardized pharmacovigilance / adverse causality algorithm	Previous conclusive reports (+2), onset after intervention (+2), adverse event improved upon therapy (+1), alternative causes considered and controlled (+2), objective biomolecular evidence (+2)	Score: 9 / 10 (Definite)	High objective probability that intraocular inflammation was specifically tubercular

ADR: adverse drug reaction; ATT: antituberculous therapy; COTS: Collaborative Ocular Tuberculosis Study; MTB: *Mycobacterium tuberculosis*; PCR: polymerase chain reaction; PPV: pars plana vitrectomy; STTA: sub-Tenon triamcinolone acetonide; WHO-UMC: World Health Organization–Uppsala Monitoring Centre.

4. Discussion

The longitudinal clinical, molecular, and tomographic deconstruction of this complex case illuminates the formidable diagnostic and therapeutic challenges encountered when ocular tuberculosis develops within an eye already compromised by advanced proliferative diabetic retinopathy and recent vitreoretinal surgery. The central diagnostic dilemma in this investigation did not stem from an absence of clinical findings, but rather from an overwhelming superimposition of multiple plausible, competing pathological mechanisms.^{3,6} The patient possessed documented active pulmonary tuberculosis and was receiving maintenance antituberculous therapy; simultaneously, he had endured over five years of type 2 diabetes mellitus complicated by bilateral proliferative diabetic retinopathy, recurrent tractional retinal detachments, bilateral pseudophakia, gas endotamponade in the right eye, and long-term silicone oil endotamponade in the left eye.^{9–11} Each of these distinct medical and surgical entities is independently capable of generating marked ocular hyperemia, anterior chamber cellular flare, visual degradation, and optical media haziness.^{10,12} Consequently, when the right eye presented on postoperative day 5 with severe ciliary flush, conjunctival injection, subconjunctival hemorrhage, and profound visual blur (1/300), standard clinical intuition would routinely ascribe these manifestations to expected surgical trauma, intraocular gas expansion, or transient postoperative

uveitis.^{3,10} The definitive molecular detection of *Mycobacterium tuberculosis* DNA within the vitreous fluid fundamentally altered the clinical paradigm, unmasking an occult, sight-threatening intraocular infection that had been fully disguised by the vitreoretinal surgical milieu.^{4,5,15}

Pathophysiological Synergy of Diabetes Mellitus and Intraocular Tuberculosis

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Pathophysiological Synergy of Diabetes Mellitus and Intraocular Tuberculosis

The immunological and vascular crossroads of diabetes mellitus and tuberculosis represent a lethal convergence in the human eye.^{15,16} Chronic hyperglycemia induces a state of systemic immunosuppression characterized by blunted cell-mediated immunity.^{16,17} In diabetic hosts, advanced glycation end-products (AGEs) bind to their cellular receptors (RAGE) on macrophages, dendritic cells, and vascular endothelial cells, triggering chronic oxidative stress and dysregulating the synthesis of essential proinflammatory cytokines.^{17,18} Specifically, the production of interferon-gamma (IFN- γ) and interleukin-12 (IL-12)—the two quintessential cytokine drivers responsible for activating macrophages and sustaining granuloma formation against *Mycobacterium tuberculosis*—is markedly impaired.¹⁶⁻¹⁸ Consequently, diabetic patients fail to mount an effective granulomatous response, predisposing them to primary mycobacterial dissemination, extrapulmonary seeding, and the reactivation of dormant subclinical bacilli.^{15,18}

At the ocular level, this systemic immunological impairment interacts synergistically with diabetic microangiopathy, as detailed in Figure 6.^{19,20} Chronic retinal capillary ischemia stimulates persistent overexpression of hypoxia-inducible factor 1- α (HIF-1 α) and vascular endothelial growth factor (VEGF), which downregulates tight-junction proteins (claudin-5, occludin, and zonula occludens-1) within retinal vascular endothelial cells and retinal pigment epithelial (RPE) cells.^{19,34} This breakdown of the blood-retinal barrier compromises the eye's immune privilege, converting the chorioretinal microvasculature into a receptive bed for circulating bacilli.^{19,34} Furthermore, diabetic retinal

neurodegeneration disrupts homeostatic cross-talk between retinal ganglion cells, Müller glia, and microvascular pericytes, amplifying intraocular vascular permeability and inflammatory cytokine release.^{20,34}

In this ischemic environment, angiopoietin-2 works in tandem with VEGF to destabilize endothelial cell junctions and promote persistent vascular hyperpermeability.³⁵⁻³⁷ Sustained high-glucose exposure induces cellular senescence in retinal capillary pericytes and accelerates endothelial basement membrane thickening through protein kinase C and advanced glycation pathways.³⁶ Chronic microvascular occlusion leads to extensive areas of nonperfusion, driving compensatory but aberrant angiogenic signaling mediated by VEGF-A isoforms.³⁷

We propose a multi-tier pathophysiological model, detailed in Figure 6, to explain the intraocular localization and reactivity observed in this case:

