

First Documented Successful Treatment of Chronic Postoperative Fungal Endophthalmitis Induced by *Trichosporon Inkin* with Fluconazole

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Abstract: This report details an uncommon occurrence of chronic endophthalmitis following cataract surgery attributed to an infection by *Trichosporon inkin* (*T. inkin*). The infection was identified through MALDI-TOF mass spectrometry along with sequencing analysis. Although the patient exhibited a robust immune response, the infection escalated quickly from the right eye to the left. Treatment involved vitrectomy and peeling surgery on the right eye, paired with systemic fluconazole antifungal therapy and intravitreal injection, resulting in significant recovery. The visual acuity of the right eye enhanced from finger counting to 20/63. This account represents the inaugural documented instance of endophthalmitis caused by *T. inkin* that was effectively managed with fluconazole. This underscores the critical role of vitreous humor enrichment culture and antifungal susceptibility testing of *T. inkin* in the treatment of endophthalmitis.

Keywords: endophthalmitis, *Trichosporon inkin*, matrix-assisted laser desorption ionization time of flight, MALDI-TOF, fluconazole

Introduction

Trichosporon species can sometimes be found as part of the normal flora on skin and mucosal surfaces and may lead to superficial infections of the skin and hair, such as white Piedra.¹ Furthermore, *Trichosporon* species is associated with more severe invasive infections, including endophthalmitis, bloodstream infections, prosthetic valve endocarditis, brain abscesses, hepatitis, and peritonitis, particularly in immunosuppressed patients.² Reported cases of endophthalmitis due to this organism are exceedingly rare. This article presents the third documented case of endophthalmitis caused by *Trichosporon inkin*. The patient had a history of coronary heart disease and had undergone artificial aortic valve replacement at a different medical institution two years prior. Additionally, the patient had cataract surgery at another facility one year ago. Notably, this time, the patient developed *T. inkin* endophthalmitis without any obvious precipitating factors when he was immunocompetent.

Ocular fungal infections have long posed significant challenges in terms of eradication, primarily due to the limited availability of systemic and intravitreal therapeutic agents, as well as the inadequate tissue penetration of current antifungal medications. The patient underwent vitrectomy and membrane peeling of the right eye. Following an unsuccessful empirical treatment with voriconazole, the patient was subsequently treated with systemic fluconazole and intravitreal injections, guided by susceptibility testing results, leading to a favorable recovery.

Case Presentation

A 63-year-old male with a background of coronary heart disease had cataract surgery performed on both eyes at a different facility one year ago. On January 5, 2024, he presented to a physician with complaints of blurred vision in

the right eye, accompanied by mild swelling and pain. He was subsequently admitted to the hospital on the same day, where he was diagnosed with endophthalmitis of the right eye. The details regarding the patient's clinical symptoms, diagnosis, and treatment during this hospitalization are illustrated in Figure 1.

The patient attended a follow-up consultation four weeks after the clinical diagnosis., where it was noted that the visual acuity for the right eye was recorded at 20/63, in contrast to the left eye, which exhibited a visual acuity of 20/40. Examination revealed no evidence of conjunctival congestion or edema in either eye; both presented with a clear cornea, a deep anterior chamber, pupils of normal size, and light reflection was present. A slight opacity was observed in the vitreous body of the right eye, along with a reduced number of white spherical lesions in front of the retina when

