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Case report

Delayed-onset *Candida parapsilosis* cornea tunnel infection and endophthalmitis after cataract surgery: Histopathology and clinical course

Sotiria Palioura, Nidhi Relhan, Ella Leung, Victoria Chang, Sonia H. Yoo, Sander R. Dubovy, Harry W. Flynn Jr.*

Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, FL, USA

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ABSTRACT

Purpose: To describe a patient with late post-operative endophthalmitis and clear cornea tunnel infection caused by *Candida parapsilosis* that was masquerading as chronic anterior uveitis.

Observations: A 62-year old woman with history of uncomplicated cataract surgery 7 months prior and chronic postoperative anterior uveitis, presented with an endothelial plaque, hypopyon, and infiltrates in the capsular bag and within the clear corneal tunnel. Anterior chamber cultures identified *C. parapsilosis* and pathology of the endothelial plaque showed fungus. Anterior chamber washout, scraping of the endothelial plaque, serial intracameral and intravitreal injections with amphotericin B (10 mcg) failed to control the infection. Pars plana vitrectomy, removal of the intraocular lens and capsular bag, a corneal patch graft, and administration of intravitreal antifungal agents were performed. One year later the patient remains free of recurrence and her best-corrected vision is 20/25 with a rigid gas permeable contact lens.

Conclusions: and Importance: Persistent intraocular and intracorneal inflammation after cataract surgery should raise suspicion of endophthalmitis caused by fungi non-responsive to topical and intravitreal antibiotics. Surgical intervention and removal of the nidus of infection, which is often the intraocular lens and capsular bag, may be necessary for a successful outcome.

1. Introduction

Candida parapsilosis has emerged as an opportunistic fungal pathogen over the last two decades especially in debilitated patients and low birth weight neonates.[1] Though typically a commensal of human skin, its capacity to form biofilms on catheters and implants accounts for its increased incidence within the nosocomial setting.[2] *Candida parapsilosis* is a well-known cause of delayed-onset postoperative endophthalmitis with at least 3 epidemics in the mid-1980s due to contaminated irrigating solutions used intraoperatively.[3–5] It has also been described as the causative organism for suppurative fungal keratitis and crystalline keratopathy after corneal transplantation,[6,7] laser in situ keratomileusis (LASIK),[8] insertion of intracorneal ring segments,[9] treatment of epithelial ingrowth post-LASIK,[10] trauma with vegetable matter,[11] and Boston type 1 keratoprosthesis implantation.[12]

Herein, a case of *Candida parapsilosis* cornea tunnel infection with late-onset endophthalmitis is reported after cataract surgery via phacoemulsification and all similar cases in the literature of fungal tunnel infections post-cataract surgery are reviewed.

2. Findings

A 62-year old female self-referred to the Bascom Palmer Eye Institute (BPEI) Emergency Department for further management of chronic postoperative anterior uveitis in her left eye. The patient had history of uncomplicated cataract surgery with insertion of a posterior chamber intraocular lens (IOL) 7 months prior to presentation. She had been treated with topical difluprednate 0.05% and bromfenac 0.07% eye drops for recurrent inflammation in the anterior chamber. At least 3 attempts were made by her surgeon and an outside retina specialist to taper her anti-inflammatory regimen without success. Past medical history did not reveal other predisposing factors or increased risks for developing a Candida infection. An extensive uveitis work-up, which included a complete blood count, sedimentation rate, Quantiferon gold test, chest X-ray, rapid plasma reagin (RPR), fluorescent treponemal antibody (FTA-ABS), angiotensin converting enzyme, serum lysozyme, anti-nuclear antibody (ANA), toxoplasmosis IgM and IgG antibodies, HLA B27 antigen, HLA B51 antigen and Lyme titers, was performed and was negative.

Two weeks prior to presentation to us she experienced increased

* Corresponding author. Department of Ophthalmology Bascom Palmer Eye Institute University of Miami, Miller School of Medicine, 900 N.W. 17th Street, Miami, FL, 33136, USA.
E-mail address: hflynn@med.miami.edu (H.W. Flynn).

