CHAPTER 14

Endophthalmitis

Highlights

- Chronic postoperative endophthalmitis may be difficult to diagnose and may require invasive diagnostic testing; treatment may include antibiotic or antifungal injection and, in many cases, explantation of an intraocular lens.
- Endogenous endophthalmitis should be suspected in immunosuppressed patients and in patients with a recent history of infection, surgery, diabetes, or intravenous drug use who are found to have anterior and posterior segment inflammation. The diagnosis can be definitively established by cultures, stains, or molecular studies (eg, polymerase chain reaction analysis) of vitreous aspirate.
- Endogenous endophthalmitis requires evaluation for a systemic source of infection and treatment with intravitreal antibiotic or antifungal injection and often systemic antimicrobials.

Definitions

Endophthalmitis is a clinical diagnosis made when intraocular inflammation involving both the anterior and posterior segments is attributable to bacterial or fungal infection within the eye. The retina or the choroid may be involved. Occasionally, concomitant infectious scleritis or keratitis is present. Endophthalmitis may be either exogenous, as in postoperative or posttraumatic cases, or endogenous, as in hematogenous spread from a systemic infection. Acute postoperative endophthalmitis and posttraumatic endophthalmitis are typically manifested by aggressive intraocular inflammation within days of ocular surgery or trauma. Their incidence varies between 0.04% and 0.2%. In contrast, chronic postoperative endophthalmitis occurs weeks or months after surgery and can be caused by a myriad of bacteria and fungi. Because this condition often goes undiagnosed for long periods, its incidence has not been established. Endogenous endophthalmitis occurs when bacteria or fungi are hematogenously disseminated into the ocular circulation from a systemic infection.

Acute postoperative and posttraumatic endophthalmitis are covered in BCSC Section 12, *Retina and Vitreous,* and are not discussed further here. For a detailed discussion of post–cataract surgery endophthalmitis, including proper surgical techniques and perioperative antibiotic prophylaxis, see BCSC Section 11, *Lens and Cataract*.

Chronic Postoperative Endophthalmitis

Clinical Findings

Chronic postoperative endophthalmitis has a distinctive clinical course, with multiple recurrences of chronic indolent inflammation in an eye that has previously undergone surgery, typically cataract extraction. Unlike the explosive onset of acute postoperative endophthalmitis, in chronic disease the initial inflammation may occur at any point during the postoperative course; however, it is often delayed by many months. Chronic anterior segment inflammation, hypopyon, keratic precipitates, intracapsular plaques, and/or vitritis may be present (Fig 14-1). Inflammation may respond to corticosteroid therapy but often recurs after corticosteroids are tapered. In the most severe cases, inflammation may cause corneal decompensation or even iris neovascularization.

Chronic postoperative endophthalmitis can be divided into bacterial and fungal varieties. Chronic postoperative bacterial endophthalmitis is most commonly caused by *Cutibacterium acnes* (formerly *Propionibacterium acnes*). Gram-positive bacteria with limited virulence (eg, *Staphylococcus epidermidis* and *Corynebacterium* species), gram-negative bacteria, or *Mycobacterium* species may also be causative agents. *C acnes,* a commensal, anaerobic, pleomorphic, gram-positive rod, is commonly found on the eyelid skin or conjunctiva. The organism may also sequester itself between an intraocular lens (IOL) implant and the posterior capsule. In this relatively anaerobic environment, *C acnes* grows and forms colonies, which manifest as whitish plaques between the posterior capsule and the IOL implant. Nd:YAG capsulotomy may trigger chronic endophthalmitis in these eyes by liberating the organism into the vitreous cavity, resulting in more severe vitreous inflammation and exacerbation of the underlying infection.