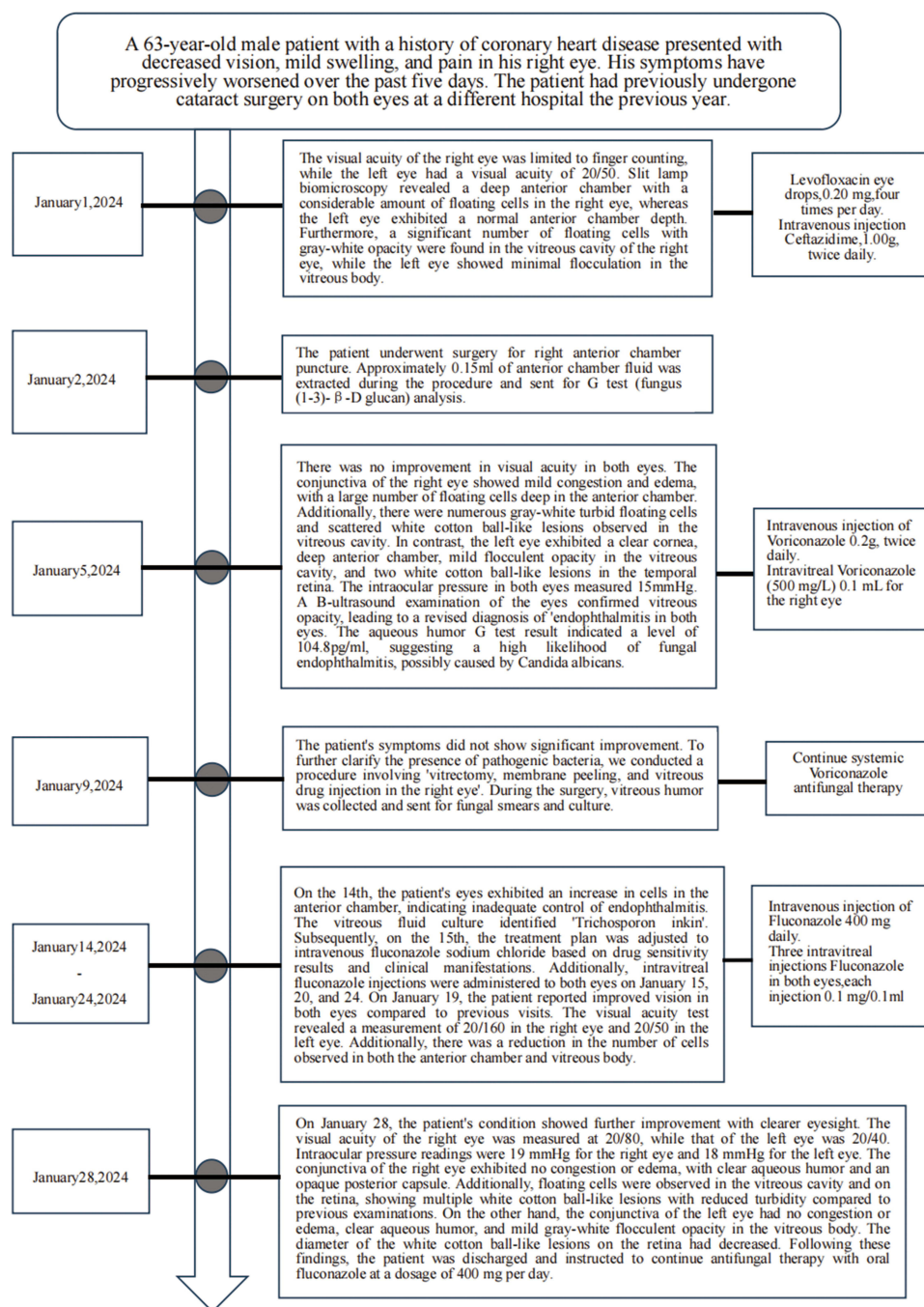


Figure 1 Patient's diagnosis and treatment process.

compared to prior examinations. The patient was administered systemic fluconazole over a period of 16 weeks, which led to an absence of endophthalmitis recurrence after the treatment was discontinued, contributing to an enhancement in the patient's quality of life. **Figure 2** presents scanning laser ophthalmoscopy (SLO) images captured on the day of the patient's admission (January 5), as well as two weeks (January 18) and four weeks (February 5) after the clinical diagnosis. Additionally, **Figure 3** displays an optical coherence tomography (OCT) image of the macula of the right eye, obtained concurrently.

The vitreous humor smear was examined under the microscope after Gram staining, revealing the presence of hyphae, as depicted in **Figure 4A**. Subsequently, the vitreous humor was directly inoculated into Columbia blood agar plate, Sabouraud dextrose agar (SDA), and MacConkey plate, while also being injected into blood culture bottles for enrichment culture. After a 5-day incubation period, no growth was detected on the Columbia blood agar plates, SDA, or MacConkey plates. However, the blood culture bottle yielded positive results within 1.23 days, with fungal hyphae and spores visible in the smear, as illustrated in **Figure 4B**. The sample was then transferred to Columbia blood agar plates and SDA and placed in a 35°C CO₂ environment for 3 days. This resulted in the growth of white, smaller, slightly dry colonies on the blood agar plates (**Figure 4C**), and white yeast-like colonies on SDA (**Figure 4D**). The microscopic morphology of the colonies, as observed after Gram staining and lactophenol cotton blue staining, is presented in **Figure 4E** and **F**.

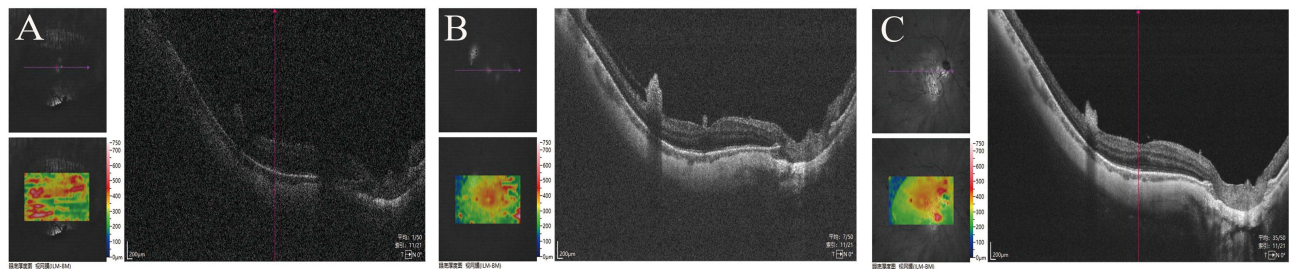


Figure 2 OCT (optical coherence tomography) examination of the right eye's macula. On the fifth day of hospitalization (January 5): white lesions are faintly visible in front of the retina (**A**). Post vitrectomy (January 18): white lesions visible in the preretina (**B**). At the follow-up visit (February 5): Preretinal white lesions become smaller and lighter in color (**C**).