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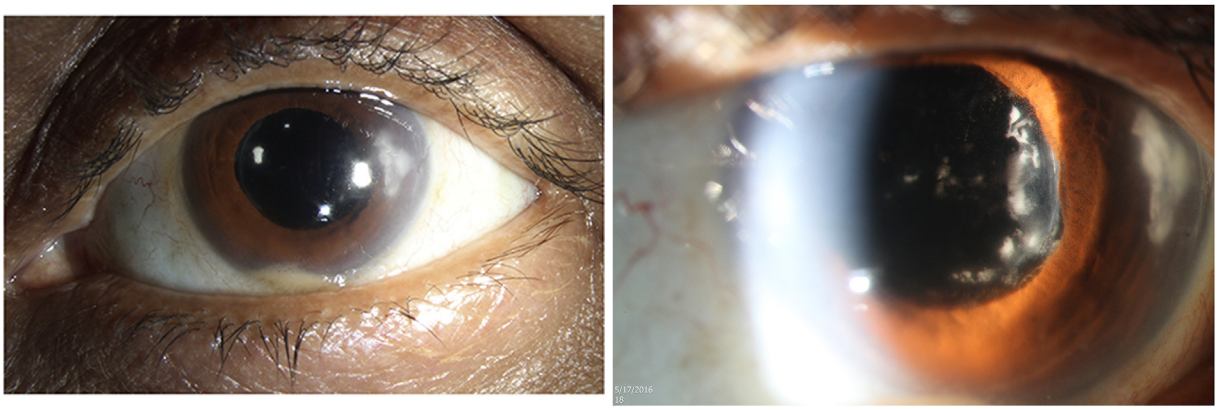

Fig. 1. Slit lamp photograph at presentation (7 months after cataract surgery in the patient's left eye). 1A - A stromal infiltrate along the clear cornea cataract tunnel is present temporally, while a 1 mm hypopyon and endothelial plaque are visible inferiorly. 1B - White fluffy-appearing deposits between the IOL and the capsular bag are seen temporally. There was no evidence of vitritis and the patient's visual acuity was 20/50.

redness and light sensitivity. Her outside retina specialist noted new keratic precipitates, 1 + cell in the anterior chamber, a new infiltrate along the clear cornea cataract incision tract and new focal deposits on the posterior surface of the IOL and inside the capsular bag. Given the concern for chronic postoperative endophthalmitis, an anterior chamber culture was sent by her outside physician and vancomycin and moxifloxacin were injected intracamerally and ceftazidime was injected intravitreally. On postoperative day 3, the patient experienced recurrence of the anterior chamber inflammation and reported to BPEI for further management.

Upon presentation to us, her left eye had mild perilimbal injection, a noticeable infiltrate along the clear cornea cataract tunnel temporally, a small hypopyon and endothelial plaque inferiorly, and white fluffy-appearing deposits between the IOL and the capsular bag temporally (Fig. 1). There was no vitritis and her vision was 20/50. At this time, the anterior chamber cultures from the outside medical center came back positive for *Candida*. A repeat anterior chamber washout and cultures, scraping of the endothelial plaque and injections of intracameral and intravitreal amphotericin B (0.2 mL of 5 mcg/0.1 mL) were performed. She was also started on hourly topical amphotericin B 0.5 mg/mL drops and topical steroids were stopped. Cultures showed *C. parapsilosis* and pathology of the endothelial plaque that was removed revealed fungal elements.

Despite a repeat intracameral amphotericin B injection 3 days after the anterior chamber washout, the hypopyon, capsular/IOL deposits and intrastromal wound infiltrate persisted (Fig. 2). Thus, 7 days after the washout at BPEI, the patient was brought back to the operating room for definitive surgical management of the *C. parapsilosis* endophthalmitis. A 23-gauge pars plana vitrectomy was performed, the IOL and the capsular bag were removed *in toto* through a superior 7 mm long scleral tunnel incision 2 mm posterior to the limbus and a 6.5 mm corneal patch graft was performed temporally at the site of the prior cataract wound. The patient was left aphakic and intravitreal voriconazole (0.2 mL of 100 mcg/0.1 mL) and amphotericin B (0.2 mL of 5 mcg/0.1 mL) were injected at the end of the procedure. In view of persistent ocular infection despite prior treatment with intravitreal amphotericin-B, a combination approach was utilized at the time of the definitive surgical procedure. Her post-operative regimen included topical amphotericin B 0.5 mg/mL, voriconazole 1% and cyclosporine 0.5% drops which were slowly tapered (Fig. 3). Histopathology examination revealed budding yeast along the cornea tunnel (Fig. 4A) and within the capsular bag (Fig. 4B). At her 1-year follow up visit her best-corrected vision in that eye is 20/25 with a rigid gas permeable lens and she remains free of recurrence (Fig. 5).