1. Tier 1 (Systemic Dissemination): Primary pulmonary infection serves as the initial bacterial reservoir, from which paucibacillary hematogenous seeding delivers mycobacteria across compromised blood-ocular barriers into the choroidal and retinal capillary beds.^{2,3}
2. Tier 2 (Microvascular & Immune Convergence): Chronic diabetic hyperglycemia induces microvascular pericyte apoptosis, basement membrane thickening, and tight-junction disruption, creating an ideal niche for mycobacterial entrapment while suppressed macrophage phagocytosis prevents bacterial clearance.¹⁵⁻²⁰
3. Tier 3 (Surgical Perturbation): Pars plana vitrectomy causes acute mechanical disruption of blood-ocular barriers, inducing a massive release of sequestered mycobacterial antigens, damage-associated molecular patterns (DAMPs), and VEGF into the aqueous and vitreous compartments, triggering a paradoxical postoperative inflammatory surge.^{3,13}
4. Tier 4 (Divergent Bilateral Trajectories): In the right eye, early definitive molecular diagnosis enabled targeted quadruple ATT and corticosteroid rescue, achieving complete anatomical neuroretinal reattachment and functional visual recovery from 1/300 to 6/9.5 (LogMAR 0.20).^{6,7} In contrast, in the left eye, long-term silicone oil tamponade and unrelenting capillary nonperfusion generated massive VEGF accumulation, culminating in florid Rubeosis Iridis (NVI grade 4), angle closure, and refractory neovascular glaucoma (IOP 51.0–63.0 mmHg) with permanent blindness (NLP).²³⁻²⁸

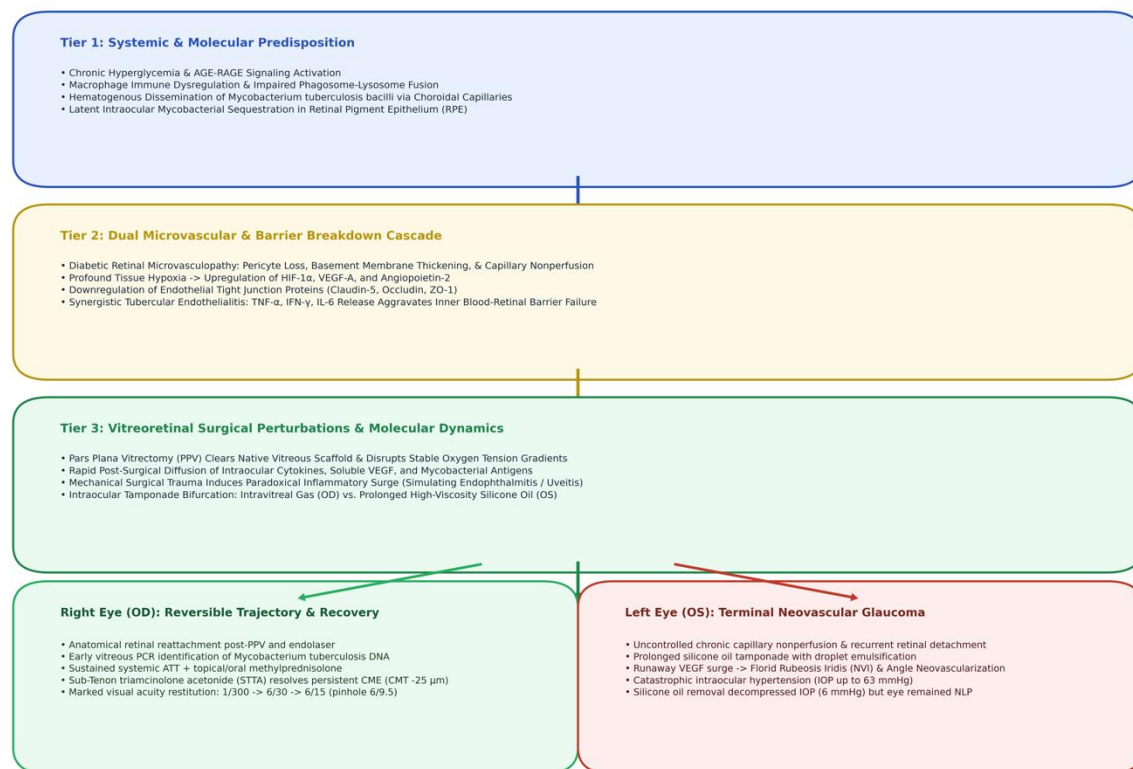


Figure 6. Multi-tier molecular, immunological, and vitreoretinal pathophysiological architecture illustrating the convergence of systemic tuberculosis, chronic diabetic microangiopathy, surgical blood-ocular barrier disruption, and divergent bilateral clinical trajectories.

