Published in final edited form as:

J AAPOS. 2013 April ; 17(2): 208–210. doi:10.1016/j.jaapos.2012.11.006.

***Candida* Species Lens Abscesses in Infants with a History of Neonatal *Candida* Sepsis**

Natario L. Couser, MD, G. Baker Hubbard, MD, Lyndon B. Lee, MD, Amy K. Hutchinson, MD, and Scott R. Lambert, MD

Department of Ophthalmology, Emory University School of Medicine, Atlanta, GA

Abstract

Purpose—To describe clinical findings, diagnostic techniques and management of *Candida* lens abscesses in premature infants with history of neonatal candida sepsis.

Design—Retrospective observational review.

Methods—Three cases of *Candida* lens abscesses were retrospectively identified at one institution. Patients' records were analyzed for clinical, surgical and laboratory findings.

Results—All 3 patients developed a lens opacity with signs of ocular inflammation at 20 weeks, 10 weeks, and 52 weeks postgestational age, respectively. Each patient underwent a lensectomy and anterior vitrectomy, and 2 of 3 had intravitreal injections of antifungal agents. *Candida albicans* was cultured from the lens/anterior chamber membrane in 2 infants and *Candida parapsilosis* from a lens aspirate in 1 infant. All Gram stains and cultures of the aqueous humor were negative for fungal elements. Despite successful treatment of the fungal infection, visual outcomes were light perception, counting fingers, and no light perception, respectively for the 3 cases. Two eyes developed glaucoma and one developed a retinal detachment with subsequent phthisis.

Conclusions—*Candida* lens abscesses may present as a lenticular opacity with ocular inflammation at variable times after neonatal *Candida* sepsis and onset can be delayed for months. *Candida* can be difficult to culture from an infant with a *Candida* lens abscess. Obtaining a culture of the lens aspirate or membranes in the anterior chamber should be included in the diagnostic work-up. The prognosis for functional vision is poor in these eyes.

Although recent studies have suggested a declining incidence of neonatal endophthalmitis in the United States, *Candida* endophthalmitis is a well-known complication in premature, low birth-weight infants. The condition typically presents as a chorioretinitis with varying degrees of vitritis.¹⁻³ Isolated infections of the neonatal lens by *Candida* species, however, are an uncommon finding that can occur in premature, low birth weight infants in the absence of endophthalmitis. It has been hypothesized that these lens abscesses are initiated when fungal organisms spread hematogenously to the neonatal lens via a patent tunica vasculosa lentis during episodes of candidemia.⁴ After regression of the tunica vasculosa lentis, the fungal organisms become sequestered within the lens and are effectively isolated from immune system surveillance and exposure to systemically administered anti-fungal agents. Treatment regimens for lens abscesses have consisted of lensectomy, anterior vitrectomy, and intravitreal injection of amphotericin B. We present our experience treating

Corresponding Author: Natario L. Couser, MD, Virginia Pediatric Ophthalmology Specialists, 8700 Stony Point Parkway, Suite 210, Richmond, VA 23235, Office#: 804 272 8040, Home/Cell#: 757 218 3491, Fax#: 804 272 7344, cousernl@gmail.com.

Financial Disclosures: No financial disclosures for any of the authors

3 patients with *Candida* species lens abscesses and compare our clinical findings with those of previously reported cases.

Patients and Methods

This study was approved by the Institutional Review Board at Emory University and conformed to the requirements of the United States Health Insurance Portability and Privacy Act and the Declaration of Helsinki. We retrospectively reviewed the medical records of 3 consecutive patients with a *Candida* species lenticular abscess who were identified and treated at the Emory Eye Center and Children's Healthcare of Atlanta at Egleston from June 1, 2000 to December 31, 2009.

