Onset of an Outbreak of *Bipolaris hawaiiensis* Fungal Endophthalmitis after Intravitreal Injections of Triamcinolone

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Purpose: To report a series of cases with fungal endophthalmitis occurring after intravitreal injection of triamcinolone derived from a single lot prepared by a compounding pharmacy.

Design: Retrospective, observational case series.

Participants: Seventeen eyes treated with triamcinolone obtained from a single lot subsequently found to be contaminated with *Bipolaris hawaiiensis*.

Methods: A retrospective chart review in a single retina practice was performed for 15 patients (n = 17 eyes) who received intravitreal injections of triamcinolone obtained from a single compounding pharmacy. Medical records and cytologic and microbiologic results were reviewed from December 2011 through January 2013.

Main Outcome Measures: Visual acuity; presence of vitreous cell, anterior chamber cell, or both; and fungal detection in samples obtained by vitreous needle aspiration or vitreous biopsy.

Results: Fungal endophthalmitis developed in 82% (14/17) of eyes after intravitreal triamcinolone obtained from the same lot. Median onset was 83 days (range, 6–322 days). Preinjection visual acuity ranged from 20/20 to counting fingers (median, 20/50). Median visual acuity at last follow-up was 20/400 (range, 20/30–no light perception). The most common signs and symptoms included decreased vision (57% [8/14]), vitreous cell (64% [9/14]), and anterior chamber cell (50% [7/14]). Fungus was detected by cytologic or culture examination in 7% (1/14) from initial vitreous tap. By comparison, vitreous samples obtained by pars plana vitrectomy (PPV) resulted in fungus-positive cytologic results in 43% (6/14) of eyes and positive culture results in 36% (5/14) of eyes. All culture-positive specimens (100% [5/5]) were identified as *B. hawaiiensis*. Overall, fungal infection was confirmed in 57% (8/14) of eyes by either cytologic or microbiologic analysis.

Conclusions: Fungal endophthalmitis resulting from *B. hawaiiensis* developed in a series of eyes after intravitreal injections of triamcinolone obtained from a single compounding pharmacy. Clinical presentation of infection can be delayed up to 10 months. Vitreous tap may be inadequate, and direct vitreous biopsy by PPV may be preferred to identify fungal endophthalmitis and facilitate prompt diagnosis and treatment. *Ophthalmology 2014;121:952-958 © 2014 by the American Academy of Ophthalmology.*

Endophthalmitis has become an increasing concern as the need for intravitreal injections has exponentially increased in recent years. Signs and symptoms of bacterial infections typically occur within 1 week of the procedure. A meta-analysis of endophthalmitis after intravitreal anti–vascular endothelial growth factor injections reported an infection rate of 0.049% (52/105 536), with nearly half (48%) reported as having culture-negative results and the remainder having positive results for bacterial isolates.[1] Similarly, rates of endophthalmitis after intravitreal triamcinolone injections have ranged between 0.10% and 0.87%.[2,3] The cases had either negative or positive culture results for bacterial isolates.

Fungal endophthalmitis is even rarer than bacterial endophthalmitis with more devastating visual outcomes. Exogenous fungal endophthalmitis (after trauma or surgery) is more common than endogenous endophthalmitis and is more prevalent in tropical climates. Exogenous fungal endophthalmitis accounts for nearly 85% to 98% of all cases of fungal endophthalmitis.[4]

In this study, we examined a series of eyes at initial presentation in which fungal endophthalmitis developed after intravitreal injections of preservative-free triamcinolone acquired from a single lot prepared by a single compounding pharmacy (Franck's Compounding Pharmacy, Ocala, FL). This outbreak of endophthalmitis after contamination of triamcinolone solution preceded that of fungal meningitis arising from contamination of methylprednisolone solution, which also occurred in a single compounding facility (New England Compounding, Framingham, MA). The data from our study of fungal endophthalmitis may have broader implications regarding the epidemiologic factors and diagnosis and treatment of patients affected by the outbreak of fungal meningitis.