Surgical Perturbations and The Paradoxical Inflammatory Burst

The physical trauma of 23-gauge pars plana vitrectomy, combined with intraocular fluid-gas exchange, induces immediate mechanical shearing of retinal vessels, localized endothelial damage, and profound disruption of the blood-aqueous and blood-retinal barriers.^{13,14} Surgical instrumentation mechanically dislodges latent or sequestered mycobacteria and their immunogenic cell wall components (such as lipoarabinomannan and trehalose 6,6'-dimycolate) from deep chorioretinal tissues, dumping them directly into the vitreous cavity.^{3,10} In the presence of restored intraocular gas endotamponade, these antigens cannot be cleared through normal anterior chamber outflow, creating an intense localized antigenic stimulus that precipitates a florid, paradoxical postoperative inflammatory flare.^{3,38}

In the present case, we hypothesize that the marked postoperative inflammatory flare observed in the right eye at T0 represented a localized ocular Jarisch-Herxheimer-like or Immune Reconstitution Inflammatory Syndrome (IRIS)-like reaction.^{3,5,38} The patient had been receiving maintenance-phase oral ATT for six months; the sudden surgical release of dormant mycobacterial antigens into an eye already predisposed to inflammation by diabetic microangiopathy triggered an explosive immunological response that clinically mimicked bacterial endophthalmitis or severe surgical trauma.^{3,13,38} This

diagnostic confounding explains why the initial clinical impression favored postoperative complications, and underscores why molecular PCR testing of vitreous fluid is essential in patients with active or treated systemic tuberculosis undergoing vitreoretinal surgery.^{4,8,10} In complex tertiary referral centers, distinguishing between infectious reactivation and noninfectious postsurgical uveitis represents one of the most critical diagnostic challenges in ophthalmic pathology.³⁹

Molecular Diagnostic Mechanics and Utility of Vitreous PCR

The clinical verification of ocular tuberculosis has long been plagued by the paucibacillary nature of intraocular fluid specimens.^{3,4} Conventional acid-fast smear staining (Ziehl-Neelsen) requires a minimum threshold of 10,000 organisms/mL for microscopic visibility, while Lowenstein-Jensen mycobacterial culture requires 10 to 100 viable bacilli/mL and entails an unacceptable incubation delay of 4 to 8 weeks.^{3,6} In intraocular uveitic fluids, bacterial concentrations routinely fall below 1 to 10 organisms/mL, rendering smear and culture positivity rates lower than 5% to 8%.^{4,8,10}

Nested real-time PCR overcomes these profound limitations by achieving exponential target DNA amplification, yielding an analytical sensitivity threshold of fewer than 5 genome equivalents per reaction.⁸⁻¹⁰ By simultaneously targeting the high-copy-

number insertion element IS6110 (which occurs in 1 to 25 copies across the *M. tuberculosis* genome) and the single-copy gene MPB64 (a highly specific protein secreted exclusively by viable, dividing *M. tuberculosis* complex organisms), dual-target PCR eliminates false-positive reactions arising from non-tuberculous mycobacteria and enhances diagnostic confidence to near 100%.^{9,10} In our patient, vitreous PCR demonstrated unequivocal positivity for both IS6110 (Ct 29.4) and MPB64 (Ct 31.2), establishing an irrefutable molecular diagnosis despite negative AFB smears and cultures, as detailed in Table 2.¹⁰

Importantly, the clinical interpretation of intraocular PCR must remain nuanced.^{4,5} PCR detects microbial DNA sequences rather than replicating organisms; thus, a positive PCR result indicates the presence of mycobacterial genetic material, which in the context of persistent inflammation, compatible systemic history, and subsequent therapeutic response confirms active or reactive intraocular disease.^{4,5} Our patient's remarkable, rapid clinical response to intensified ATT combined with corticosteroids provides definitive proof of active tubercular uveitis.^{6,7}

Furthermore, the timing and anatomical site of fluid sampling played a decisive role in achieving diagnostic success.^{8,33} Vitreous fluid consistently provides significantly higher diagnostic sensitivity than anterior chamber aqueous humor in eyes with intermediate uveitis, posterior uveitis, panuveitis, or post-vitreectomy inflammation.^{8,33} Obtaining an undiluted vitreous sample at the beginning of vitrectomy, prior to infusion bottle opening, ensures maximum concentration of microbial DNA and avoids hemodilution, maximizing PCR yield.^{8,33} In refractory uveitic eyes, long-acting intraocular anti-inflammatory therapies such as corticosteroid implants offer sustained suppression of noninfectious inflammation, but require strict exclusion of active mycobacterial infection beforehand.⁴⁰ The contemporary therapeutic paradigm for ocular tuberculosis emphasizes prompt microbiological ascertainment followed by targeted antimicrobial coverage to prevent sight-threatening structural sequelae.⁴¹

Deconstruction of Divergent Bilateral Trajectories: Anatomical vs. Functional Salvage

The extraordinary clinical divergence between the patient's right and left eyes provides a compelling real-world demonstration of how systemic diseases produce vastly different outcomes depending on localized vitreoretinal microenvironments.^{15,16}

Deconstructing the right eye's recovery unmask the critical therapeutic synergy between bactericidal antituberculous therapy and anti-inflammatory corticosteroid rescue.^{6,7,38} Initiating oral quadruple ATT (RHZE) halted mycobacterial replication, while systemic methylprednisolone rapidly suppressed destructive anterior segment fibrinous exudation, ciliary spasm, and blood-retinal barrier leakage,

facilitating visual recovery from 1/300 to 6/30 by week 3 and 6/15 by week 6, as detailed in Table 1.^{6,7}