Chronic postoperative fungal endophthalmitis may have a presentation similar to that of *C acnes–related disease*. Numerous fungal organisms have been implicated in this chronic inflammatory process, including *Candida parapsilosis, Aspergillus flavus, Torulopsis candida,* and *Paecilomyces lilacinus,* as well as *Verticillium* species. Certain clinical signs may be helpful in differentiating a fungal from a bacterial etiology, including the presence of corneal infiltrate or edema, a mass in the iris or ciliary body, or development of necrotizing scleritis. The

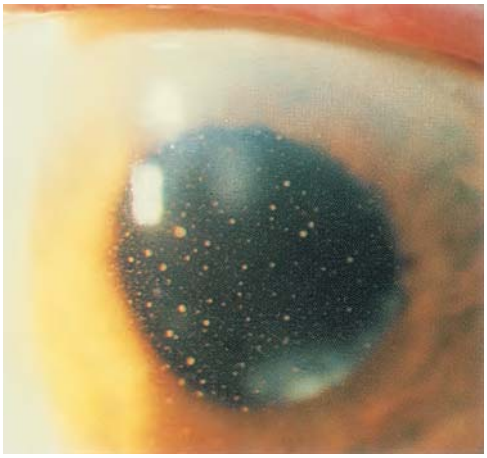

Figure 14-1 Chronic postoperative endophthalmitis caused by *Cutibacterium acnes* infection. Anterior segment photograph shows keratic precipitates and white plaque in the capsular bag. *(Courtesy of David Meisler, MD.)*

presence of vitreous snowballs with a "string-of-pearls" appearance in the vitreous may also be indicative of a fungal infection. The intraocular inflammation may worsen after topical, periocular, or intraocular corticosteroid therapy, which should automatically raise suspicion for a fungal infection.

Maalouf F, Abdulaal M, Hamam RN. Chronic postoperative endophthalmitis: a review of clinical characteristics, microbiology, treatment strategies, and outcomes. *Int J Inflam*. 2012:313248. doi:10.1155/2012/313248

Shirodkar AR, Pathengay A, Flynn HW Jr, et al. Delayed- versus acute-onset endophthalmitis after cataract surgery. *Am J Ophthalmol*. 2012;153(3):391–398.e2.

Diagnosis

The diagnosis of chronic postoperative endophthalmitis is based on clinical suspicion and confirmed by obtaining aerobic, anaerobic, and fungal cultures of intraocular fluids. The aqueous, capsular plaques (if present), and vitreous should be sampled using needle aspiration or pars plana vitrectomy. Gram and fungal stains should also be obtained. The value of such stains should not be underestimated, especially in cases of fungal endophthalmitis. In addition, polymerase chain reaction (PCR) testing with primers for *C acnes* and pan-fungal and pan-bacterial targets may be helpful. The bacterial and fungal stains or PCR may yield information rapidly, enabling the clinician to tailor therapy and improve clinical prognosis long before the results of the cultures become positive. Because of the slow-growing and fastidious nature of the organisms that cause chronic endophthalmitis, cultures must be retained by the microbiology laboratory for 2 or more weeks. If initial cultures are negative for infection but clinical suspicion remains high, cultures may need to be repeated.

The differential diagnosis of chronic postoperative endophthalmitis includes noninfectious causes such as lens-induced uveitis (from retained cortical material or retained intravitreal lens fragments), uveitis-glaucoma-hyphema syndrome (IOL malposition leading to iris chafing and intraocular inflammation), sympathetic ophthalmia (if the fellow eye has had prior surgery or trauma), and masquerade syndromes such as vitreoretinal lymphoma. See the Clinical Pearl for the differential diagnosis of chronic postsurgical intraocular inflammation.

Lai J-Y, Chen K-H, Lin Y-C, Hsu W-M, Lee S-M. *Propionibacterium acnes* DNA from an explanted intraocular lens detected by polymerase chain reaction in a case of chronic pseudophakic endophthalmitis. *J Cataract Refract Surg*. 2006;32(3):522–525.

Meisler DM, Mandelbaum S. *Propionibacterium*-associated endophthalmitis after extracapsular cataract extraction: review of reported cases. *Ophthalmology*. 1989;96(1):54–61.

CLINICAL PEARL

The differential diagnosis for chronic postoperative intraocular inflammation includes the following conditions:

- persistent postoperative noninfectious inflammation
- chafing by an intraocular lens, including uveitis-glaucoma-hyphema syndrome
- viral anterior uveitis
- chronic infectious endophthalmitis

Treatment

Treatment of chronic postoperative bacterial endophthalmitis ranges from intravitreal antibiotic alone (see Appendix B) to pars plana vitrectomy and intravitreal antibiotic with or without partial capsulectomy. These measures may not completely eradicate the infection, especially if the microorganism is sequestered in the equatorial lens capsule. In such cases, IOL explantation, complete capsulectomy, and intravitreal vancomycin injection may be curative. The decision to explant an IOL is made on a case-by-case basis depending on the clinical course, the severity of the intraocular inflammation, and the level of vision loss. Although there is no preferred method for treating this chronic infection, existing literature suggests that more than one surgical procedure may be necessary to eradicate it.