Methods

In a retrospective case series from December 2011 through January 2013, the incidence of fungal endophthalmitis at a single institution was evaluated in 15 patients after intravitreal injections (n = 17

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Table 1. Demographics and Indication for Treatment

Patient No.	Age (yrs)	Sex	Diagnosis	Lens Status
1	68	M	DME	PCIOL
2*	55	M	CME	Aphakia
3	64	M	DME	PCIOL
4	72	F	BRVO, CME	PCIOL
5†	67	F	DME	Phakic
6†	67	F	DME	Phakic
7	53	M	DME	Phakic
8	62	M	DME	PCIOL
9	73	M	CRVO, CME	Phakic
10	30	M	DME	Phakic
11	64	M	CRVO, CME	Phakic
12	65	M	DME	Phakic
13†	58	M	DME	PCIOL
14†	58	M	DME	PCIOL
15*	72	F	DME	PCIOL
16	83	F	BRVO, CME	PCIOL
17	88	F	DME	PCIOL

BRVO = branch retina vein occlusion; CME = cystoid macular edema; DME = diabetic macular edema; F = female; M = male; PCIOL = posterior chamber intraocular lens.
*Bilateral injections (2 patients).
†Same eye injected twice (approximately 1.5 months apart).

eyes) of triamcinolone. Intravitreal injections were performed by a single retina specialist (K.W.S.) using preloaded syringes containing what was believed to be sterile, preservative-free triamcinolone acquired from a single lot from a single compounding pharmacy (Franck's Compounding Pharmacy). The lot numbers of the intravitreal medications received and injected in the patients had been recorded in their respective charts, allowing for efficient tracking of the medications.

The initial patients 1 and 2 sought treatment for vitreitis at 6 and 12 days (Tables 1–4), respectively, after the last intravitreal triamcinolone injection and were treated with a vitreous tap and initial intravitreal injection of vancomycin (1 mg/0.1 ml) and ceftazidime (2.25 mg/0.1 ml), as well as dexamethasone (400 μg/0.1 ml). The initial vitreous biopsy results showed no organisms by Gram and Giemsa stains and by culture. One month later, the inflammation reoccurred and the procedure was repeated, and again the specimen showed no organisms by stains or by culture. Another 1 month later, the inflammation reoccurred in patient 1, and this time, the patient was taken to the operating room for a formal pars plana vitrectomy and vitreous biopsy of the white material in the vitreous. The sample was sent for culture and cytologic analysis. Two days later, one of the authors (K.W.S.) received a phone call from Franck's Compounding Pharmacy inquiring as to whether we had had "any suspicious cases of inflammation" and was provided the lot number of the "possibly contaminated triamcinolone." Ten minutes later, a phone call was received from the pathologist that hyphae were found in the vitreous specimen. At this point, a review of all charts of all patients who had received intravitreal triamcinolone from this lot number were identified. These patients were notified and advised to return immediately for evaluation and possible vitreous tap and intravitreal injection of voriconazole or amphotericin B. The Centers for Disease Control and Prevention (CDC) also was notified immediately.

Most patients were treated prophylactically at that time with an in-office vitreous tap and intravitreal injection of voriconazole (100 μm in 0.01 ml) regardless of whether there was clinical infection. All patients were monitored closely for development of endophthalmitis and were treated again with intravitreal antifungal agents on presentation as needed, including vitreous tap.