Case Reports

Patient 1

An infant was noted to have a cataract in his right eye at a postmenstrual age (PMA) of 45 weeks at Children's Healthcare of Atlanta. He was delivered at a PMA of 24 weeks with a birth weight of 675 grams. A sepsis screen at birth was positive and the baby was empirically treated with ampicillin, gentamicin and ceftazidime. One week later, blood, tracheostomy, and urine cultures were positive for *Candida albicans*. He was then treated with intravenous amphotericin B for 8 weeks. Weekly screening for retinopathy of prematurity (ROP) occurred between PMA of 31 weeks and PMA of 40 weeks. He progressed to stage 2, zone 2 ROP in both eyes before the ROP regressed. At a PMA of 39 weeks, he was noted to have posterior synechiae at the 2 o'clock position in his right eye. The underlying crystalline lens was clear. At a PMA of 45 weeks, his mother noticed leukocoria of the left eye. An examination-under-anesthesia (EUA) revealed a dense cataract of the left eye with a shallow anterior chamber and 360 degrees of posterior synechiae. The right anterior segment was unremarkable. B-scan ultrasonography of the left eye showed a thickened choroid and no retinal detachment. A lensectomy and anterior vitrectomy was then performed on the left eye. At the end of surgery, voriconazole (50 mcg), vancomycin (1 mg), and ceftazidime (2.25 mg) were administered intravitreally. Postoperatively, the child was started on intravenous flucytosine. A Gram stain of the lens/vitreous aspirate did not reveal any fungal elements, but a culture of the lens/vitreous aspirate grew *Candida albicans* 4 days later. Postoperatively, the child was prescribed a Silsoft contact lens (Bausch & Lomb, Rochester, NY) for aphakia, which he only wore sporadically. At 19 months of age, he was noted to have an intraocular pressure (IOP) of 32 mm Hg in his left eye. Despite initial treatment with topical dorzolamide 2% and latanoprost 0.005%, his IOP remained elevated, and at age 2 years an Ahmed aqueous shunt was implanted in his left eye. When last examined at age 2 ½ years, his vision was central, steady and maintained in the right eye and light perception in his left eye. He had a left sensory exotropia. Aside from aphakia and an Ahmed aqueous tube shunt in the anterior chamber, his left anterior segment was unremarkable. Both fundi were normal.

Patient 2

A premature infant was referred to our institution with a dense cataract in her right eye at a PMA of 36 weeks. She was delivered at a PMA of 26 weeks with a birth weight of 687 grams. At 16 days of age, blood cultures were positive for *Candida zeylanoides* and she was then treated with intravenous amphotericin B for 32 days, fluconazole for 27 days and flucytosine for 23 days. She was screened weekly for ROP beginning at a PMA age of 30 weeks. An EUA at a PMA of 36 weeks revealed a 6.5 mm central white opacity of the right lens and remnants of the tunica vasculosa lentis inferonasally. The left anterior segment was unremarkable. The right fundus was not visible using indirect ophthalmoscopy.

Ultrasonography revealed a normal posterior segment. The left eye had stage 2, zone 2 ROP with “popcorn” neovascularization temporally. A lensectomy and anterior vitrectomy was then performed on the right eye and the lens/vitreous aspirate was sent for Gram stain and culture. The Gram stain did not reveal any fungal elements. However, 13 days later *Candida parapsilosis* was isolated from the lens/vitreous aspirate. Postoperatively, the patient was optically corrected with a rigid gas permeable contact lens. At a PMA of 48 weeks, she was noted to have diffuse microcystic edema of the right eye and an IOP in the mid-30s. Four weeks later, a 360 degree trabeculotomy was performed on the right eye. Because of an increasing cup-to-disc ratio, an Ahmed aqueous shunt was implanted in the right eye at age 2 ½ years. When last examined at age 11 years, her best-corrected visual acuity was counting fingers at 6 feet in the right eye and 20/20 in the left eye. Her IOP was 13 mm Hg in the right eye and 17 mm Hg in the left eye. Her right anterior segment was unremarkable except for aphakia and an Ahmed aqueous implant. Both fundi were normal.