The treatment of chronic fungal endophthalmitis is more difficult and requires the use of weekly intravitreal antifungal injections (amphotericin or voriconazole) and possibly systemic antifungal drugs in the most severe cases. In vitrectomized eyes, antifungals are often injected twice a week. Multiple vitrectomies may be necessary.

Clark WL, Kaiser PK, Flynn HW Jr, Belfort A, Miller D, Meisler DM. Treatment strategies and visual acuity outcomes in chronic postoperative *Propionibacterium acnes* endophthalmitis. *Ophthalmology*. 1999;106(9):1665–1670.

Endogenous Endophthalmitis

Endogenous Bacterial Endophthalmitis

Endogenous bacterial endophthalmitis is caused by hematogenous dissemination of the organisms, resulting in intraocular infection. This disease is uncommon and accounts for less than 10% of all endophthalmitis cases. Patients who have compromised immune systems are most at risk for endogenous endophthalmitis. Predisposing conditions include type 1 and type 2 diabetes, systemic malignancy, sickle cell anemia, and systemic lupus erythematosus. Endogenous endophthalmitis may also develop in patients with immunosuppression from HIV infection; however, it is unclear whether HIV infection is an independent risk factor. In addition, extensive gastrointestinal surgery, endoscopy, dental procedures, and intravenous drug use may increase the risk of endogenous endophthalmitis. Systemic immunomodulatory therapy and chemotherapy may also put patients at risk. Although the eye may be the only location where the infection is found, an extraocular focus exists in as many as 90% of cases. Possible sources of infection include cellulitis, tooth abscess, pneumonia, endocarditis, urinary tract infection, bacterial meningitis, and liver abscess. Previous use of an indwelling line or port may also be related.

A wide variety of bacteria can cause endogenous endophthalmitis. The most common gram-positive organisms are *Streptococcus* species (endocarditis), *Staphylococcus aureus* (cutaneous infections), *Bacillus* species (from intravenous drug use), and *Nocardia* species (in immunocompromised patients, discussed in further detail in Chapter 11). The most common gram-negative organisms are *Neisseria meningitidis, Haemophilus influenzae,* and enteric organisms such as *Escherichia coli* and *Klebsiella* species. In Asia, the most common cause of endogenous endophthalmitis is infection from *Klebsiella* species in liver abscesses.

Jackson TL, Paraskevopoulos T, Georgalas I. Systematic review of 342 cases of endogenous bacterial endophthalmitis. *Surv Ophthalmol.* 2014;59(6):627–635.

Clinical findings

Although some patients with endogenous bacterial endophthalmitis are ambulatory and afebrile, others may show signs of an ongoing systemic infection, such as fever greater than 101.5°F, elevated peripheral leukocyte count, and positive bacterial cultures from extraocular sites (blood, urine, sputum). Patients who present with endogenous endophthalmitis may also be ill and undergoing treatment for a primary underlying disease, such as cancer treated with prolonged intravenous chemotherapy or other chronic infections that may subsequently sequester in the eye. A nonocular infection serving as a nidus for bacterial dissemination to the eye may be very difficult to diagnose, especially in cases of osteomyelitis, sinusitis, or pneumonia misdiagnosed as a simple upper respiratory tract infection. In these situations, laboratory tests cannot substitute for a detailed history and review of systems.

Ocular symptoms of endogenous bacterial endophthalmitis include acute onset of eye pain, photophobia, and blurred vision. Examination usually reveals severely reduced visual acuity. Substantial inflammation may be seen in the anterior chamber, including fibrin and hypopyon, as well as in the vitreous cavity (Fig 14-2). Both eyes may be affected simultaneously. Chorioretinal abscess and retinal hemorrhages, including white-centered Roth spots, may also be present (Fig 14-3). Very rarely, there is periorbital and eyelid edema.