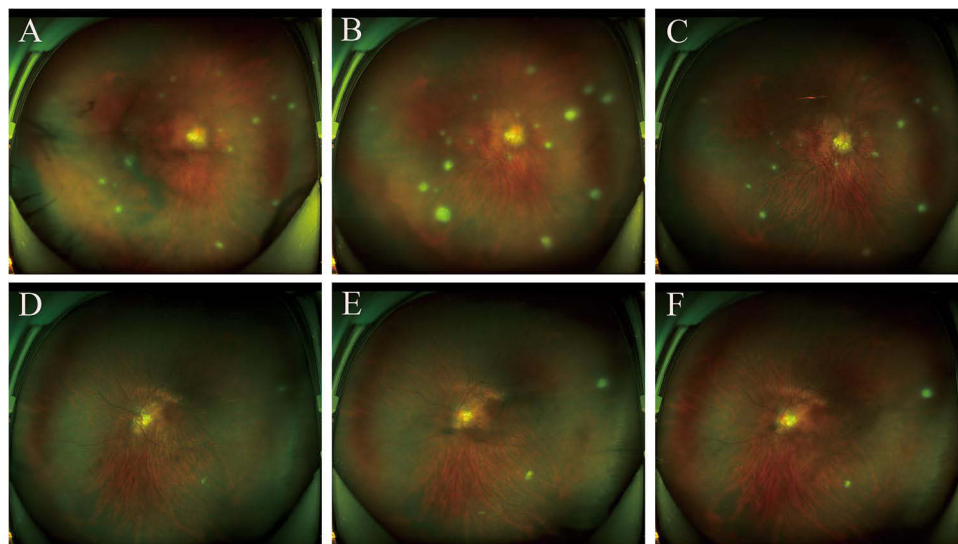


Figure 3 Scanned laser ophthalmoscope (SLO) images of the patient. On the 5th day of admission, a significant number of floating cells were observed in the vitreous cavity of the right eye, exhibiting gray-white turbidity, with multiple white cotton ball-like lesions vaguely discernible. Following vitrectomy (4 days post fluconazole treatment), the scattered white cotton ball-like lesions became more apparent. The size of these lesions decreased after 20 days of fluconazole treatment (**A–C**). On the fifth day of admission and four days post fluconazole treatment, two white cotton ball-like lesions were detected in the superior and inferior temporal retina of the left eye. After 20 days of fluconazole treatment, the diameter of these lesions reduced compared to before (**D–F**).

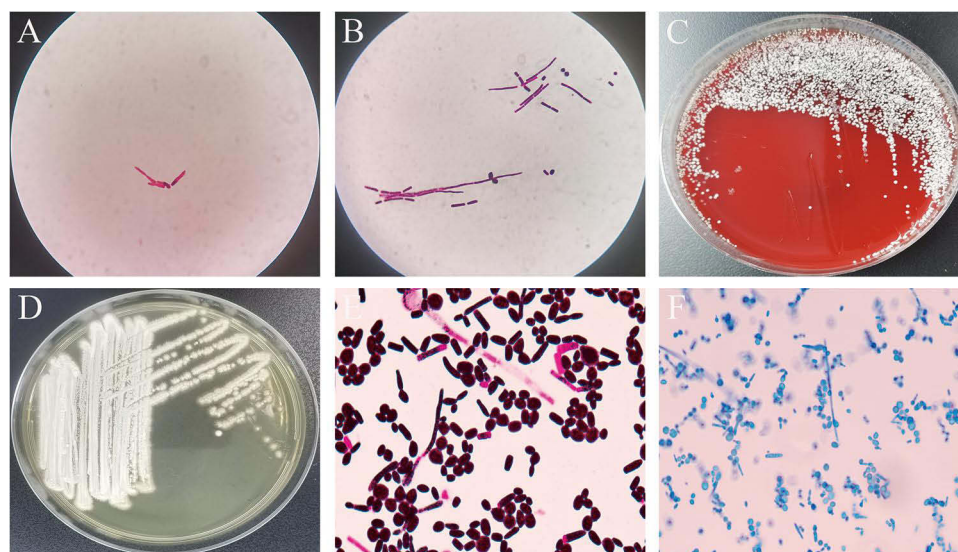


Figure 4 Microbiological examination pictures of the patient. Direct smear microscopy of vitreous humor revealed the presence of hyphae (Gram stain, ×1000) (A). Following positive enrichment culture of vitreous humor, smear microscopy showed conidia and hyphae (Gram stain, ×1000) (B). White dry colonies cultured on Columbia blood agar at 35°C for 3 days (C). Incubate on Sabouraud dextrose agar (SDA) at 35°C for 3 days, white yeast-like colonies will appear (D). The strain shows blastocyst conidia, articular conidia and hyphae under a microscope (Gram stain, ×1000) (E). Stained with lactic acid phenol and cotton blue, blastocyst conidia and hyphae can be seen (×1000) (F).