Clinical data collected included patient demographics, diagnosis, indication for intravitreal triamcinolone injection, and preinjection visual acuity. Information at presentation regarding onset of signs and symptoms of infection, visual acuity, intraocular pressure, fundus photography, fluorescein angiography, and ultrasonography also was recorded. Vitreous fluid pathologic and culture results from vitreous taps and pars plana vitrectomy samples also were documented. This study was conducted adhering to the tenets of the Declaration of Helsinki for research involving human subjects and was in compliance with the regulations of the Health

Table 2. Initial Presentation after Intravitreal Injection of Contaminated Triamcinolone

Patient No.	Visual Acuity	Pain	Keratic Precipitates	Hypopyon	Anterior Chamber Cell	Vitreous Cell	Chorioretinitis
1	Y	N	N	Y	2+	2–3+	N
2*	Y	N	Y	N	2+	1+	N
3	N	N	N	N	Trace–1+	1+	N
4	Y	N	N	N	1+	2+	Y
5†	Y	N	N	N	N	1–2+	N
6†	N	N	N	N	N	N	N
7	N	N	N	N	N	N	N
8	Y	N	N	N	N	N	N
9	Y	Y	N	N	2+	4+	Y
10	N	N	N	N	N	Trace	N
11	N	N	N	N	N	N	N
12	Y	N	N	N	N	Trace	N
13†	N	Y	N	N	Trace	N	N
14†	Y	Y	N	N	Trace	4+	N
15*							
16							
17							

N = no; Y = yes.
Patients 15, 16, and 17 had no signs or symptoms.
*Bilateral injections (2 patients).
†Same eye injected twice (approximately 1.5 months apart).

Table 3. Visual Acuity Changes and Onset of Signs and Symptoms Presentation

Patient No.	Preoperative Visual Acuity	Visual Acuity at Presentation	Presentation, Days (Months)	Intraocular Pressure at Presentation
1	20/30	CF @ 1′	6 (0.2)	17
2*	20/400	HM	12 (0.4) and 60 (2.0)	26
3	CF @ 2′	20/50	64 (2.1)	9
4	20/50	HM	84 (2.8)	11
5†	20/30	20/200	77 (2.6)	19
6†	20/60	20/50	76 (2.5)	17
7	20/100	20/50	83 (2.8)	29
8	20/30	20/200	63 (2.1)	32
9	20/50	CF @ 2′	97 (3.2)	10
10	20/50	20/40	110 (3.7)	17
11	20/100	20/80	174 (5.8)	19
12	20/50	20/70	204 (6.8)	23
13†	20/20	20/20	162 (5.4)	19
14†	20/20	20/100	322 (10.7)	15
15*	20/400	20/200		
16	20/70	20/60		
17	20/60	20/50		

CF = counting fingers; 1′ = 1 foot; 2′ = 2 feet; HM = hand movements.
Patients 15, 16, and 17 had no signs or symptoms.
*Bilateral injections (2 patients).
†Same eye injected twice (approximately 1.5 months apart).

Insurance Portability and Accountability Act. The institutional review board ruled that approval was not required for this retrospective chart review.

Results

Over a period of 3 months (December 2011 through February 2012), 15 patients (n = 17 eyes) received intravitreal triamcinolone injections derived from a single lot obtained from a single compounding pharmacy (Tables 1–4). Of these patients, 10 were men and 5 were women, with a median age of 65 years (range, 30–88 years). Indications for receiving intravitreal triamcinolone injections included diabetic macular edema (n = 12), macular edema associated with retinal vascular occlusion (n = 4), and pseudophakic macular edema (n = 1). Lens status of the patients at the time of injection was phakic (n = 7), pseudophakic (n = 9), aphakic (n = 1). Bilateral injections were performed in 2 patients on separate days. The same eye was injected twice in 2 other patients approximately 1.5 months apart.

Table 4. Cytologic and Culture Results

Patient No.	Tap Cytospin Periodic Acid–Schiff Positive Results?	Tap Culture Positive Results?	Pars Plana Vitrectomy Cytospin Periodic Acid–Schiff Positive Results?	Pars Plana Vitrectomy Culture Positive Results?
1	N	N	Y	Y
2*	N	N	N	N
3	N	N	Y	Y
4	N	N	Y	N
5†	Y	N	Y	Y
6†	N	N	N/A	N/A
7	N	N	N	Y
8	N	Y	N	N
9	N	N	Y	Y
10	N	N	N	N
11	N	N	N	N
12	N	N	Y	N
13†	N	N	N	N
14†	N	N	N	N
15*				
16				
17				
Total	7%	7%	43%	36%

N/A = not applicable; N = no; Y = yes.
Patients 15, 16, and 17 had no signs or symptoms.
*Bilateral injections (2 patients).
†Same eye injected twice (approximately 1.5 months apart).