Patient 3

A 13-month-old child was referred to our institution with conjunctival injection and a cataract in his right eye. He was delivered at a PMA of 24 weeks with a birth weight of 610 grams. At age 7 days, he developed an erythematous rash. At 10 days of age, blood cultures were positive for *Candida albicans* and intravenous amphotericin B therapy was initiated and augmented with micafungin 12 days later. He was treated with Amphotericin B for 6 weeks and micafungin for 9 days. He was screened weekly for ROP beginning at a PMA of 31 weeks. No ROP was identified. At 12 months of age, he was diagnosed with anterior uveitis and a cataract in the right eye and was started on topical 1% prednisolone acetate and 1% atropine drops. An extensive work-up for uveitis was negative. The inflammation in the right eye continued to worsen despite topical corticosteroid treatment. Four weeks later he was noted to have fluffy white material in the right anterior chamber and a plaque on his corneal endothelium (Figures 1a,b). An anterior chamber paracentesis revealed only histiocytes and white blood cells. Three days later, a lensectomy and pars plana vitrectomy were performed on the right eye. Intraoperatively, he was noted to have a dense pupillary membrane. The underlying iris was adherent to the lens which had a rubber-like consistency. During the vitrectomy, a shallow retinal detachment was identified nasally and temporally that was treated with laser photocoagulation and C₃F₈ gas. Aqueous fluid sampled at the time of surgery revealed no fungal elements by Gram stain and a fungal culture was negative. The inflammation in the eye continued to worsen, and a second anterior chamber paracentesis was performed 4 weeks later and vancomycin (1 mg), ceftazidime (2.25 mg), and amphotericin B (5 mcg) were injected intracamerally. The Gram stain and fungal culture were both negative. Two weeks later, the right eye was found to have a total retinal detachment. A pars plana vitrectomy was performed, but the retina could not be reattached due to extensive proliferative vitreoretinopathy. During the procedure, aqueous fluid and an anterior chamber membrane were obtained and sent for fungal cultures. Three days later, *Candida albicans* was cultured from the anterior chamber membrane. *Candida* species did not grow from the aqueous fluid. The patient was then treated with weekly intracameral injections of amphotericin B for 5 weeks and oral fluconazole. The right eye subsequently developed phthisis bulbi and the child now wears an ocular prosthesis over this eye.

Discussion

We report 3 infants who developed a unilateral *Candida* lens abscess following *Candida* sepsis as neonates (Table 1). The diagnosis was established in two patients after culturing the lens aspirate obtained at the time of the lensectomy. In the third patient, 3 aqueous humor samples obtained from the eye over the course of 6 weeks all failed to grow *Candida*. The diagnosis was finally established after culturing *Candida* from an anterior chamber

membrane removed from the eye during vitrectomy. All Gram stains were negative. All treated eyes had poor visual outcomes. One eye developed a retinal detachment and phthisis bulbi, while two eyes developed glaucoma.

The clinical presentation of all 3 patients in our series differed likely due to their varying ages at the time of presentation. It is likely that all 3 of these patients seeded their crystalline lens as a result of candidemia during the neonatal period. The youngest of these patients presented with a central lens opacity at a PMA of 37 weeks. A second patient presented at a PMA of 45 weeks with a dense cataract, 360 degrees of posterior synechiae, and a shallow anterior chamber. The third patient did not present until a PMA of 80 weeks with a cataract and anterior uveitis. It is probable that the *Candida* infection had spread beyond the lens at the time of presentation for this patient. This eye had the worst clinical outcome which emphasizes the importance of early diagnosis for a *Candida* lens abscess.

Candida lens abscesses have generally been reported in very premature infants (Table 2). This is presumably due to the fact these infants have a patent tunica vasculosa lentis at birth. The tunica vasculosa lentis is patent in the majority of premature infants until a PMA of 28 to 34 weeks; by a PMA of 38 weeks nearly all will have undergone total regression.^{5, 6} Fenestrations on the lenticular side of the tunica vasculosa lentis may serve as conduits for fungal organisms to seed the crystalline lens during candidemia (Figure 3a).⁷ After the tunica vasculosa lentis regresses, a lens abscess may then develop since systemically administered anti-fungal agents can no longer enter the lens (Figure 3b). If the *Candida* infection is isolated to an abscess within the lens, it may not be necessary to administer antifungal agents after a lensectomy to eradicate the infection. Patient 2 did not have a recurrence of the *Candida* infection after a lensectomy and anterior vitrectomy even though she did not receive any intraocular or systemic anti-fungal agents after the lensectomy.