Morbidity due to endogenous bacterial endophthalmitis can be significant. If the associated systemic infection is missed, sepsis may develop and the patient may die. Recurrent or persistent intraocular infection may require numerous surgical procedures and repeated injections of intravitreal antibiotics. In the most severe cases, complications such as cataract development, retinal detachment, suprachoroidal hemorrhage, vitreous hemorrhage, macular scar, hypotony, and phthisis bulbi can also occur. The prognosis is directly related to the offending organism and the systemic status of the patient.

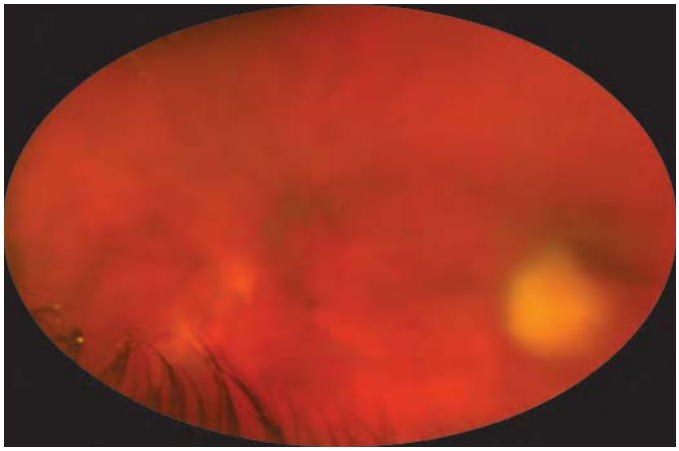

Figure 14-2 Endogenous bacterial endophthalmitis. Fundus photograph of the left eye shows substantial vitreous haze with a large chorioretinal abscess and associated hemorrhage in the temporal periphery. *(Courtesy of Jared E. Knickelbein, MD, PhD.)*

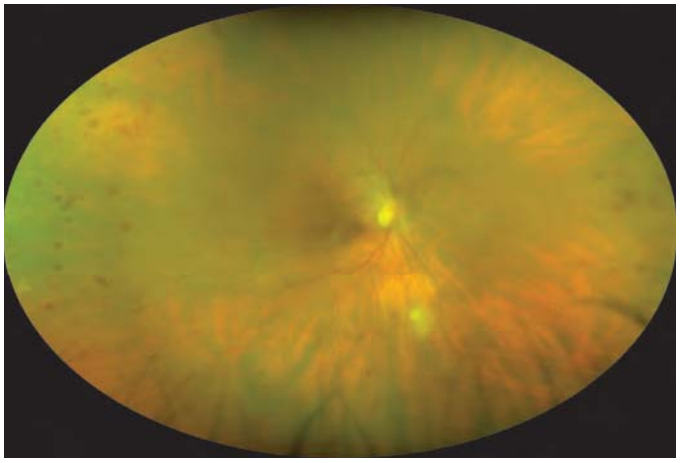

Figure 14-3 Endogenous bacterial endophthalmitis. Fundus photograph shows vitreous haze, a small chorioretinal abscess in the inferior midperiphery, and peripheral intraretinal hemorrhages. *(Courtesy of Jared E. Knickelbein, MD, PhD.)*

Diagnosis

Endogenous bacterial endophthalmitis is diagnosed on the basis of vitreous and aqueous cultures and appropriate stains. PCR evaluation of ocular fluids with pan-bacterial primers can also be useful. Vitrectomy may be required. Cultures of blood and other body fluids can help confirm the diagnosis and establish therapy.

Treatment

Intravitreal antibiotics, typically vancomycin and ceftazidime, are given at the time of vitreous sampling (see Appendix B). When fungal organisms may be involved, empiric treatment of both fungal and bacterial causes is indicated. Patients with endogenous bacterial endophthalmitis should be evaluated by a specialist in infectious diseases to identify and treat the systemic source of infection. Intravenous antibiotic treatment may be needed for several weeks, depending on the organism isolated. Initial antimicrobial choices may be empiric and subsequently tailored to the culture results.

Endogenous Fungal Endophthalmitis

Endogenous fungal endophthalmitis develops acutely to subacutely and is associated with poor visual outcomes. Affected patients often have a history of type 1 or type 2 diabetes, immunosuppression, or intravenous drug use. Ocular infection stems from hematogenous spread from a systemic source and usually begins in the choroid, appearing as yellow-white chorioretinal lesions with indistinct borders that can range in size from <1 mm to several disc diameters. Organisms can subsequently break through into the vitreous, producing localized cellular and fungal aggregates overlying the original site(s). Chorioretinal lesions may be difficult to detect on initial presentation, with vitreous inflammation being the

main sign of infection. Anterior segment inflammation, including keratic precipitates and hypopyon, as well as iris nodules and rubeosis, may also be observed.