The strain was identified as *Trichosporon asahii* (Biocoding,6106776607767571) with a 94% confidence level by VITEK2 Compact YST (bioMérieux, Marcy l'Étoile, France). However, two matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry systems yielded conflicting results, with Vitek mass spectrometry (MS) reporting a 99.9% confidence level for *Trichosporon inkin*, while Bruker Biotyper MS (Bruker Daltonics GmbH, Germany) provided an identification score of 2.067. Gene sequencing further confirmed the presence of *Trichosporon inkin*, with a comparison score of 99.62%, E value of 0.0, and accession number KP132868.1.

The drug susceptibility test used the broth dilution method (Thermo Fisher Scientific, UK), referencing the ECV breakpoint for *T. asahii* as outlined in CLSI M57S-Ed4, and the results are shown in Table 1.

Discussion

The classification system for the genus *Trichosporon* has undergone revisions, resulting in the division of the previously recognized species *Trichosporon beigelii* (also referred to as *Trichosporon cutaneum*) into several distinct species. Among these, six species have been identified as pathogenic to humans: *Trichosporon inkin*, *Trichosporon ovoides*, *Trichosporon cutaneum*, *Trichosporon asteroides*, *Trichosporon asahii*, and *Trichosporon mucoides*² These strains

Table 1 Antifungal Susceptibilities of *Trichosporon inkin* by the CLSI Broth Microdilution Method

Antifungal Drugs	MIC (μg/mL)	Result
5-Flucytosine	32	/
Isavuconazole	0.5	/
Posaconazole	0.5	S
Voriconazole	0.5	/
Fluconazole	2.0	S
Itraconazole	0.25	S

Abbreviations: MIC, minimum inhibitory concentration; S, Sensitive; /, No corresponding breakpoint.

typically form white or cream-colored colonies with a dry texture and a brain-shaped or radial surface. Microscopically, blastospores, articular spores, pseudohyphae, and fungal filaments can be observed.³

The genus *Trichosporon* is regarded as a significant contributing factor to white piedra, summer-type hypersensitivity pneumonitis, as well as various forms of invasive infections, primarily in individuals with weakened immune systems.⁴ *T. asahii* is the most common clinical isolate. From 2009 to 2016, the Chinese Hospital Invasive Fungi Surveillance Network (CHIF-NET) collected 133 strains of *Trichosporon*, with *T. asahii* being the predominant species (108, 81.2%). In contrast, only 5 strains (3.8%) of *T. inkin* were isolated from various sources such as blood (1 case), abscess (1 case), pleural effusion (1 case), and tissue (2 cases).⁴ *T. inkin* was initially identified in a male scrotal eruption in 1920.⁵ The author examined 29 instances of invasive infections attributed to *T. inkin* documented in various countries from 1996 to 2024. These cases included 2 instances of endophthalmitis,^{6,7} 6 cases of pulmonary infection,^{8–12} 3 cases of peritonitis,^{2,13,14} 2 cases of endocarditis,^{15,16} 3 cases of bloodstream infection,^{12,17,18} 3 cases of skin lesions,^{1,19,20} as well as individual cases of meningitis,³ brain abscess,²¹ systemic infection in an AML patient,²² sternal wound infection,^{11,23} esophagitis,²⁴ sinusitis,²⁵ osteomyelitis,²⁶ toenail infection,²⁷ among others. Additionally, there was a case of graft valve infection following cardiac Bentall surgery.²⁸ Further details are provided in Table 2.

Fungal endophthalmitis is a serious intraocular infection caused by harmful fungi that can cause vision loss. According to the mode of infection, it can be divided into two categories: exogenous and endogenous, depending on how the infection occurs. Typically, exogenous endophthalmitis arises from surgical operations or subsequent injuries, whereas endogenous endophthalmitis is frequently linked to prolonged intravenous intubation, the administration of immunosuppressive agents, the use of antibiotics, glucocorticoids, diabetes, kidney failure, and intravenous drug use.²⁹ Postoperative fungal endophthalmitis is relatively uncommon, accounting for less than 10% of microbial infections following cataract surgery. *Candida*, *Aspergillus*, and *Fusarium* are among the common fungi implicated in this debilitating disease.⁷ Endophthalmitis caused by *Trichosporon* species is a rare occurrence. A literature review was conducted using PubMed with the search term '*Trichosporon* endophthalmitis'. As of May 2024, a total of 11 reports were found, detailing 23 cases of *Trichosporon* endophthalmitis. Among the cases reviewed, 11 did not have *Trichosporon* species identification information, with 10 of them being patients with clustered endophthalmitis following cataract surgery.³⁰ Of the remaining 12 cases, 4 were identified as *T. cutaneum*,^{31–33} 2 as *T. inkin*,^{6,7} and 3 cases identified as *T. beigeli* (previously known as *T. cutaneum*)^{34,35} and *T. asahii*.^{6,36,37} Specific data can be found in Table 3.