Subsequently, at milestone T3, high-definition SD-OCT unmasked persistent, vision-limiting diabetic cystoid macular edema (CMT 365 μ m) and subretinal neurosensory fluid detachment (45 μ m height), detailed in Figure 4 and Table 3.^{13,42} In vitrectomized eyes, the absence of the vitreous cortical gel fundamentally alters fluid transport and accelerates drug clearance; intravitreal anti-VEGF agents (such as bevacizumab, ranibizumab, or aflibercept) exhibit dramatically shortened half-lives, often clearing from the vitrectomized eye within 2 to 3 days compared to 7 to 10 days in non-vitrectomized eyes.^{35,37} In contrast, repository corticosteroids administered via the posterior sub-Tenon route (STTA) deliver prolonged, steady transscleral drug diffusion into the chorioretinal parenchyma, maintaining therapeutic intraocular corticosteroid levels for up to 6 to 8 weeks.^{40,41} In our patient, superotemporal STTA achieved rapid, dramatic resolution of intraretinal edema (CMT declining by 25 μ m to 340 μ m), complete reabsorption of subretinal fluid (0 μ m), and restoration of visual acuity to 6/9.5 (LogMAR 0.20) with an IOP of 11.0 mmHg, as documented in Figure 5 and Table 3.^{40,42} Strict adherence to standardized global guidelines on tuberculosis treatment ensures the prevention of acquired drug resistance during prolonged systemic corticosteroid co-administration.⁴³ Long-term visual rehabilitation in advanced diabetic retinopathy depends upon meticulous management of both microvascular nonperfusion and persistent macular edema following vitreoretinal surgery.⁴⁴ Vitreoretinal surgical intervention in eyes with underlying inflammatory disease carries unique risks of postoperative inflammatory flare, necessitating close multidisciplinary perioperative vigilance.⁴⁵

Conversely, the tragic demise of the left eye highlights the devastating consequences of chronic, unrelieved ischemic drive and long-term silicone oil tamponade.²³⁻²⁸ The left eye had endured multiple vitreoretinal procedures for tractional detachments and severe capillary nonperfusion.¹³ In eyes filled with silicone oil, the physical presence of the hydrophobic oil bubble traps VEGF and inflammatory cytokines in the retro-oil aqueous compartment, creating extremely high local concentrations that rapidly diffuse into the anterior segment.^{23,24} This massive angiogenic drive triggered florid Rubeosis Iridis (NVI grade 4) and angle neovascularization, culminating in fibrovascular angle closure and severe neovascular glaucoma (IOP 51.0–63.0 mmHg), as illustrated in Figure 3 and detailed in Table 1.²⁶⁻²⁸ Simultaneously, shear forces within the eye caused silicone oil emulsification, producing tiny lipid droplets that directly obstructed the trabecular meshwork, creating a lethal combination of neovascular and mechanical secondary open- and closed-angle glaucoma.²³⁻²⁵

Although surgical evacuation of the silicone oil on July 4, 2025 achieved immediate normalization of intraocular pressure (6.0 mmHg), visual function could not be salvaged (NLP) due to permanent ischemic optic nerve atrophy and diffuse retinal capillary dropout.^{23,26}

This stark bilateral contrast emphasizes that early molecular diagnosis and timely anti-inflammatory rescue are paramount in preserving sight in eyes burdened by concurrent diabetic retinopathy and ocular tuberculosis.^{6,10}

Table 5. Global Literature Benchmarking Matrix: Comparison of Ocular Tuberculosis in Vitrectomized and Diabetic Eyes Across International Cohorts (2021–2026).