Endogenous fungal endophthalmitis may be mistaken for noninfectious uveitis and treated with corticosteroids alone. This treatment usually worsens the clinical course of the disease, necessitating further investigation to establish the correct diagnosis. The condition requires aggressive systemic and local antifungal therapy and often surgical intervention. Co-management with a specialist in infectious diseases is essential.

Endogenous fungal endophthalmitis is most commonly caused by *Candida* species, followed by *Aspergillus* species (see the following sections for further discussion). *Cryptococcus neoformans, Coccidioides immitis, Histoplasma capsulatum, Sporothrix schenckii,* and *Blastomyces dermatitidis* are less common causes.

Sridhar J, Flynn HW Jr, Kuriyan AE, Miller D, Albini T. Endogenous fungal endophthalmitis: risk factors, clinical features, and treatment outcomes in mold and yeast infections. *J Ophthalmic Inflamm Infect*. 2013;3(1):60.

Candida *endophthalmitis*

Candida species are an important cause of nosocomial infections and are the most common cause of endogenous fungal endophthalmitis. *Candida albicans,* a yeast naturally found on the skin and mucous membranes as well as in the gut, is the most common pathogenic species, but non-*albicans* species (eg, *Candida glabrata*) have also been identified in patients with fungal endophthalmitis. Fungal organisms reach the eye hematogenously through metastasis to the choroid. Fungi may then break through Bruch membrane, form subretinal abscesses, and secondarily involve the retina and vitreous. Histologically, *Candida* species are recognized as budding yeast with a characteristic pseudohyphate appearance (Fig 14-4; see also BCSC Section 4, *Ophthalmic Pathology and Intraocular Tumors*).

In patients with candidemia, the reported prevalence rates of *Candida* endophthalmitis vary widely. In a systematic review that included a rigorous definition of endophthalmitis and involved more than 1,000 prospectively identified patients with candidemia, the endophthalmitis rate was <1%. Of note, patients with candidemia often have major comorbidities, such as anemia, thrombocytopenia, and hypertension. These comorbidities

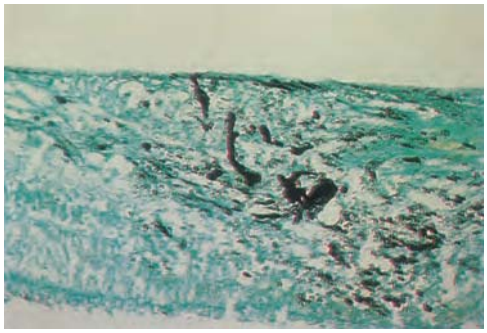

Figure 14-4 *Candida* retinitis in fungal endophthalmitis. Histologic examination with a Gomori methenamine silver stain reveals fungi *(black)* in the retina.

may cause ocular findings, including intraretinal hemorrhages (and Roth spots) and cotton-wool spots, which do not necessarily represent intraocular infection.

Predisposing conditions associated with candidemia and the development of intraocular infection include the following:

- intravenous drug use
- immunosuppressive therapy
- prolonged neutropenia
- organ transplant
- poorly controlled chronic diseases (eg, diabetes)
- use of indwelling catheters
- history of recent major gastrointestinal surgery
- hospitalized neonates
- hyperalimentation
- bacterial sepsis
- systemic antibiotic use

Breazzano MP, Day HR Jr, Bloch KC, et al. Utility of ophthalmologic screening for *Candida* bloodstream infections: a systematic review. *JAMA Ophthalmol*. 2019;137(6):698–710.

Shah CP, McKey J, Spirn MJ, Maguire J. Ocular candidiasis: a review. *Br J Ophthalmol*. 2008;92(4):466–468.

Clinical findings Patients with *Candida* endophthalmitis may present with floaters or blurred vision resulting from vitreous opacities or macular chorioretinal involvement. Patients may also have eye pain arising from associated anterior uveitis, which may be severe. Typically, *Candida* chorioretinitis is characterized by multiple, bilateral, white, well-circumscribed lesions less than 1 mm in diameter. Lesions are typically distributed throughout the postequatorial fundus and are associated with overlying vitreous inflammation (Fig 14-5). The chorioretinal lesions may be associated with vascular sheathing and intraretinal hemorrhages. The vitreous opacities may assume a string-of-pearls appearance.