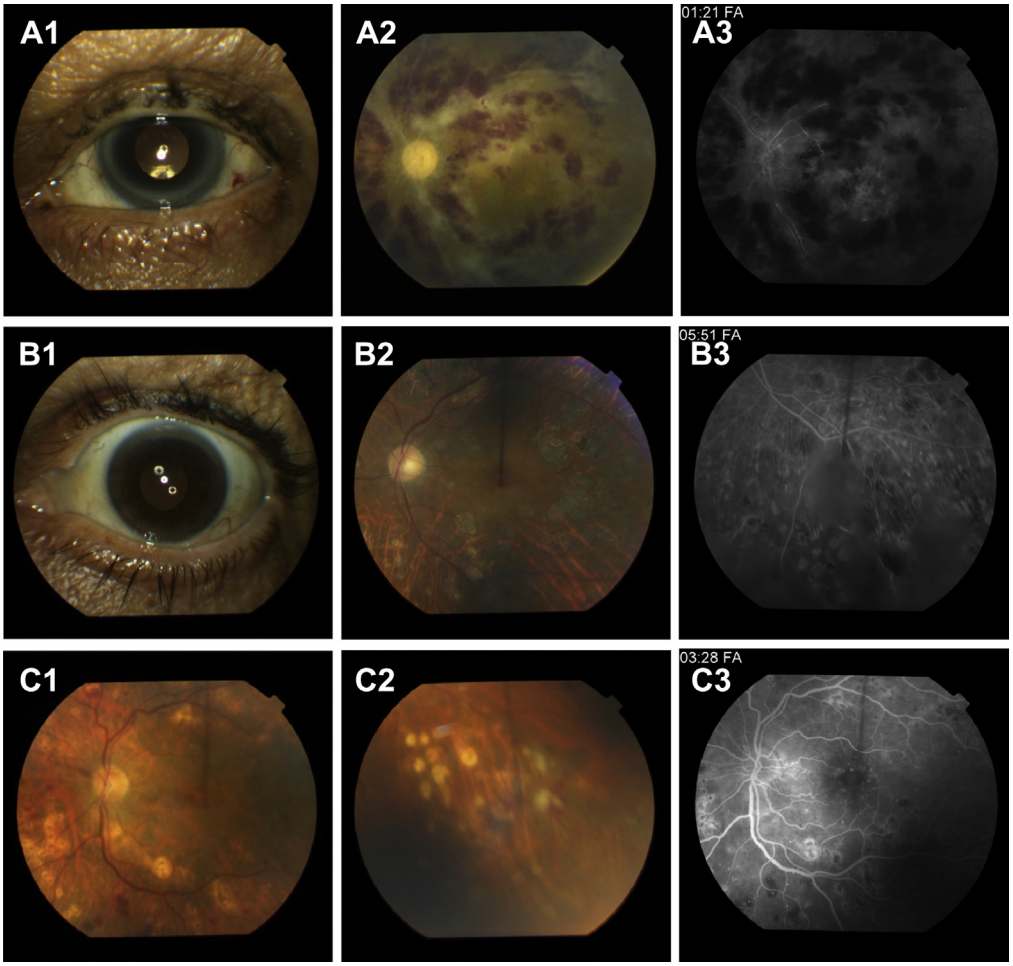

Figure 1. A1, Anterior segment photograph showing a quiet anterior segment noting the lack of conjunctival injection and discharge. **A2**, Fundus photograph and (**A3**) fluorescein angiography image of a patient with an initial branch retina vein occlusion showing white hyphae infiltrates and retinitis and diffuse retinal hemorrhages. Visual acuity, 20/400. **B1**, Anterior segment photograph showing a quiet anterior segment. Note the lack of conjunctival injection and discharge. **B2**, Fundus photograph and (**B3**) fluorescein angiography image of a patient with diabetic retinopathy with vitreous opacities that are difficult to distinguish from an old vitreous hemorrhage. These opacities proved to be hyphae on vitreous biopsy. Visual acuity, 20/40. **C1** and **C2**, Fundus photographs and (**C3**) fluorescein angiography image of a patient with diabetic retinopathy showing 2 small (500 μm) white vitreous opacities overlying the surface of the retina that proved to be hyphae.