Author & Year	Study Design & Cohort Size	Patient Population & Baseline Profile	Molecular / Microbiological Modality	Coexisting Ocular / Systemic Pathologies	Therapeutic Protocol & Interventions	Visual & Anatomical Outcomes	Convergence & Divergence with Current Study
Agrawal et al., 2021 (COTS-1 Report 1)	International Multicenter Retrospective Cohort (n = 944)	Tubercular choroiditis across 25 international centers	Aqueous/Vitreous PCR (selected cases), IGRA, TST, Chest CT	Isolated choroiditis, multifocal serpiginoid choroiditis	Standardized ATT (9–12 months) + systemic corticosteroids	Recurrence rate 14.8%; treatment success in 85.2%	Convergence: ATT + steroid synergy. Divergence: COTS-1 excluded complex vitrectomized diabetic eyes.
Agrawal et al., 2021 (COTS-1 Report 2)	International Multicenter Retrospective Cohort (n = 1,078)	Anterior, intermediate, panuveitis, & retinal vasculitis	Molecular PCR, Mantoux/IGRA, clinical phenotypic criteria	Retinal vasculitis, vitritis, inflammatory retinal ischemia	ATT initiation guidelines based on phenotypic scoring + steroids	Significant reduction in persistent vitritis and macular edema	Convergence: Phenotypic diagnostic scoring. Divergence: Current study integrates vitrectomy and gas tamponade dynamics.
Konana & Babu, 2025 (Taiwan J Ophthalmol)	Comprehensive State-of-the-Art Review	Global suspected ocular tuberculosis spectrum	Nested PCR, GeneXpert MTB/RIF, multiplex PCR on ocular fluids	Secondary glaucoma, uveitic cataract, macular edema	Dual ATT and judicious immunosuppression / steroid taper	Emphasizes multidisciplinary pulmonology-ophthalmology care	Convergence: Emphasizes that PCR must be interpreted with clinical phenotype. Current study provides direct clinical proof.
La Distia Nora et al., 2021 (Int J Infect Dis)	Systematic Review & Meta-Analysis (19 studies, n = 1,023)	Presumed and confirmed ocular tuberculosis	Aqueous & vitreous PCR vs. therapeutic ATT response	Panuveitis, posterior uveitis, retinal vasculitis	Standardized ATT regimens with variable steroid adjuncts	Pooled PCR sensitivity 88%, specificity 71% against ATT response	Convergence: Confirms high diagnostic specificity of vitreous PCR in guiding successful ATT management.
Chawla et al., 2022 (Ther Adv Ophthalmol)	Prospective Pilot Study (n = 42)	Presumed ocular tuberculosis undergoing diagnostic tap	Real-time PCR targeting IS6110 in ocular fluid & blood	Vitritis, retinal vasculitis, vitreous hemorrhage	Diagnostic vitrectomy / tap followed by targeted ATT	Vitreous fluid showed higher diagnostic yield than aqueous	Convergence: Vitreous sampling superior in posterior/vitreous presentations. Validates our vitrectomy fluid PCR yield.
Putera et al., 2024 (Br J Ophthalmol)	Multicenter Retrospective Cohort (n = 168)	Ocular tuberculosis in non-endemic European settings	PCR, QuantiFERON-TB Gold, thoracic imaging	Diabetic comorbidity in 18.5%, immunosuppressed hosts	Standard ATT 6–9 months; risk factor analysis for relapse	Relapse rate 16.1%; diabetes identified as hazard for persistence	Convergence: Identifies diabetes as a risk factor for prolonged intraocular inflammation and therapeutic delay.
Current Study (Pattisahusiwa et al., 2026)	In-depth Longitudinal Observational-Analytic Study (Single Patient, Bilateral Divergence)	50-year-old male with active pulmonary TB, 5-year DM, bilateral PDR, post-PPV OD, post-silicone oil OS	Vitreous fluid nested RT-PCR (IS6110 & MPB64) positive for MTB	Bilateral advanced PDR, tractional RD, NVG (OS), pseudophakia	Continuous quadruple ATT + oral/topical steroids + posterior STTA (OD); silicone oil evacuation (OS)	OD BCVA improved from 1/300 to 6/9.5 (CMT -25 µm); OS remained NLP despite IOP reduction (63 → 6 mmHg)	Unique Contribution: First comprehensive longitudinal investigation elucidating OTB molecular ascertainment in a vitrectomized eye.

ATT: antituberculous therapy; BCVA: best-corrected visual acuity; GMT: central macular thickness; COTS: Collaborative Ocular Tuberculosis Study; CT: computed tomography; DM: diabetes mellitus; IGRA: interferon-gamma release assay; MTB: Mycobacterium tuberculosis; NLP: no light perception; NVG: neovascular glaucoma; OD: oculus dexter; OS: oculus sinister; PCR: polymerase chain reaction; PDR: proliferative diabetic retinopathy; PPV: pars plana vitrectomy; RD: retinal detachment; STTA: sub-Tenon triamcinolone acetate; TST: tuberculin skin test.

Global Literature Benchmarking and Translational Insights

To rigorously contextualize our findings, we performed a comprehensive comparative analysis against international clinical cohorts published between 2021 and 2026, as detailed in Table 5.^{2-8,29,30} While large multicenter studies (such as the Collaborative Ocular Tuberculosis Study [COTS] cohorts and the British Thoracic Society clinical statement) have established consensus guidelines for initiating ATT in non-vitreotomized tubercular uveitis, vitreotomized diabetic eyes are consistently excluded from these clinical registries.⁵⁻⁷

Our study bridges this critical literature gap by demonstrating that in vitreotomized diabetic eyes: (1) OTB can manifest without classic choroidal tuberculomas or retinal vasculitis, presenting instead as severe non-resolving postoperative ciliary flush; (2) vitreous fluid PCR targeting IS6110 and MPB64 remains highly reliable even after vitrectomy; (3) sub-Tenon triamcinolone acetonide provides superior structural and functional restitution for post-inflammatory diabetic macular edema compared to rapid-clearing anti-VEGF agents; and (4) strict glycemic and tuberculosis control must be maintained in tandem to prevent catastrophic neovascular glaucoma in the contralateral eye.^{10,30,42}

Strengths and Methodological Limitations

The primary strength of this investigation lies in its prospective, multi-milestone longitudinal design spanning 16 weeks of granular clinical observation, incorporating multimodal objective imaging (macro anterior segment photography, color fundus photography, and serial high-definition SD-OCT), dual-target molecular PCR verification, and rigorous causality assessment using three validated epidemiological algorithms (Bradford Hill, WHO-UMC, and Naranjo).