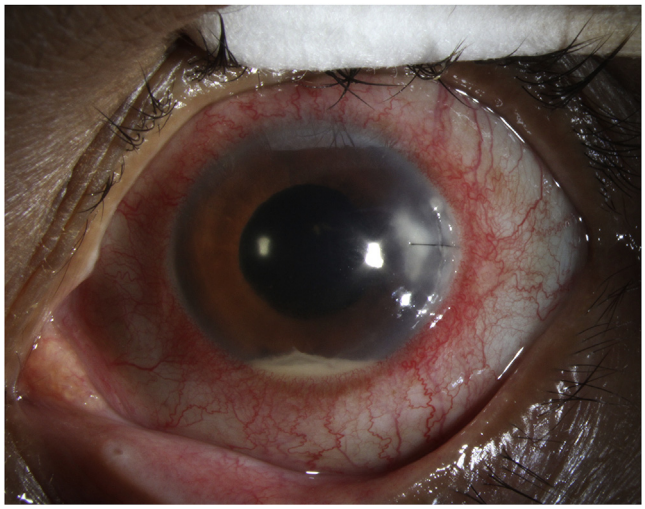

Fig. 2. Slit lamp photograph of the patient's left eye 6 days after anterior chamber washout, scraping of the endothelial plaque, and two intracameral and intravitreal amphotericin B (5 mg/mL) injections. The stromal infiltrate along the cornea tunnel and the hypopyon persisted.

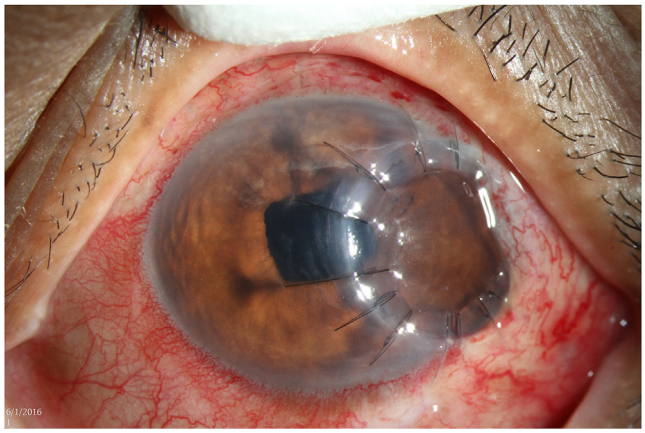

Fig. 3. Slit lamp photograph of the patient's left eye 1 week after pars plana vitrectomy, removal of the intraocular lens and capsular bag, cornea patch graft and intravitreal voriconazole and amphotericin B injections.