Rao NA, Hidayat AA. Endogenous mycotic endophthalmitis: variations in clinical and histopathologic changes in candidiasis compared with aspergillosis. *Am J Ophthalmol*. 2001;132(2):244–251.

Diagnosis The diagnosis of ocular candidiasis is suggested by the presence of chorioretinitis or endophthalmitis in the appropriate clinical context and is confirmed by positive results from blood or vitreous culture. It has been suggested that all patients with candidemia undergo baseline dilated ophthalmoscopic examinations and monitoring for the development of metastatic ocular candidiasis for at least 2 weeks after an initial eye examination. However, the American Academy of Ophthalmology currently recommends ophthalmic consultation only for patients with a clinical rationale, such as signs or symptoms concerning for endophthalmitis, or those who are intubated or otherwise unable to communicate ocular symptoms; routine screening for all patients with candidemia is not necessary.

The presence of vitreous snowballs and endophthalmitis may require diagnostic and therapeutic vitrectomy, especially with severe disease or when systemic infection has yet to be confirmed. Fungal stains and cultures on Sabouraud agar plates, as well as pan-fungal

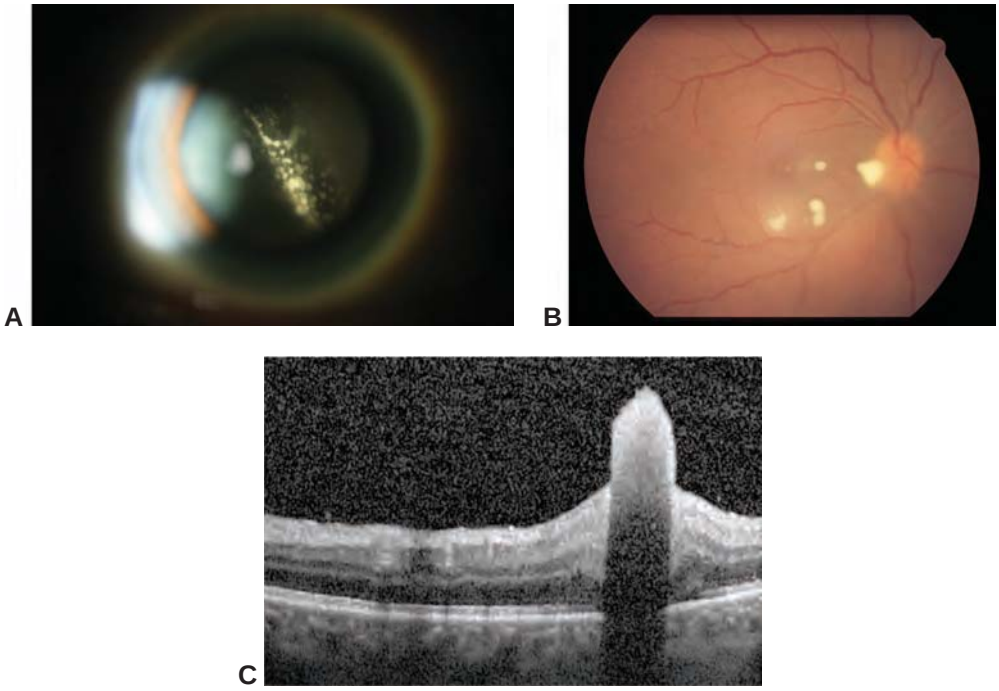

Figure 14-5 Endogenous *Candida* endophthalmitis. **A,** Slit-lamp photograph shows a "string of pearls" in the vitreous. **B,** Fundus photograph shows vitreous opacities and underlying white chorioretinal lesions. **C,** Optical coherence tomography line scan shows a fungal lesion breaking through the retina into the vitreous cavity. *(Part A courtesy of H. Nida Sen, MD, and Henry Wiley, MD/National Eye Institute; part B courtesy of Debra A. Goldstein, MD; part C courtesy of Jared E. Knickelbein, MD, PhD.)*

PCR and PCR for *Candida* species if available, should be obtained on undiluted vitreous fluid samples. Blood cultures should also be obtained if systemic infection has yet to be confirmed.