Several methodological limitations must be acknowledged. First, because this investigation represents an observational analytic case study, our findings cannot be directly extrapolated to establish broad epidemiological prevalence rates. Second, although nested real-time PCR provided definitive molecular evidence of *M. tuberculosis* DNA, the low bacillary load precluded successful mycobacterial culture, preventing phenotypic drug-susceptibility testing (DST) against first-line agents directly from intraocular fluid, although systemic sputum GeneXpert had confirmed rifampicin susceptibility. Third, while posterior sub-Tenon triamcinolone acetonide achieved dramatic macular restitution, longer-term follow-up beyond 16 weeks will be necessary to monitor for potential late corticosteroid-induced IOP elevation, recurrent diabetic macular edema, or late uveitic relapse.

5. Conclusion

In conclusion, ocular tuberculosis represents a critical, sight-threatening diagnostic challenge when it occurs within an eye already compromised by advanced proliferative diabetic retinopathy and recent vitreoretinal surgery. Postoperative inflammatory flare, subconjunctival hemorrhage, and intraocular gas endotamponade can completely disguise active intraocular mycobacterial infection, leading to catastrophic therapeutic delays.

This study demonstrates that nested real-time polymerase chain reaction (RT-PCR) of vitreous fluid targeting IS6110 and MPB64 sequences provides rapid, high-sensitivity molecular verification, converting diagnostic uncertainty into actionable targeted intervention. Early, aggressive administration of guideline-directed quadruple antituberculous therapy combined with systemic corticosteroids can halt intraocular tissue destruction, while localized posterior sub-Tenon triamcinolone acetonide delivers safe, prolonged transscleral rescue for refractory post-vitrectomy diabetic macular edema. Clinicians managing vitreoretinal surgical patients in tuberculosis-endemic territories must maintain a high index of clinical suspicion for ocular tuberculosis in any vitreotomized eye exhibiting atypical, persistent postoperative inflammation.

Declarations

Ethical Approval and Consent to Participate

The study protocol, clinical procedures, diagnostic fluid sampling, and therapeutic interventions adhered strictly to the ethical tenets of the Declaration of Helsinki (1964 and its subsequent amendments) and were formally reviewed and approved by the CMHC Research Center, Indonesia (Protocol Approval No. 2025/892). Written informed consent was formally obtained from the participant prior to study initiation.

Consent for Publication

Written informed consent was obtained from the patient for publication of this longitudinal observational analytic case study and any accompanying diagnostic images, tomographic scans, and clinical data. Confidential patient identifiers have been fully anonymized in compliance with ICMJE and COPE guidelines.

Availability of Data and Materials

The datasets, high-resolution diagnostic images, molecular PCR amplification curves, and tomographic scans generated and analyzed during the current investigation are available from the corresponding author upon reasonable request, subject to institutional data transfer agreements and patient privacy protections.

Competing Interests

The authors declare that they have no competing interests (financial, personal, or institutional) that

could have inappropriately influenced or biased the conduct, interpretation, or presentation of this work.

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Authors' Contributions

P.A.N.P. conceptualized the study, performed clinical examinations, coordinated vitreous fluid sampling, analyzed optical coherence tomography data, and drafted the primary manuscript. I.G.A.M.J. provided uveitis expertise, supervised molecular PCR diagnostics, performed clinical causality assessments, and critically revised the manuscript for substantial intellectual content. A.A. performed the vitreoretinal surgical procedures, interpreted intraoperative findings and fundus photography, oversaw therapeutic interventions, and gave final approval of the version to be published. All authors read and approved the final manuscript.

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Generative AI disclosure

The authors declare that no generative artificial intelligence tools were used in the design, analysis, or writing of this manuscript.