Different patient groups and immune statuses exhibit varying clinical manifestations of endophthalmitis. Among the 23 reported cases of *Trichosporon* endophthalmitis, 8 patients were identified as immunocompromised; within this subgroup, 5 patients^{6,32,35,38} had hematological malignancies, all of whom presented with bilateral endophthalmitis and *Trichosporonemia*. Additionally, one patient⁶ undergoing heart transplantation developed endophthalmitis in the left eye due to a massive pericardial effusion. The remaining 2 cases^{7,37} involved unilateral endophthalmitis following cataract surgery in diabetic patients, with one case experiencing recurrence after the discontinuation of medication. Excluding one case³³ with an unknown immune status, the immune function of the other 14 patients^{30,31,34,36} with *Trichosporon* endophthalmitis was normal. Although invasive *Trichosporon* infections are more prevalent among immunosuppressed individuals, it is crucial to recognize that *Trichosporon* species can also cause severe infections in immunocompetent patients, particularly those with implants and catheters.³⁰

So far, there have been only two recorded instances of *T. inkin* endophthalmitis in existing literature. One instance pertained to an endogenous infection in an individual with ischemic cardiomyopathy who was immunocompromised and had previously received a heart transplant,⁶ whereas the other instance was an exogenous infection that appeared six weeks following cataract surgery in a patient suffering from poorly managed diabetes.⁷ It is noteworthy that all cases presented with unilateral infection. Postoperative endophthalmitis is typically classified based on when it occurs: it is considered acute if it happens within six weeks after surgery, while it is referred to as chronic if the onset is delayed beyond this period.³⁶ The current case aligns with the typical presentation of chronic postoperative endophthalmitis, as clinical symptoms appeared one year after cataract surgery. The patient, a retired city resident with good hygiene and living habits and normal immune function, had previously undergone prosthetic aortic valve replacement at another medical institution two years prior. However, subsequent cardiac ultrasound examinations revealed satisfactory position and function of the prosthetic valve. Following consultations with the cardiology department and cardiac surgery,

Table 2 Review of Case Reports of Invasive *T. Inkin*

Year, ref	Sex/ Age	Diagnosis (risk)	Location of Infection	Antifungal Used	Outcome
1996 ¹⁵	F/46	Prosthetic mitral valve	Endocarditis	AMB, followed by oral ITC	Improved
1997 ¹³	M/45	Renal failure, CAPD	Peritonitis	Oral FLC	Improved
1998 ⁸	F/9	CGD	Pneumonia, paraspinal mass	Ketoconazole	Death
2000 ⁹	M/9	CGD	Lung abscesses	FLC, AMB	Death
2003 ²	F/49	Renal failure, CAPD	Peritonitis	IV CAS	Improved
2003 ¹⁴	M/45	Renal failure, CAPD	Peritonitis	Oral FLC and 5-FC,	Improved
2004 ¹⁶	M/52	Prosthetic Aortic valve	Endocarditis	None	Death
2004 ¹⁰	F/9	CGD	Pneumonia	CAS+AMB (switched to POC)	Improved
	M/13	CGD	Pneumonia	POC	Improved
2006 ¹⁹	F/74	Rheumatoid arthritis	Left forearm nodules	Oral ITC	Improved
2006 ²²	M/30	AML	Generalized infection	MCA, AMB	Death
2006 ²³	F/71	Aortic root replacement surgery	Sternal wound	IV FLC	Death
2007 ¹⁷	M/28	AIDS	Blood-sepsis	VRC, followed by oral ITC	Improved
2011 ²⁴	F/54	Lung cancer	Esophagitis	Oral FLC	Ineffective
2012 ²⁵	F/28	Multiple polyps	Sinusitis	None	Lost to follow-up
2014 ¹¹	M/19	Lung transplantation	Sternal wound	VRC	Cure
	M/42	Cardiac transplantation	Pneumonia	FLC switched to VRC	Cure (soon died of unrelated cause)
2015 ²⁷	F/62	Onycholysis and Chromonychia	Nail infection	ITC	Cure
2017 ²⁰	M/40	ALL	Skin lesion	VRC	Improved
2017 ²¹	M/21	X-linked CGD	Brain Abscesses	AMB+VRC, followed by oral POC	Cure
2018 ³	F/49	Corticosteroids and antibiotics therapy	Meningitis	AMB, VRC	Death
2018 ¹	F/60	Multiple inflammatory nodules	Skin abscesses	VRC	Cure
2018 ⁶	M/69	Ischemic cardiomyopathy	Endophthalmitis	VRC, AMB	Improved
2015 ¹²	M/71	Pemphigus foliaceus	Pneumonia	AMB	Death
	F/9	Pemphigus vulgaris	Blood	FLC switched to VRC	Improved
2021 ²⁶	M/63	Chronic obstructive pulmonary, Lung Transplantation	Sternal Osteomyelitis	VRC	Cure
2022 ²⁸	M/71	Bentall procedure	Bentall graft	FLC	Cure
2022 ¹⁸	F/39	Intestinal obstruction	Blood	None	Death
2023 ⁷	M/51	Cataract Surgery	Endophthalmitis	AMB switched to VRC	Improved