3. Discussion

Candida endophthalmitis after cataract surgery typically has a

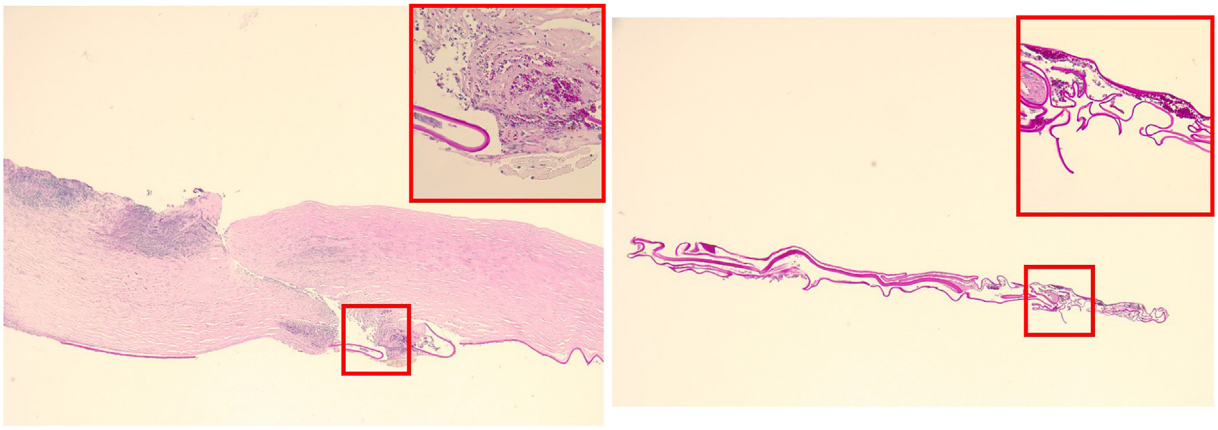

Fig. 4. Histopathology examination revealed PAS-positive budding yeast in 4A–40x magnification and 400x magnification (in inset) of corneal tissue including clear corneal incision. 4B - 40x magnification and 400x magnification (in inset) of the capsular bag.

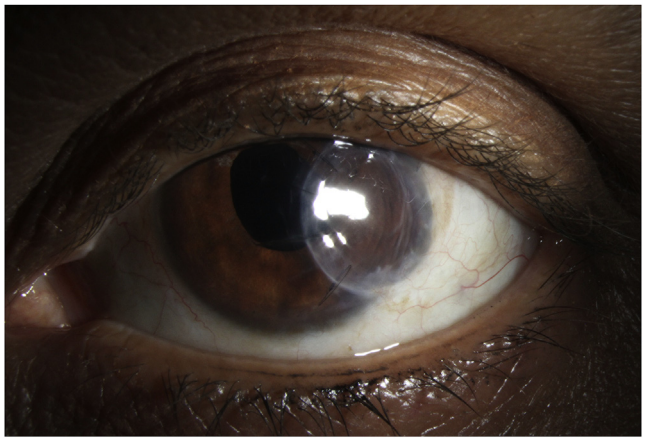

Fig. 5. Slit lamp photograph of the patient's left eye 6 months after pars plana vitrectomy, removal of the IOL/capsular bag complex, a corneal patch graft and intravitreal amphotericin B (5 mg/mL) and voriconazole (10 mg/mL) injections. Following removal of all sutures and fitting of a rigid gas permeable lens 1 year post operatively she remains free of recurrence with a best-corrected visual acuity of 20/25 with a rigid gas permeable contact lens.

delayed-onset presentation, as it is often masked by a favorable response to the frequent steroid use immediately after surgery. Candida species is well known for its tendency to form biofilms and, thus, successful treatment of the infection often requires removal of the IOL/capsular bag complex along with pars plana vitrectomy and intravitreal antifungals.[13]

Fungal corneal tunnel infections after phacoemulsification cataract surgery are rare with only 23 cases having been reported in the literature (Table 1).[14–29] Twelve eyes (52.2%) progressed to endophthalmitis with poor visual outcomes (visual acuity ≤ 20/400) in 3 patients and loss of the eye in 4 patients (3 became phthisical and one underwent evisceration). In 14 of the 23 cases (60.9%) the main incision was clear corneal and in 9 (39.1%) it was sclerocorneal. The latency period between the date of the cataract surgery and the presentation of the fungal tunnel infection ranged from 3 days to 15 years (median, 30 days). Most infections were caused by *Aspergillus* spp. (n = 12, 52.2%), two by *Fusarium* spp. (8.7%), two by *Alternaria* spp. (8.7%), two by *Candida albicans* (8.7%), one by *Candida parapsilosis* (4.3%), one by *Scedosporium apiospermum* (4.3%) and one by *Phialemonium curvatum* (4.3%). In two (9.1%) of the reported cases the fungal elements were seen on smear, but the organisms did not grow on culture media.

The current patient represents the second case reported in the literature of *C. parapsilosis* cornea tunnel infection complicated by endophthalmitis. The first case, reported by Gregori et al., in 2007, also failed medical management with intravitreal amphotericin B and pars plana vitrectomy with removal of the IOL/capsular bag complex and therapeutic penetrating keratoplasty were required.[25] The final visual acuity for that patient was 20/400. The two cases of tunnel infections caused by the related species *C. albicans* did not result in endophthalmitis and were treated with topical and oral antifungals (Table 1).