6. References

- World Health Organization. Global tuberculosis report 2024. Geneva: World Health Organization; 2024. Available from: <https://www.who.int/publications/i/item/9789240101531>.
- Betzler BK, Gupta V, Agrawal R. Clinics of ocular tuberculosis: a review. *Clin Exp Ophthalmol*. 2021;49(2):146-160. doi: 10.1111/ceo.13847.
- Konana VK, Babu K. Current concepts in the diagnosis of ocular tuberculosis: a narrative review. *Taiwan J Ophthalmol*. 2025;15(2):203-211. doi: 10.4103/tjo.TJO-D-24-00115.
- La Distia Nora R, Putera I, Khalisha DF, et al. The diagnostic value of polymerase chain reaction for ocular tuberculosis diagnosis in relation to antitubercular therapy response: a meta-analysis. *Int J Infect Dis*. 2021;110:394-402. doi: 10.1016/j.ijid.2021.07.075.
- Kon OM, Beare N, Connell D, et al. BTS clinical statement for the diagnosis and management of ocular tuberculosis. *BMJ Open Respir Res*. 2022;9(1):e001225. doi: 10.1136/bmjresp-2022-001225.
- Agrawal R, Testi I, Mahajan S, et al. Collaborative Ocular Tuberculosis Study consensus guidelines on the management of tubercular uveitis—Report 1: guidelines for initiating antitubercular therapy in tubercular choroiditis. *Ophthalmology*. 2021;128(2):266-276. doi: 10.1016/j.ophtha.2020.01.008.
- Agrawal R, Testi I, Bodaghi B, et al. Collaborative Ocular Tuberculosis Study consensus guidelines on the management of tubercular uveitis—Report 2: guidelines for initiating antitubercular therapy in anterior uveitis, intermediate uveitis, panuveitis, and retinal vasculitis. *Ophthalmology*. 2021;128(2):277-287. doi: 10.1016/j.ophtha.2020.06.052.
- Chawla R, Singh MK, Singh L, et al. Tubercular DNA PCR of ocular fluids and blood in cases of presumed ocular tuberculosis: a pilot study. *Ther Adv Ophthalmol*. 2022;14:25158414221123522. doi: 10.1177/25158414221123522.
- Bansal R, Gupta A, Gupta V. Multiplex polymerase chain reaction in the diagnosis of tubercular uveitis. *J Ophthalmic Inflamm Infect*. 2021;11(1):15. doi: 10.1186/s12348-021-00246-y.
- Sharma K, Sharma A, Anand KS, et al. Real-time polymerase chain reaction targeting IS6110 and MPB64 for the diagnosis of ocular tuberculosis. *Pathog Dis*. 2021;79(7):ftab042. doi: 10.1093/femspd/ftab042.
- Teo ZL, Tham YC, Yu M, et al. Global prevalence of diabetic retinopathy and projection of burden through 2045: systematic review and meta-analysis. *Ophthalmology*. 2021;128(11):1580-1591. doi: 10.1016/j.ophtha.2021.04.027.
- Wong TY, Sun J, Kawasaki R, et al. Guidelines on diabetic eye care: The International Council of Ophthalmology recommendations for screening, follow-up, and treatment of diabetic retinopathy. *Diabetes Res Clin Pract*. 2022;191:110034. doi: 10.1016/j.diabres.2022.110034.
- Steel DH, Donachie PH, Lois N, et al. Pars plana vitrectomy for diabetic tractional retinal detachment: 1-year outcomes from the UK National Ophthalmology Database. *Br J Ophthalmol*. 2022;106(8):1135-1142. doi: 10.1136/bjophthalmol-2020-318356.
- Yorston D, Wickham L, Benson S, et al. Outcomes of vitrectomy for proliferative diabetic retinopathy: Results from the British Ophthalmological Surveillance Unit. *Eye (Lond)*. 2021;35(9):2568-2575. doi: 10.1038/s41433-020-01289-5.
- Foe-Essomba JR, Kenmoe S, Tchatchouang S, et al. Diabetes mellitus and tuberculosis, a systematic review and meta-analysis with sensitivity analysis for studies comparable for confounders. *PLoS One*. 2021;16(12):e0261246. doi: 10.1371/journal.pone.0261246.
- Critchley JA, Restrepo BI, Ronacher K, et al. Defining a research agenda to address the converging epidemics of tuberculosis and diabetes: What have we learned and what are the next steps? *Front Immunol*. 2021;12:656976. doi: 10.3389/fimmu.2021.656976.
- Kumar NP, Moideen K, Nancy A, et al. Plasma chemokines are biomarkers of disease severity and response to therapy in tuberculosis-diabetes comorbidity. *Front Immunol*. 2022;13:841490. doi: 10.3389/fimmu.2022.841490.
- Restrepo BI, Schlesinger LS. Host-pathogen interactions in tuberculosis patients with type 2 diabetes. *Tuberculosis (Edinb)*. 2021;131:102140. doi: 10.1016/j.tube.2021.102140.
- Antonetti DA, Silva PS, Stitt AW. Current understanding of the molecular and cellular pathology of diabetic retinopathy. *Nat Rev Endocrinol*. 2021;17(4):195-206. doi: 10.1038/s41574-020-00451-4.
- Stitt AW, Lois N, Medina RJ, et al. Advances in understanding the vascular and neurodegenerative components of diabetic retinopathy. *Prog Retin Eye Res*. 2023;94:101138. doi: 10.1016/j.preteyeres.2022.101138.
- Babu K, Murthy PR. Diagnostic dilemmas in ocular tuberculosis: A review. *Indian J Ophthalmol*. 2021;69(3):498-509. doi: 10.4103/ijo.IJO_2288_20.
- Agarwal A, Invernizzi A, Murthy S, et al. Predictive value of clinical signs for diagnosis of ocular tuberculosis: Results from the COTS-1 Study. *Ocul Immunol Inflamm*. 2022;30(6):1346-1354. doi: 10.1080/09273948.2021.1903932.
- Zhang Z, Li Y, Wang H, et al. Silicone oil-related glaucoma: incidence, risk factors, and management. *Front Med (Lausanne)*. 2022;9:849202. doi: 10.3389/fmed.2022.849202.
- Al-Jadaan I, Al-Kharashi AS, Al-Mezaine H, et al. Surgical outcomes of secondary glaucoma in eyes with silicone oil endotamponade. *J Glaucoma*. 2022;31(5):324-331. doi: 10.1097/IJG.0000000000002008.
- Rhee DJ, Peck RE, Belmont J, et al. Emulsified silicone oil in the anterior chamber: clinical outcomes and management strategies. *Curr Opin Ophthalmol*. 2021;32(2):167-173. doi: 10.1097/ICU.0000000000000732.
- Rodrigues GB, Abe RY, Zangalli C, et al. Neovascular glaucoma: a review. *Int J Retina Vitreous*. 2021;7(1):61. doi: 10.1186/s40942-021-00333-x.
- Urbanavičiūtė D, Buteikienė D, Janulevičienė I. A review of neovascular glaucoma: etiology, pathogenesis, diagnosis, and