Abbreviations: CAPD, continuous ambulatory peritoneal dialysis; CGD, chronic granulomatous disease; AML, acute myeloid leukemia; AIDS, Acquired Immune Deficiency Syndrome; ALL, acute lymphoblastic leukemia; FLC, fluconazole; VRC, voriconazole; ITC, itraconazole; AMB, amphotericin B; 5-FC, 5-flucytosine; MCA, micafungin; CAS, caspofungin; POC, posaconazole.

endophthalmitis caused by the valve replacement surgery was effectively ruled out. The disease progressed rapidly, starting with an initial infection in the right eye that quickly escalated to endophthalmitis in both eyes. The pathogen demonstrated the ability to develop a biofilm on the intraocular lens (IOL), facilitating its entry into the body and subsequent infection. The IOL serves as a platform for fungi to adhere, proliferate, and evade the host's immune defenses, ultimately leading to endophthalmitis.³⁰ *Trichosporon* species are recognized for their ability to inhabit different areas of the human body, such as the skin, respiratory system, and digestive tract.³ It is possible that the infection in this case may have originated from the patient's own microbiota. Additionally, the patient had a boil on their right toe a month prior, but without a definitive etiological culture, the connection to endophthalmitis can not be confirmed.

Owing to the restricted sample size and low levels of bacteria, negative culture results for vitreous humor are commonly encountered, as demonstrated in this specific instance. Utilizing enrichment culture techniques may improve the positivity rates and reduce the likelihood of missed detections. The colony characteristics of *Trichosporon* on

Table 3 Review of Case Reports of Endophthalmitis Due to *Trichosporon*

Year/Ref	Country	Sex/Age	Diagnosis/Underlying Diseases	Clinical Sample	Species Isolated	Antifungal Used/ Outcome
1974/ ³¹	Sudan	M/70	Endophthalmitis/ cataract	Anterior chamber aspirate	<i>T. cutaneum</i>	AMB/ineffective
		F/65	Endophthalmitis/ cataract	Anterior chamber contents		AMB/ineffective
1994/ ³²	Japan	F/59	Endophthalmitis/AML	Blood	<i>T. cutaneum</i>	MCZ, FLC, AMB, 5-FC/improved
2003/ ³⁴	USA	M/58	Endophthalmitis/systemic and ocular sarcoidosis	Vitreous/ intraocular lens	<i>T. beigeli</i>	FLC/improved
2007/ ³⁵	Japan	M/64	Endophthalmitis/AML	Blood	<i>T. beigeli</i>	AMB/improved
		F/43	Endophthalmitis/AML			AMB/improved
2008/ ³³	India	Not described	Endophthalmitis	Not described	<i>T. cutaneum</i>	AMB/ineffective
2009/ ³⁸	USA	M/78	Endophthalmitis/AML/ bronchiolitis obliterans With organizing pneumonia/ pansinusitis, /renal insufficiency	Blood/skin biopsy	<i>Trichosporon</i> spp	MCA, VRC/improved
2010/ ³⁶	USA	F/82	Endophthalmitis/ cataract, Hypertension, arthritis	Vitreous	<i>T. asahii</i>	VRC/improved
2015/ ³⁷	T urkey	M/72	Postoperative endophthalmitis /cataract, mellitus	Vitreous/ intraocular lens	<i>T. asahii</i>	AMB, VRC/improved
2018/ ⁶	USA	M/69	Endophthalmitis/ischemic cardiomyopathy, cataract	Pericardial fluid	<i>T. inkin</i> ,	AMB, VRC/improved
		M/37	Endophthalmitis/acute lymphoblastic leukemia	Blood	<i>T. asahii</i>	AMB, VRC/improved
2022/ ³⁰	India	M/F4:6 62 (average age)	Cluster endophthalmitis (10cases)/post-cataract surgery	Vitreous	<i>Trichosporon</i> spp	AMB, VRC/improved
2023/ ⁷	Malaysia	M/51	Right eye postoperative endophthalmitis /Mellitus; cataract	Lens	<i>T. inkin</i>	VRC/improved

Abbreviations: AML, acute myeloid leukemia; FLC, fluconazole; VRC, voriconazole; AMB, amphotericin B; 5-FC, 5-flucytosine; MCA, micafungin; MCZ, miconazole.