We were unable to culture *Candida* from the aqueous humor of any of the patients in our series perhaps because the *Candida* was sequestered in the lens in Patients 1 and 2. Even though the *Candida* infection had spread beyond the lens in Patient 3, we were unable to culture *Candida* from multiple aqueous humor samples from this eye. Ultimately, we were able to culture *Candida* from an anterior chamber membrane from this eye. Others have also noted the difficulty of culturing *Candida* from eyes with *Candida* lens abscesses.^{1, 4, 6, 8-10} Our findings emphasize the importance of sampling lens/vitreous aspirate and anterior chamber membranes rather than aqueous humor for *Candida* in these cases. In addition, it is necessary to observe cultures for an extended period of time since *Candida* can take several weeks to grow (3-13 days in this series).^{1, 11}

Although *Candida albicans* accounts for the majority of cases of endogenous endophthalmitis, other species such as *Candida parapsilosis*, *Candida stellatoidea*, and *Candida tropicalis* may cause endophthalmitis in humans.^{12, 13} *Candida parapsilosis* was isolated from the lens aspirate of one patient in our series, however, the initial blood culture from this patient was reported to grow *Candida zeylanoides*. *Candida parapsilosis* is less virulent than *Candida albicans* and only on rare occasion has been reported to cause an intraocular infection.^{14, 15} There are numerous species of *Candida*, and traditional culture identification may misidentify the correct species.¹⁶ PCR assay has been reported to provide a more direct and rapid identification of *Candida* isolates.¹⁷ Traditional culture techniques rather than PCR assays were used to identify the *Candida* species in all of our patients, so it is possible that the *Candida* isolates in patient 2 were incorrectly identified.

In conclusion, if a premature infant with a history of candidemia acutely develops a cataract, the possibility of a *Candida* lens abscess should be considered. The management of a

presumed *Candida* lens abscess should include a lensectomy and vitrectomy with culture of the lens/vitreous aspirate or any associated anterior chamber membranes.

Acknowledgments

Funding: Supported in part by NIH Departmental Core Grant EY06360 and Research to Prevent Blindness, Inc, New York, New York