The differential diagnosis of *Candida* endophthalmitis includes infection with other fungi or bacteria as well as *Toxoplasma* retinochoroiditis, which can exhibit similar posterior pole lesions. *Candida* snowball lesions may also resemble pars planitis.

Breazzano MP, Bond JB III, Bearelly S, et al; for the American Academy of Ophthalmology. American Academy of Ophthalmology recommendations on screening for endogenous *Candida* endophthalmitis. *Ophthalmology*. 2022;129(1):73–76.

Hidalgo JA, Alangaden GJ, Eliott D, et al. Fungal endophthalmitis diagnosis by detection of *Candida albicans* DNA in intraocular fluid by use of a species-specific polymerase chain reaction assay. *J Infect Dis*. 2000;181(3):1198–1201.

Treatment The treatment of intraocular candidiasis includes systemic and often intravitreal administration of antifungal drugs. Consultation with a specialist in infectious diseases is essential. Chorioretinal lesions not yet involving the vitreous body may be treated effectively with the oral triazole antifungal drugs fluconazole or voriconazole (200 mg, twice daily, for 2–4 weeks), with vigilant monitoring for evidence of progression. Voriconazole is often preferred as it has good oral bioavailability, achieving therapeutic intravitreal levels with a broad spectrum of antifungal activity. When the vitreous body is involved, intravitreal injection

of antifungal drugs (amphotericin B, 5–10 μg/0.1 mL, or voriconazole, 100 μg/0.1 mL; see Appendix B) should be considered, usually in conjunction with pars plana vitrectomy. Long-acting corticosteroid injections should be avoided. Vitrectomy may be useful diagnostically by providing intraocular fluid for microbiologic and molecular analyses and therapeutically by debulking the pathogen load and clearing the vitreous inflammation.

More severe infections may require intravenous amphotericin B with or without flucytosine. Major dose-limiting toxicities (renal, cardiac, and neurologic) associated with conventional amphotericin B therapy have been greatly reduced by the use of liposomal lipid complex formulations. Finally, intravenously administered caspofungin, an antifungal drug in the echinocandin class (ie, drugs that inhibit synthesis of glucan in the cell wall) with activity against *Candida* and *Aspergillus* species, has been successfully employed in a small number of patients with *Candida* endophthalmitis; however, some treatment failures have also been reported with this drug. Another echinocandin agent, intravenous micafungin, is also available in the United States and Europe for treatment of candidiasis. Oral voriconazole, flucytosine, fluconazole, or rifampin may be administered in addition to intravenous amphotericin B or caspofungin. Systemic antifungal treatment may be necessary for 6 weeks or longer.

Hariprasad SM, Mieler WF, Holz ER, et al. Determination of vitreous, aqueous, and plasma concentration of orally administered voriconazole in humans. *Arch Ophthalmol.* 2004;122(1):42–47.

Paulus YM, Cheng S, Karth PA, Leng T. Prospective trial of endogenous fungal endophthalmitis and chorioretinitis rates, clinical course, and outcomes in patients with fungemia. *Retina*. 2016;36(7):1357–1363.

Riddell J IV, Comer GM, Kauffman CA. Treatment of endogenous fungal endophthalmitis: focus on new antifungal agents. *Clin Infect Dis*. 2011;52(5):648–653.

Aspergillus *endophthalmitis*

Aspergillus species are molds found in soils and decaying vegetation. The spores of these ubiquitous saprophytic molds become airborne and seed the lungs and paranasal sinuses of humans. Human exposure is very common, but infection is rare and depends on the virulence of the fungal pathogen and immunocompetence of the host. Ocular disease occurs via hematogenous spread of *Aspergillus* organisms to the choroid.

Endogenous *Aspergillus* endophthalmitis is a rare disorder associated with disseminated aspergillosis among patients with severe chronic pulmonary diseases, cancer, organ transplant, endocarditis, severe immunocompromise, or intravenous drug use. In isolated instances, *Aspergillus* endophthalmitis occurs in immunocompetent patients with no apparent predisposing factors. Disseminated infection most commonly involves the lungs; the eye is the second most common site of infection. *Aspergillus fumigatus* and *A flavus* are the species most frequently isolated from patients with intraocular infection.