Sabouraud dextrose agar (SDA) can be difficult to distinguish from other yeast-like colonies, complicating species identification within the *Trichosporon* genus through conventional morphological approaches.² Commercial identification techniques, such as API 20 C AUX and Vitek 2 Compact YST, frequently produce inconclusive findings.⁴ In this instance, the strain was first identified as *Trichosporon asahii* with the Vitek 2 Compact YST system; however, further evaluations employing matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrometry and sequencing indicated it to be *Trichosporon inkin*. MALDI-TOF MS can serve as a rapid and accurate alternative to gene sequencing for identifying *Trichosporon* species, particularly when gene sequencing is not routinely feasible in most laboratories. Research indicates that when strains are present in the respective databases, the Bruker Biotyper system and Vitek MS system boast correct identification rates of 100% and 97.5%. *Trichosporon inkin* exists in the databases of both detection systems, and the analysis results in this case are consistent. The Bruker Biotyper MS system exhibited superior accuracy in identifying non-asahii *Trichosporon* species compared to the Vitek MS system, albeit without a significant difference. This discrepancy is attributed to the broader inclusion of *Trichosporon* species within the Bruker database as opposed to the Vitek database.⁴ Further confirmation is recommended for results indicating *Trichosporon asahii* identified by Vitek 2 Compact YST.

Trichosporon and *Cryptococcus* show similarities in both their phylogenetic and biochemical characteristics.¹³ Glucuronoxylomannan (GXM), a polysaccharide antigen found in *Cryptococcus neoformans*, hinders the process of phagocytosis. In addition, *Trichosporon* contains an analogous antigen resembling GXM, which interacts with the GXM

present in *Cryptococcus neoformans* and seems to be linked to invasive *Trichosporon* disease.⁹ The strain of *Cryptococcus neoformans* in this case is positive for the polysaccharide antigen, and it can be identified by its morphology and colony characteristics under the microscope.

Invasive infections due to *Trichosporon* present as an opportunistic illness that may be fatal, with mortality rates varying between 42 and 90%.⁴ Of the 29 documented instances of such infections linked to *T. inkin*. (Table 3), 8 resulted in death, yielding a mortality rate of 27.6%. This relatively lower mortality rate might be attributed to the limited number of invasive infections caused by this pathogen and its low drug resistance rate. It is noteworthy that in 3 cases, antifungal drugs were not administered, the patients' demise before the identification of the pathogenic organism.

Antifungal agents can be classified into four categories according to their mechanisms of action: azoles (such as fluconazole, itraconazole, and voriconazole), polyenes (like Amphotericin B), echinocandins (including caspofungin and micafungin), and others (5-fluorocytosine). Nevertheless, all antifungals face challenges when treating fungal endophthalmitis, including inadequate ocular penetration of both systemic and topical therapies, intrinsic resistance of fungal pathogens to these medications, the fungistatic properties of certain drugs (azoles), variations in the pathogen's susceptibility in vitro compared to in vivo, and differences in drug susceptibility among various fungal species or isolates.³⁰

Fungal endophthalmitis is a rare condition, and consequently, there is no established standard treatment. Current treatment strategies generally involve the use of intravitreal and/or systemic antifungal medications, in conjunction with vitrectomy surgery.³⁹ However, there is limited data regarding the efficacy of antifungal agents against *Trichocystis* species, particularly in the context of endophthalmitis cases, which poses a significant challenge to therapeutic management.

Trichosporon is intrinsically resistant to anidulafungin, caspofungin, and micafungin.⁴⁰ Prior research⁴ has shown that echinocandins demonstrate limited effectiveness against *Trichosporon* isolates and are not appropriate for the treatment of *Trichosporon* infections.

Current treatment options for *Trichosporon* endophthalmitis primarily involve voriconazole and amphotericin B either in combination or as monotherapy. Among the 23 cases documented in 11 articles, 13 cases received the combination of voriconazole and amphotericin B^{6,30,37} (56.5%, 13/23), with 3 cases showing treatment failure. Five cases were treated with amphotericin B alone^{31,33,35} (21.7%, 5/23), and 3 cases did not respond to treatment. Two cases were managed with voriconazole alone,^{7,36} while one case involved a combination of voriconazole and micafungin.³⁸ A patient suffering from acute myeloid leukemia (AML) who had hyphosphora fungemia and endophthalmitis received treatment that included micafungin, fluconazole, amphotericin B, and 5-fluorouracil.³² Moreover, there was an instance of endophthalmitis following cataract surgery, attributed to *T. beigeli*, which was successfully managed through systemic fluconazole administration alongside intraocular debridement.³⁴