Fungal endophthalmitis developed in 82% (14/17) of eyes receiving intravitreal triamcinolone from the same lot (Table 2). The mean interval between onset of signs or symptoms was 106.3 days (3.5 months), ranging from 6 to 322 days. At the time of intravitreal triamcinolone injection, median visual acuity was 20/50 (range, 20/20—counting fingers). In comparison, median visual acuity at the onset of signs and symptoms of fungal endophthalmitis was 20/80 (range, 20/20—hand movements). Intraocular pressure was elevated in some eyes at presentation (median, 17 mmHg; range, 9—32 mmHg). As yet, 3 patients have not demonstrated signs or symptoms of fungal endophthalmitis after 18 months and continue to be monitored closely.

The most common symptom at presentation was painless decreased vision in 57% (8/14) of eyes in which fungal endophthalmitis developed (Table 3). Pain was associated with only 21% (3/14) of affected eyes. The most common signs were vitreous cell in 64% (9/14) of eyes and anterior chamber cell, which occurred in 50% (7/14) of eyes with fungal endophthalmitis (Fig 1). Less frequent findings included hypopyon (7% [1/14]), keratitic precipitates (7% [1/14]), and chorioretinitis (7% [1/14]). Rubeosis or conjunctival injection was not seen in any of the eyes at presentation.

Vitreous tap specimens obtained in the office resulted in low yields for the detection of fungus by either cytologic analysis of cytospin specimens with periodic acid—Schiff-positive hyphae (7% [1/14]) or fungal cultures (7% [1/14]; Table 4). In contrast, vitreous samples obtained by pars plana vitrectomy resulted in higher yields in the detection of fungus. Fungus positive yield rates were better between periodic acid—Schiff-positive hyphae using cytologic analysis (43% [6/14]) than detection of fungus in cultures (36% [5/14]). Additionally, all pars plana vitrectomy specimens that showed positive culture results for fungus (100% [5/5]) were identified as the same organism by DNA sequencing performed by the CDC: *Bipolaris hawaiiensis* (Fig 2) species. Overall, vitreous specimens obtained by either vitreous tap or pars plana vitrectomy yielded fungus in 57% (8/14) of eyes by either cytologic or culture analysis.

Discussion

In this article, we describe an outbreak of fungal endophthalmitis occurring after exposure to a single lot of intravitreal triamcinolone injections. There was an extremely high incidence of