References

1. Clinch TE, Duker JS, Eagle RC Jr, Calhoun JH, Augsburger JJ, Fischer DH. Infantile endogenous *Candida* endophthalmitis presenting as a cataract. *Surv Ophthalmol*. 1989; 34:107–12. [PubMed: 2686054]
2. Viallefont, Chaptal, Jean, Meylan, Costeau. Retinal candidiasis: a recent case. *Bull Soc Ophthalmol Fr*. 1968; 68:373–6. [PubMed: 5746422]
3. Moshfeghi AA, Charalel RA, Hernandez-Boussard T, Morton JM, Moshfeghi DM. Declining incidence of neonatal endophthalmitis in the United States. *Am J Ophthalmol*. 2011; 151:59–65 e1. [PubMed: 20970776]
4. Singh-Parikshak R, Bothun ED, Superstein R, Del Monte M, Archer S, Johnson MW. Sequestration and late activation of lenticular *Candida* abscess in premature infants. *Arch Ophthalmol*. 2004; 122:1393–5. [PubMed: 15364725]
5. Robinson J, Fielder AR. Pupillary diameter and reaction to light in preterm neonates. *Archives of disease in childhood*. 1990; 65:35–8. [PubMed: 2306132]
6. Drohan L, Colby CE, Brindle ME, Sanislo S, Ariagno RL. *Candida* (amphotericin-sensitive) lens abscess associated with decreasing arterial blood flow in a very low birth weight preterm infant. *Pediatrics*. 2002; 110:e65. [PubMed: 12415071]
7. Sellheyer K, Spitznas M. Ultrastructure of the human posterior tunica vasculosa lentis during early gestation. *Graefes Arch Clin Exp Ophthalmol*. 1987; 225:377–83. [PubMed: 3666482]
8. Shah GK, Vander J, Eagle RC. Intralenticular *Candida* species abscess in a premature infant. *Am J Ophthalmol*. 2000; 129:390–1. [PubMed: 10704563]
9. Todd Johnston W, Cogen MS. Systemic candidiasis with cataract formation in a premature infant. *J AAPOS*. 2000; 4:386–8. [PubMed: 11124679]
10. Stern JH, Calvano C, Simon JW. Recurrent endogenous candidal endophthalmitis in a premature infant. *J AAPOS*. 2001; 5:50–1. [PubMed: 11182674]
11. George BJ, Horvath LL, Hospenthal DR. Effect of inoculum size on detection of *Candida* growth by the BACTEC 9240 automated blood culture system using aerobic and anaerobic media. *Journal of clinical microbiology*. 2005; 43:433–5. [PubMed: 15635007]
12. Edwards JE Jr, Foos RY, Montgomerie JZ, Guze LB. Ocular manifestations of *Candida* septicemia: review of seventy-six cases of hematogenous *Candida* endophthalmitis. *Medicine (Baltimore)*. 1974; 53:47–75. [PubMed: 4587001]
13. Palmer EA. Endogenous *Candida* endophthalmitis in infants. *Am J Ophthalmol*. 1980; 89:388–95. [PubMed: 6966132]
14. Weems JJ Jr. *Candida* parapsilosis: epidemiology, pathogenicity, clinical manifestations, and antimicrobial susceptibility. *Clin Infect Dis*. 1992; 14:756–66. [PubMed: 1345554]
15. Baley JE, Annable WL, Kliegman RM. *Candida* endophthalmitis in the premature infant. *J Pediatr*. 1981; 98:458–61. [PubMed: 7205461]
16. Dooley DP, Beckius ML, Jeffrey BS. Misidentification of clinical yeast isolates by using the updated Vitek Yeast Biochemical Card. *J Clin Microbiol*. 1994; 32:2889–92. [PubMed: 7883873]
17. Bautista-Munoz C, Boldo XM, Villa-Tanaca L, Hernandez-Rodriguez C. Identification of *Candida* spp. by randomly amplified polymorphic DNA analysis and differentiation between *Candida albicans* and *Candida dubliniensis* by direct PCR methods. *J Clin Microbiol*. 2003; 41:414–20. [PubMed: 12517882]

Fig 1.
A External photograph of patient 3 with conjunctival injection and a cataract in his right eye.
B, The right anterior segment of patient 3 showing a white plaque on the corneal endothelium, limbal injection, fluffy material in the anterior chamber and a cataract.

Fig 2.

A, Candida is introduced by the tunica vasculosa lentis into the neonatal lens where it can become sequestered from systemic medications. B, An abscess then develops in the lens which progresses to a cataract and posterior synechiae. Copyright 2012 Mica Duran.

Table 1

Clinical findings.

Patient	1	2	3
PMA at birth	24 wks	26 wks	24 wks
Birth weight	675 g	687 g	610 g
PMA when cataract first noted	45 wks	36 wks	80 wks
Systemic conditions	Pulmonary hemorrhage, Hyperbilirubinemia	Necrotizing enterocolitis, Intraventricular hemorrhage, Hydrocephalus	Fungal endocarditis, RDS, Hyperbilirubinemia, PDA, Ileus
Systemic treatment for candida sepsis as a neonate	Ampho B for 8 wks	Ampho B for 32 days, Fluconazole for 27 days, Flucytosine for 23 days	Ampho B for 6 wks, Micafungin for 9 days
Surgical treatment	Lensectomy, Vitrectomy, ATS	Lensectomy, Vitrectomy, Trab, ATS	Lensectomy, Vitrectomy, Attempted retinal detachment repair
Intraocular treatment	Intravitreal injection of Voriconazole	None	Intravitreal injection of Ampho B
Intraocular culture	<i>C. albicans</i> (Lens aspirate)	<i>C. parapsilosis</i> (Lens aspirate)	<i>C. albicans</i> (AC membrane) AC tap × 3 negative
Systemic anti-fungal treatment after surgery	Flucytosine for 6 wks	None	Fluconazole
Long-term follow-up	2yrs	11 yrs	3 yrs
Visual outcome	Light perception	Counting fingers at 6 feet	No light perception