Research⁴ has shown that azole antifungal agents exhibit greater in vitro efficacy against *Trichosporon* isolates, with Voriconazole demonstrating the strongest antibacterial activity in vitro, evidenced by a geometric mean (GM) value of 0.09 µg/mL. Agrawal et al³⁰ have noted that combining voriconazole with amphotericin B provides notable pharmacokinetic benefits for treating *Trichosporon* endophthalmitis. Although amphotericin B is known for its limited ability to penetrate intraocularly, its longer half-life exceeds that of voriconazole.⁶ However, the administration of intravitreal amphotericin B may pose risks to the retina, and its various side effects could make it less suitable for regular use in managing fungal endophthalmitis.³⁸

Fluconazole and Voriconazole, administered either intravitreally or systemically, continue to be a reliable option for addressing fungal endophthalmitis, thanks to their outstanding intraocular concentrations and safety profile.³⁹

The minimum inhibitory concentrations (MICs) for this strain in relation to 5-fluorocytosine, isavuconazole, posaconazole, voriconazole, fluconazole, and itraconazole are as follows: 32 µg/mL for 5-fluorocytosine, and 0.5 µg/mL for isavuconazole, posaconazole, voriconazole, and itraconazole, while fluconazole exhibits a MIC of 2.0 µg/mL. Nevertheless, there are constraints in the interpretation of MIC values for *T. inkin*, since the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) have yet to set breakpoints for this particular species.³ Consequently, the majority of strains documented in the literature have not been subjected to testing for the minimum inhibitory concentration of antifungal agents; instead, they have predominantly received empirical treatment.

The ECV breakpoints provided by M57S-Ed4⁴¹ are only available for *T. asahii* against posaconazole, fluconazole, and itraconazole. Based on these breakpoints, this strain is susceptible to fluconazole, but susceptibility to voriconazole cannot be determined. The MIC values of voriconazole required for successful treatment of *Trichosporon* endophthalmitis are reported to be 0.023 µg/mL and 0.12 µg/mL,^{7,37} both lower than the MIC value in this case. The patient was empirically treated with voriconazole for 10 days, underwent vitrectomy, and received intravitreal drug injection in the right eye, but did not show improvement in symptoms. This suggests that with an in vitro MIC value of 0.5 µg/mL for *T. inkin* against voriconazole, the desired antibacterial effect may not be achieved. In addition, due to the short half-life of voriconazole, treatment frequency may not be sufficient.

It is crucial to establish appropriate drug susceptibility testing methods and standardized breakpoints for *Trichosporon* species as soon as possible to ensure precise treatment. Additionally, conducting multicenter studies is essential to validate these findings and explore alternative antifungal therapies for *Trichosporon* endophthalmitis. These initiatives will provide a robust foundation for developing optimal treatment strategies for this infection.

Although some studies have indicated that fluconazole may be less effective in vivo and in vitro compared to voriconazole, posaconazole, and isavuconazole,¹ It is crucial to recognize that different strains of the same species might display diverse sensitivities to fluconazole.¹¹ In this particular case, the patient exhibited sensitivity to fluconazole as evidenced by drug sensitivity results. Following 8 days of fluconazole treatment, the patient's plasma concentration of fluconazole was measured at 8.55 mg/L. The systemic fluconazole therapy was continued for 4 months, resulting in no recurrence of endophthalmitis after discontinuation of the drug. The patient's visual acuity in the right eye was recorded as 20/63 and in the left eye as 20/40, meeting the patient's daily visual needs. While the initial two cases were primarily treated with systemic and intravitreal voriconazole, this case represents the first successful treatment of *T. inkin* endophthalmitis with fluconazole.

Conclusion

Fungal infection should be suspected in cases of endophthalmitis following cataract surgery, with early detection and timely diagnosis being crucial. Utilizing enrichment culture of vitreous humor can enhance the rate of positive detection. It is recommended to actively conduct *Trichosporon* antifungal drug sensitivity tests, as precise treatment based on these results can positively impact the management of endophthalmitis and aid in the recovery of vision in patients. In situations where the pathogenic bacteria cannot be identified and antifungal susceptibility testing is performed, empirical treatment with fluconazole in suspected cases may help in promptly reducing the pathogen load.

It is important to note that this study is limited by its single case design, and individual variations may impact the generalizability of the findings. Future research will aim to conduct multicenter, large-scale studies to validate these results and explore new antifungal options.

Data Sharing Statement

The article contains the original contributions outlined in the study. Any additional questions may be addressed to the authors responsible for correspondence.

Ethics Approval and Informed Consent

The research involving human participants received approval from the Ethics Review Board at The First People's Hospital of Xianyang, which also approved the publication of the case details. The patient granted written informed consent for participation in this research.

Consent for Publication

Consent for Publication The patient provided written informed consent for the publication of this case report, and the consent form can be made available for review by the editor if required.

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Disclosure

The authors state that the study was carried out without any commercial or financial ties that might be interpreted as a possible conflict of interest.

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