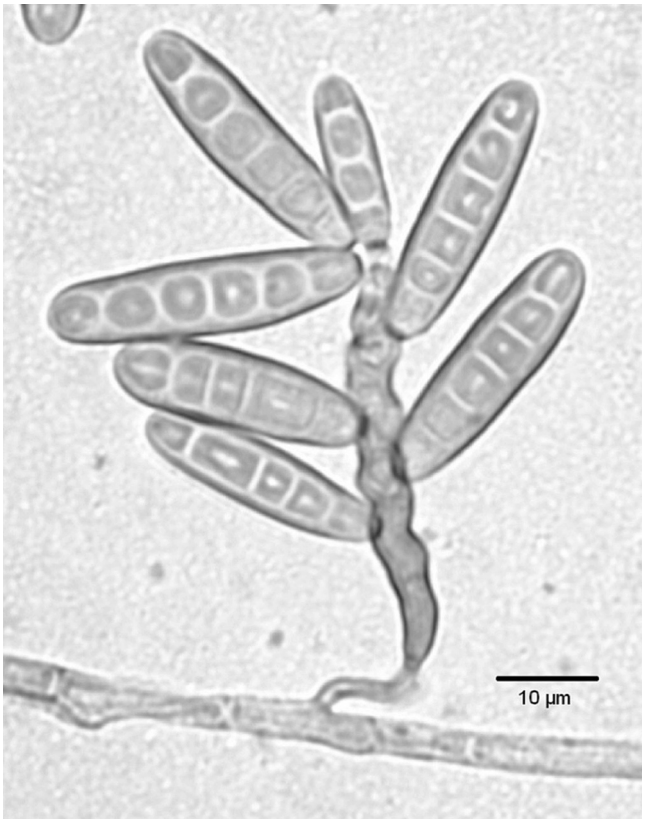

Figure 2. Photomicrograph obtained from a culture sample from patient 1 showing *Bipolaris hawaiiensis*. (Courtesy of Kent W. Small, MD.)

fungal endophthalmitis (82% [14/17]) in the exposed patients. The investigations by the CDC established that this outbreak was the result of contamination by Franck's Compounding Pharmacy.[5–7] Cytologic or culture-positive confirmation of fungal infection eventually was obtained in 53% (8/15) of eyes after many vitreous taps and biopsies. Furthermore, all culture-positive specimens obtained by pars plana vitrectomy (100% [5/5]) were identified as *B. hawaiiensis*, which is rarely a human pathogen.

A recent report by Sheyman et al[6] documents their experience in New York with the outbreak in their office after using a compounded combination triamcinolone and bevacizumab contaminated by the same pharmacy. The CDC investigations demonstrated that the *B. hawaiiensis* in their infected patients was genotypically identical to ours.[4,5,7]

B. hawaiiensis is a dematiaceous (pigmented) mold that was recognized by McGinnis et al[8] as a medically important though rare pathogen that was distinct from plant pathogens known as *Dreschlera* species and *Helminthosporium* species. *B. hawaiiensis* subsequently was reported to be the cause of granulomatous encephalitis, mycotic keratitis, fungal sinusitis with orbital invasion, subcutaneous phaeohyphomycosis, peritoneal dialysis-associated peritonitis, necrotizing pneumonia, keratomycosis, and endophthalmitis.[9]

B. hawaiiensis shares similar properties with those of *Exserohilum rostratum*, which was recovered from contaminated methylprednisolone solution and was responsible for a nationwide epidemic of fungal meningitis.[10] As a result, there are many parallels in these 2 outbreaks. Both are plant pathogens and are uncommon causes of human infection; both may cause serious infection; both are ubiquitous in soil, air, and water; and both are dematiaceous molds. The presence of melanin in the cell wall of these organisms may confer resistance to host response and may allow for persistent infection.[11] Initially, it was believed that if a patient had no signs or symptoms of meningitis within 6 weeks of being exposed to methylprednisolone contaminated by *E. rostratum* then they likely would remain disease free. Recently, the CDC has released statements warning physicians that some of these patients are showing signs of meningitis 6 months later. Both of these organisms when contaminating a steroid can have a prolonged incubation time.[12]

B. hawaiiensis can infect both immunocompromised and immunocompetent individuals and was recently identified as the second most common *Bipolaris* species, after *Bipolaris spicifera*, involved in human infections in the United States.[13] *B. hawaiiensis* most commonly causes allergic bronchopulmonary mycosis and sinusitis.[14] Orbital cellulitis involving *Bipolaris* has been reported to be associated with sino-orbital disease.[14–17] An ocular infection from *Bipolaris* has been limited to keratomycosis after trauma by vegetative material leading to endophthalmitis[9,18] and a single report of endogenous endophthalmitis in a patient with AIDS.[19] Our study and that of Sheyman et al[6] are the first to describe a series of *B. hawaiiensis* endophthalmitis cases occurring after intravitreal injection. During their investigation of Franck's Compounding Pharmacy, the CDC found multiple violations ranging from personnel not following standard sterile procedure to *B. hawaiiensis* being found in the laminar flow hood.[5,7] The recently proposed additional governmental regulations would not have prevented this outbreak and add no significant value in protecting patients.[20] According to the CDC, this outbreak in this practice occurred because of a failure of a single compounding pharmacy to follow established regulations.[5–7]