In total, in 10 (43.5%) fungal tunnel infections, medical management with topical, intraocular and systemic antifungals failed to control the infection, thus a sclerocorneal patch graft or therapeutic penetrating keratoplasty was performed and it was combined with pars plana vitrectomy in 3 of them. Two patients refused surgery upon failure of medical management of the infection and both of those eyes became phthisical. The mean best-corrected vision for all cases with a fungal tunnel infection was 20/400 and the median was 20/100.

This patient remains free of recurrence 1 year after the combined cornea IOL/capsular bag explantation and retina surgery. Current visual acuity corrects to 20/25 with a rigid gas permeable lens. In this patient, management of combined fungal cornea tunnel infection and endophthalmitis was successful after removal of all possible infectious niches and the long-term outcome was favorable.

4. Conclusions

Fungal tunnel infections after phacoemulsification cataract surgery are not common, yet when they result in fungal late-onset endophthalmitis, management can be challenging. The goal is to eradicate any source of infection within the eye and in the cornea. Medical management alone (with topical, intraocular, and systemic antifungals) often fails to control the infection and a combined surgical approach can be pursued to remove the IOL/capsular bag and to replace the infected corneal stroma with a healthy graft.

Patient consent

Consent to publish was not obtained. This report does not contain any personal information that could lead to identification of the patient.

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Table 1
Review of cases, interventions, and outcomes of fungal cornea tunnel infections after cataract surgery via phacoemulsification.

Author	Age (years)	Incision	Latent period (Days)	Organism	Method of Organism Isolation	Endophthalmitis	Intervention	Final BCVA
Kitahata et al. (2016)	77	Sclerocorneal	5400	Fusarium spp.	Culture of aqueous humor and of endothelial plaque	Yes	[a]Anterior chamber washout, then sclerocorneal patch graft Topical, Intracameral and Intravenous voriconazole Topical natamycin	20/50
	76	Sclerocorneal	360	Septate filamentous fungus	Smear of corneal wound infiltrate, culture was negative	Yes	[a]Medical management, then sclerocorneal patch graft Topical and Oral voriconazole Topical natamycin Intravitreal amphotericin B	20/320
Khochtali et al. (2016)	42	Clear Corneal	45	Alternaria spp.	Culture and pathology of corneal biopsy	No	Topical and Oral voriconazole	20/400
Jutley et al. (2015)	65	Clear Corneal	45	*Scedosporium apiospermum*	Culture of corneal scrapings	No	Topical and Oral voriconazole Topical natamycin Amniotic membrane transplantation	20/150
Erdem et al. (2015)	80	Clear Corneal	30	*Aspergillus terreus*	Culture of corneal scrapings	No	Topical voriconazole Topical natamycin	20/50
Esposito et al. (2014)	66	Clear Corneal	180	Alternaria spp.	Culture of corneal scrapings	No	Topical and Subconjunctival amphotericin B Oral ketoconazole	20/63
Hilda et al. (2014)	55	Clear Corneal	7	*Aspergillus flavus*	Culture of corneal scrapings	Yes	[a]Medical management, then PPV, removal of IOL/capsular bag, therapeutic PKP Topical, Intracameral and Intravitreal voriconazole Topical natamycin Topical fluconazole Oral itraconazole	Hand Motion
	59	Clear Corneal	7	*Aspergillus flavus*	Culture of corneal scrapings	Yes	[a]Medical management, then PPV, removal of IOL/capsular bag, therapeutic PKP Topical, Intracameral and Intravitreal voriconazole Topical natamycin Oral itraconazole	Counting Fingers
Roy et al. (2012)	75	Sclerocorneal	15	Fungus	Smear of anterior chamber exudates, culture was negative	Yes	Tissue adhesive Anterior chamber washout Topical natamycin Oral itraconazole	
Freda et al. (2011)	84	Clear Corneal	30	*Phialemonium curvatum*	Culture of corneal scrapings	Yes	[a]Medical management, then therapeutic PKP and scleral patch graft Intracameral, Intravitreal & Topical amphotericin B Topical natamycin	Evisceration
Mittal et al. (2010)	44	Clear Corneal	30	*Aspergillus flavus*	Culture of corneal scrapings	Yes	[a]Medical management, then sclerocorneal patch graft Topical, Intracameral and Oral voriconazole Topical natamycin Topical amphotericin B	20/60
Jain et al. (2010)	50	Clear Corneal	30	*Aspergillus flavus*	Culture of corneal scrapings	No	Topical and Intrastromal voriconazole Topical natamycin	20/50
Araki-Sasaki et al. (2009)	74	Clear Corneal	120	*Candida albicans*	Culture of endothelial plaque, culture of aqueous humor was negative	No	Anterior chamber washout Topical fluconazole Topical micafungin Oral itraconazole	20/100
Gregori et al. (2007)	78	Clear Corneal	7	*Candida parapsilosis*	Culture of aqueous humor	Yes	[a]Medical management, then PPV, removal of IOL/capsular bag, therapeutic PKP Topical and Intravitreal amphotericin B Oral ketoconazole	20/400