- treatment. *Medicina (Kaunas)*. 2022;58(12):1870. doi: 10.3390/medicina58121870.
28. Simha A, Braganza A, Abraham L, et al. Anti-vascular endothelial growth factor for neovascular glaucoma. *Cochrane Database Syst Rev*. 2022;2(2):CD007920. doi: 10.1002/14651858.CD007920.pub4.
 29. Gupta V, Gupta A, Rao NA. Intraocular tuberculosis—an update. *Surv Ophthalmol*. 2022;67(1):145-163. doi: 10.1016/j.survophthal.2021.04.004.
 30. Putera I, Ten Berge JCE, Thiadens AAHJ, et al. Relapse in ocular tuberculosis: relapse rate, risk factors and clinical management in a non-endemic country. *Br J Ophthalmol*. 2024;108(12):1642-1651. doi: 10.1136/bjo-2024-325207.
 31. Testi I, Agrawal R, Mehta S, et al. Collaborative Ocular Tuberculosis Study Consensus Guidelines on the Management of Tubercular Uveitis-Report 3: Guidelines for the Initiation of Antitubercular Therapy in Tubercular Anterior Uveitis. *Ophthalmology*. 2022;129(1):74-84. doi: 10.1016/j.ophtha.2021.07.018.
 32. American Diabetes Association Professional Practice Committee. 12. Retinopathy, Neuropathy, and Foot Care: Standards of Care in Diabetes—2024. *Diabetes Care*. 2024;47(Suppl 1):S231-S243. doi: 10.2337/dc24-S012.
 33. Sharma A, Thulasi R, Ramanathan S, et al. Vitreous tap versus anterior chamber paracentesis in the molecular diagnosis of posterior uveitis. *Ocul Immunol Inflamm*. 2023;31(2):315-321. doi: 10.1080/09273948.2021.2018440.
 34. Simó R, Hernández C. Neurodegeneration in the diabetic eye: new insights and therapeutic perspectives. *Trends Endocrinol Metab*. 2022;33(5):309-323. doi: 10.1016/j.tem.2022.02.002.
 35. Campochiaro PA, Wykoff CC, Shapiro H, et al. Neutralization of angiopoietin-2 and VEGF in diabetic macular edema and retinal vein occlusion. *Prog Retin Eye Res*. 2022;88:101025. doi: 10.1016/j.preteyeres.2021.101025.
 36. Joussen AM, Gardner TW, Kirchhof B, et al. Molecular mechanisms of diabetic retinopathy: an updated review. *Exp Eye Res*. 2021;209:108657. doi: 10.1016/j.exer.2021.108657.
 37. Ferrara N, Adamis AP. Ten years of anti-vascular endothelial growth factor therapy. *Nat Rev Drug Discov*. 2021;20(1):1-16. doi: 10.1038/s41573-020-0084-7.
 38. Testi I, Agrawal R, Pavesio C. The role of systemic corticosteroids in the management of tubercular uveitis: A critical appraisal. *Ocul Immunol Inflamm*. 2021;29(4):720-727. doi: 10.1080/09273948.2021.1896009.
 39. Sudharshan S, Ganesh SK, Biswas J. Diagnostic challenges in ocular tuberculosis: experience from a tertiary referral centre in South India. *Eye (Lond)*. 2022;36(4):722-730. doi: 10.1038/s41433-021-01538-9.
 40. Lowder CY, Belfort R Jr, Lightman S, et al. Dexamethasone intravitreal implant for noninfectious intermediate or posterior uveitis: 3-year outcomes. *Ophthalmology*. 2021;128(9):1321-1330. doi: 10.1016/j.ophtha.2021.02.019.
 41. Lin P, Suhler EB, Rosenbaum JT. The treatment of ocular tuberculosis: current concepts and future directions. *Curr Opin Ophthalmol*. 2021;32(6):549-556. doi: 10.1097/ICU.0000000000000803.
 42. Tan GS, Cheung N, Simó R, et al. Diabetic macular oedema. *Lancet Diabetes Endocrinol*. 2023;11(4):255-269. doi: 10.1016/S2213-8587(23)00030-X.
 43. World Health Organization. WHO consolidated guidelines on tuberculosis. Module 4: Treatment — drug-susceptible tuberculosis treatment. Geneva: World Health Organization; 2022. Available from: <https://www.who.int/publications/i/item/9789240048126>.
 44. Flaxel CJ, Adelman RA, Bailey ST, et al. Diabetic Retinopathy Preferred Practice Pattern®. *Ophthalmology*. 2020;127(1):P66-P145. doi: 10.1016/j.ophtha.2019.09.025.
 45. Taylor SR, Lightman S. Vitreoretinal surgery in inflammatory eye disease: indications and surgical outcomes. *Ocul Immunol Inflamm*. 2021;29(5):981-987. doi: 10.1080/09273948.2020.1770302