Of more immediate concern is that our patients typically sought treatment with painless loss of vision in an eye that was white (100% [14/14]) and quiet with some anterior chamber cell (50% [7/14]) and vitreous cell (64% [9/15]). Additionally, the inflammatory response initially was generally mild or minimal. However, we also acknowledge that as a correlate, the signs and symptoms of our patients in whom fungal endophthalmitis developed may be more benign as a result of a higher level of suspicion for infection. Because the contamination was traced back to a single lot number of triamcinolone and because we had methodically recorded the lot numbers for all patients, we were able to promptly contact and recall all of the subjects who were exposed to the fungus.

Additionally, the incubation period of the fungal endophthalmitis after intravitreal triamcinolone injections was highly variable (range, 6–322 days; Table 2). The variation in onset of our patients emphasizes the need to be vigilant regarding the development of fungal endophthalmitis even as far out as 10.7 months after injection. The indolent presentation of our patients with fungal endophthalmitis may have been influenced by multiple factors, including the load

of fungus inoculated during intravitreal injection, the natural pathogenicity of *B. hawaiiensis*, and the influence of triamcinolone on either host inflammatory responses or fungal pathogenicity. The diabetic status of our patients likely made minimal contribution to the onset of signs and symptoms of endophthalmitis, given that there was little difference noted between our vein occlusions and the diabetics.

It is difficult to foresee if the incidence of fungal endophthalmitis will increase with increased administration of intravitreal injections in the absence of pharmaceutical contamination. Nonetheless, there is a need to develop more effective ways to diagnose and treat fungal endophthalmitis. Recommendations of the Endophthalmitis Vitrectomy Study for bacterial endophthalmitis occurring after cataract surgery[21] may not be appropriate in this setting. Our results suggest that in-office vitreous tap may be inadequate to detect fungal endophthalmitis. Vitreous specimens obtained by direct visualization of white hyphae material from pars plana vitrectomy (Fig 2) yielded a higher identification rate of fungal infection by both cytologic analysis (43% [6/14]) and less so by fungal culture analysis (36% [5/14]; Table 4). It may be necessary to proceed directly to vitreous biopsy by surgical means to diagnose fungal endophthalmitis correctly. Moreover, among surgically obtained vitreous specimens, the cytologic identification rate of fungus-positive specimens was slightly better than that of culture identification of fungal infection. Cytologic analysis of cytospin specimens is performed in a much shorter period (1−2 days) than fungal culture analysis (weeks) and has been valuable in directing treatment of our patients. The addition of polymerase chain reaction analysis for fungal elements may enhance our ability to identify fungal endophthalmitis even more quickly and accurately.

In summary, this study described one of the first series of patients demonstrating the onset of fungal endophthalmitis outbreak after intravitreal injections. More specifically, this outbreak of *B. hawaiiensis* endophthalmitis was a result of contamination by a single compounding pharmacy. The most worrisome issues recognized from this outbreak are (1) the possible delay in clinical presentation (up to 10 months) and (2) the apparent low sensitivity of standard diagnostic procedures such as in-office vitreous tap. Most, if not all, retinal practices use products from compounding pharmacies or from hospital pharmacies that compound or repackage intravitreal medications and are exposed to this growing risk.