(*continued on next page*)

Table 1 (*continued*)

Author	Age (years)	Incision	Latent period (Days)	Organism	Method of Organism Isolation	Endophthalmitis	Intervention	Final BCVA
Jhanji et al. (2007)	69	Sclerocorneal	37	Fusarium spp.	Culture of corneal scrapings	No	Anterior chamber washout Topical and Intracameral amphotericin B Topical and Oral voriconazole Topical natamycin	20/60
Kehdi et al. (2005)	79	Clear Corneal	37	Aspergillus spp.	Culture of aqueous humor and corneal scrapings	Yes	[a]Medical management, then sclerocorneal patch graft Topical, Intravitreal and Intravenous amphotericin B Topical econazole Intravenous fluconazole Oral itraconazole	20/60
Garg et al. (2003)	70	Sclerocorneal	3	*Aspergillus flavus*	Culture of corneoscleral biopsy and aqueous humor	Yes	[a]Medical management, then PPV, removal of IOL/ capsular bag, therapeutic PKP Topical natamycin Oral ketoconazole	Phthisis
	70	Clear Corneal	9	*Aspergillus flavus*	Culture of corneoscleral biopsy and aqueous humor	Yes	[b]Medical management, then patient refused surgery Topical natamycin Oral ketoconazole	Phthisis
	68	Clear Corneal	8	*Candida albicans*	Culture of corneoscleral biopsy and aqueous humor	No	Topical and Oral fluconazole Topical amphotericin B	20/125
	74	Sclerocorneal	3	*Aspergillus terreus*	Culture of corneal scrapings	No	Topical natamycin Oral ketoconazole	20/20
	70	Sclerocorneal	5	Aspergillus spp.	Culture of corneal scrapings	Yes	[b]Medical management, then patient refused surgery Topical natamycin Oral itraconazole	Phthisis
Mendicute et al. (2000)	83	Sclerocorneal	10	*Aspergillus fumigatus*	Culture of corneal scrapings	No	[a]Medical management, then sclerocorneal patch graft Topical amphotericin B Oral itraconazole	20/40
	64	Sclerocorneal	15	*Aspergillus fumigatus*	Culture of corneal scrapings	No	Topical amphotericin B Oral itraconazole	20/35

PKP, penetrating keratoplasty; IOL, intraocular lens, PPV – pars plana vitrectomy, BCVA – best corrected visual acuity.

[a] In these cases, topical, intracameral and systemic antifungals ± anterior chamber washout was not curative. Fungal infiltrates recurred along the cornea tunnel. Thus, a tectonic (patch) graft ± pars plana vitrectomy was performed.

[b] In these cases, the infection progressed to endophthalmitis despite medical management. Therapeutic penetrating keratoplasty with IOL explantation, pars plana vitrectomy and injection of intravitreal antifungals was advised, but the patients refused. Eventually, these eyes became phthisical.

Conflicts of interest

All authors have no financial disclosures.

Authorship

All authors attest that they meet the current ICJME criteria for Authorship.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ajoc.2018.06.011.

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