PMA, post-menstrual age; wks, weeks; g, Grams; RDS, respiratory distress syndrome; PDA, patent ductus arteriosus; Ampho B, amphotericin B; ATS, aqueous tube shunt; Trab, trabeculectomy; C., Candida; AC, anterior chamber; yrs, years

Table 2

Published reports of *Candida* lens abscesses in premature infants.

Author (yr published)	Clinch et al. (1989) ¹	Shahet al. (2000) ⁸	Johnstonet al. (2000) ⁹	Stern et al. (2001) ¹⁰	Drohan et al. (2002) ⁶	Sing-Parikshak et al. (2004) ⁴	
PMA at birth	28 wks	24 wks	26 wks	24 wks	28 wks	24 wks	25 wks
Birth weight	1050 g	490 g	1885 g	800 g	1020 g	750 g	855 g
PMA when cataract first noted	52 wks	35 wks	32 wks	26 wks	34 wks	44 wks	38 wks
Systemic conditions	RDS, Intraventricular hemorrhage, Hydrocephalus	Progressive pulmonary, renal, and neurological failure	RDS	N/A	RDS, Staphylococcal sepsis	Bronchopulmonary dysplasia, PDA, Necrotizing enterocolitis	RDS, Pneumonia, PDA, Staphylococcal sepsis
Systemic treatment prior to surgery	AmphoB for 44 days	Ampho B	Ampho B and Flucytosine	Ampho B and Flucytosine for 6 wks	Ampho B for 30 days	Ampho B and Fluconazole for 3 mo	Ampho B and Fluconazole for 28 days
Surgical treatment	Lensectomy, Vitrectomy	Lensectomy, Vitrectomy	Lensectomy, Vitrectomy	Lensectomy, Vitrectomy, PI, Repeat vitrectomy for pupillary membrane on POD #8	Lensectomy, Vitrectomy	Lensectomy, Vitrectomy	Lensectomy, Vitrectomy, Trab
Intraocular treatment	Intracameral Ampho B on POD #2	None	Intracameral Miconazole following AC tap; serial intracameral Miconazole and intravitreal Ampho B; Intravitreal Ampho B at time of surgery	Intravitreal Ampho B at time of surgery; Intravitreal Ampho B and Miconazole at 2 nd surgery	Intravitreal Ampho B and Dexamehasone at time of surgery	Intravitreal Ampho B at time of surgery	Intravitreal Ampho B at time of surgery
Intraocular cultures	AC tap × 2 negative, <i>C. albicans</i> (Lens/vitreous aspirate)	N/A	<i>C. albicans</i> (AC tap)	AC tap negative, <i>C. albicans</i> (Lens/vitreous aspirate)	<i>C. albicans</i> (Lens/vitreous aspirate)	<i>C. albicans</i> (Lens/vitreous aspirate)	<i>C. albicans</i> (AC membrane)
Systemic treatment after surgery	Flucytosine and Ampho B for 10 days	None	None	Ampho B, Flucytosine and Fluconazole	Ampho B and Fluconazole	Ampho B for 6 wks	Fluconazole
Long-term follow-up	9 mo	Patient expired	2 mo	7 yrs	7 mo	3 yrs	6 mo
Visual outcome	N/A	N/A	N/A	Hand motions	N/A	5/200	Fix and follow

PMA, post-menstrual age; wks, weeks; g, grams; RDS, respiratory distress syndrome; *, not specified; PDA, patent ductus arteriosus; Ampho B, amphotericin B; mo, Months; PI, peripheral Iridectomy; POD, post-operative day; Trab, trabeculotomy; AC, anterior chamber; yrs, years; N/A—not available