References

1. McCannel CA. Meta-analysis of endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents: causative organisms and possible prevention strategies. Retina 2011;31:654–61.
2. Westfall AC, Osborn A, Kuhl D, et al. Acute endophthalmitis incidence: intravitreal triamcinolone. Arch Ophthalmol 2005;123:1075–7.
3. Moshfeghi DM, Kaiser PK, Scott IU, et al. Acute endophthalmitis following intravitreal triamcinolone acetonide injection. Am J Ophthalmol 2003;136:791–6.
4. Chhablani J. Fungal endophthalmitis. Expert Rev Anti Infect Ther 2011;9:1191–201.
5. Centers for Disease Control and Prevention (CDC). Notes from the field: multistate outbreak of postprocedural fungal endophthalmitis associated with a single compounded pharmacy—United States, March−April 2012. MMWR Morb Mortal Weekly Rep 2012;61:310–1.
6. Sheyman AT, Cohen BZ, Friedman AH, Ackert JM. An outbreak of fungal endophthalmitis after intravitreal injection of compounded combined bevacizumab and triamcinolone. JAMA Ophthalmol 2013;131:864–9.
7. U.S. Food and Drug Administration. Warning letter FLA-12-38 to Franck's Lab Inc., d.b.a. Franck's Compounding Lab 7/9/12. Available at: http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2012/ucm312645.htm. Accessed September 18, 2013.
8. McGinnis MR, Rinaldi MG, Winn RE. Emerging agents of phaeohyphomycosis: pathogenic species of *Bipolaris* and *Exserohilum*. J Clin Microbiol 1986;24:250–9.
9. Bashir G, Hussain W, Rizvi A. *Bipolaris hawaiiensis* keratomycosis and endophthalmitis. Mycopathologia 2009;167:51–3.
10. Smith RM, Schaefer MK, Kainer MA, et al. Multistate Fungal Infection Outbreak Response Team. Fungal infections associated with contaminated methylprednisolone injections—preliminary report [report online]. N Engl J Med. December 2012. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1213978. Accessed September 18, 2013.
11. Kontoyiannis DP, Perlin DS, Roilides E, Walsh TJ. What can we learn and what do we need to know amidst the iatrogenic outbreak of Exserohilum rostratum meningitis? Clin Infect Dis 2013;57:853–9.
12. Fungal meningitis risk remains for patients who received tainted drug. News in Brief—posted March 18, 2013. Available at: http://www.amednews.com/article/20130318/health/130319961/9. Accessed September 18, 2013.
13. da Cunha KC, Sutton DA, Fothergill AW, et al. Diversity of *Bipolaris* species in clinical samples in the United States and their antifungal susceptibility profiles. J Clin Microbiol 2012;50:4061–6.
14. Beasley FJ. Ocular involvement in mycotic sinusitis caused by *Bipolaris* [letter]. Am J Ophthalmol 1988;106:240–1.
15. Klapper SR, Lee AG, Patrinely JR, et al. Orbital involvement in allergic fungal sinusitis. Ophthalmology 1997;104:2094–100.
16. Jacobson M, Galetta SL, Atlas SW, et al. *Bipolaris*-induced orbital cellulitis. J Clin Neuroophthalmol 1992;12:250–6.
17. Maskin SL, Fetchick RJ, Leone CR Jr, et al. *Bipolaris hawaiiensis*-caused phaeohyphomycotic orbitopathy. A devastating fungal sinusitis in an apparently immunocompetent host. Ophthalmology 1989;96:175–9.
18. Chander J, Singla N, Agnihotri N, et al. Keratomycosis in and around Chandigarh: a five-year study from a north Indian tertiary care hospital. Indian J Pathol Microbiol 2008;51:304–6.
19. Pavan PR, Margo CE. Endogenous endophthalmitis caused by *Bipolaris hawaiiensis* in a patient with acquired immunodeficiency syndrome [letter]. Am J Ophthalmol 1993;116:644–5.
20. Parke DW II. Ophthalmology and compounding pharmacies. EyeNet15–6. Available at: http://www.aao.org/publications/eyenet/201301/current_perspective.cfm. Accessed September 18, 2013.
21. Endophthalmitis Vitrectomy Study Group. Results of the Endophthalmitis Vitrectomy Study: a randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Arch Ophthalmol 1995;113:1479–96.

Footnotes and Financial Disclosures

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