Clinical findings Endogenous *Aspergillus* endophthalmitis results in rapid onset of pain and loss of vision. A confluent yellowish infiltrate is often present in the posterior pole, beginning in the choroid and subretinal space (Fig 14-6A). A hypopyon can develop in the subretinal or subhyaloidal space. Retinal hemorrhages, retinal vascular occlusions, and full-thickness retinal necrosis may occur. The infection can spread, producing a dense vitritis and variable degrees of cells, flare, and hypopyon in the anterior chamber. When healed, the macular lesions form a central atrophic scar.

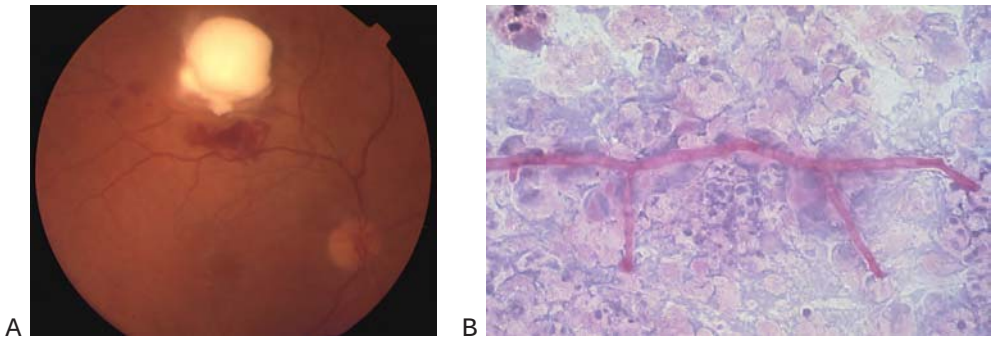

Figure 14-6 *Aspergillus* endophthalmitis. **A,** Fundus photograph shows a large granuloma in the posterior pole. **B,** Histologic specimen shows septate hyphae. *(Courtesy of Ramana S. Moorthy, MD.)*

Diagnosis The diagnosis of endogenous *Aspergillus* endophthalmitis is based on clinical findings combined with positive results from vitreous biopsy and cultures as well as results from Gram and fungal stains. Coexisting systemic aspergillosis can be a strong clue of dissemination to the eye, especially among high-risk patients. The diagnosis requires a high degree of suspicion within the correct clinical context and is confirmed by the demonstration of dichotomously branching septate hyphae on analysis of vitreous fluid specimens (Fig 14-6B). *Aspergillus* organisms may be difficult to culture from the blood.

The differential diagnosis of endogenous *Aspergillus* endophthalmitis includes *Candida* endophthalmitis, cytomegalovirus retinitis, *Toxoplasma* retinochoroiditis, coccidioidomycotic choroiditis or endophthalmitis, and bacterial endophthalmitis. In contrast to the lesions associated with *Candida* chorioretinitis and endophthalmitis, lesions produced by *Aspergillus* species are larger and more likely to be hemorrhagic, and they commonly invade the retinal and choroidal vessels, which may result in broad areas of ischemic infarction.

Rao NA, Hidayat A. A comparative clinicopathologic study of endogenous mycotic endophthalmitis: variations in clinical and histopathologic changes in candidiasis compared to aspergillosis. *Trans Am Ophthalmol Soc*. 2000;98:183–193; discussion 193–194.

Treatment Endogenous *Aspergillus* endophthalmitis usually requires aggressive treatment with diagnostic and therapeutic pars plana vitrectomy combined with intravitreal injection of amphotericin B or voriconazole. Intravitreal corticosteroids may be used in conjunction with these drugs. Because most patients with this condition have disseminated aspergillosis, systemic treatment with oral voriconazole, intravenous amphotericin B, or caspofungin is often required. Other systemic antifungal drugs, such as itraconazole, miconazole, fluconazole, and ketoconazole, may also be used. Systemic aspergillosis should be managed by a specialist in infectious diseases. Despite aggressive treatment, the visual prognosis is poor because of frequent macular involvement. Final visual acuity is usually less than 20/200. Disseminated aspergillosis has a high mortality rate.

Spadea L, Giannico MI. Diagnostic and management strategies of *Aspergillus* endophthalmitis: current insights. *Clin Ophthalmol*. 2019;13:2573–2582.