



## Bilateral infectious scleritis from *Histoplasma capsulatum* in an immunosuppressed uveitis patient

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### ABSTRACT

**Purpose:** To describe a case of bilateral infectious scleritis secondary to *Histoplasma capsulatum* in the setting of a locally and systemically immunosuppressed patient.

**Observations:** A 45-year-old man with HLA-B27 associated ankylosing spondylitis and anterior uveitis on systemic secukinumab, underwent bilateral cataract extraction which required extensive peri-operative steroids, including intravitreal triamcinolone, topical prednisolone, and oral prednisone. Six weeks after cataract surgery, the patient presented with mild eye irritation and was found to have bilateral subconjunctival purulence and necrosis. *Histoplasma capsulatum* was identified on fungal cultures and confirmed by DNA probe. The patient was treated with fortified amphotericin drops and oral itraconazole with complete resolution of scleritis.

**Conclusion and importance:** *H. capsulatum* is a rare cause of infectious scleritis that must be considered in our immunosuppressed and post-surgical patients.

### 1. Introduction

*Histoplasma capsulatum* is a ubiquitous dimorphic fungus found in soil and is endemic to the Midwest United States along the Ohio and Mississippi River valleys.<sup>1</sup> Approximately 90% of systemic infections by *H. capsulatum* are subclinical and self-limited.<sup>2</sup> Rarely, severe infections may present with acute pulmonary disease or hematogenous dissemination into multiple organ systems, most commonly the liver, spleen, gastrointestinal tract, and bone marrow.<sup>2</sup> Ocular infections are a rare complication of systemic *H. capsulatum* infection.

*H. capsulatum* is the alleged causative agent in the presumed ocular histoplasmosis syndrome (POHS) which is on the spectrum of inflammatory choroidopathies. Other less common ocular presentations of histoplasmosis include endophthalmitis,<sup>3</sup> conjunctival granulomas,<sup>4</sup> and chorioretinitis.<sup>5</sup> Infectious scleritis from *H. capsulatum* is exceedingly rare, with only two unilateral cases documented in the literature.<sup>6,7</sup> We report a case of bilateral infectious necrotizing scleritis secondary to *H. capsulatum* after cataract surgery in a patient who is both locally and systemically immunosuppressed.

### 2. Case report

A 45-year-old Caucasian male with a history of HLA-B27 associated

ankylosing spondylitis and anterior uveitis on secukinumab initially presented with progressively worsening vision in both eyes. He is a resident of rural Ohio and works as commercial truck driver. He underwent sequential cataract surgery in both eyes one month apart and was placed on extensive perioperative steroids, including intravitreal triamcinolone, topical prednisolone, and oral prednisone to control his robust inflammatory response. Post-operatively the patient was successfully tapered off of all steroids and remained inactive on secukinumab.

Six weeks after his second cataract surgery the patient presented with mild irritation in both eyes. Ocular examination revealed a visual acuity of 20/30 in his right eye (OD) and 20/50 in his left eye (OS). Examination of the right eye revealed diffuse temporal scleral injection with central whitening, sub-conjunctival purulence, and scleral necrosis (Fig. 1A). The left eye revealed similar, but more severe findings (Fig. 1B). There was no evidence of intraocular inflammation. Residual triamcinolone could be visualized in the left anterior vitreous. Anterior segment optical coherence tomography of these lesions demonstrated thickening of the temporal sclera with hypoechoic cysts within the sclera (Fig. 1C–D).

The conjunctiva was punctured, and the subconjunctival purulence was cultured from both eyes. He was initially started on oral and topical moxifloxacin. After 3 days there was no growth of the cultures and the

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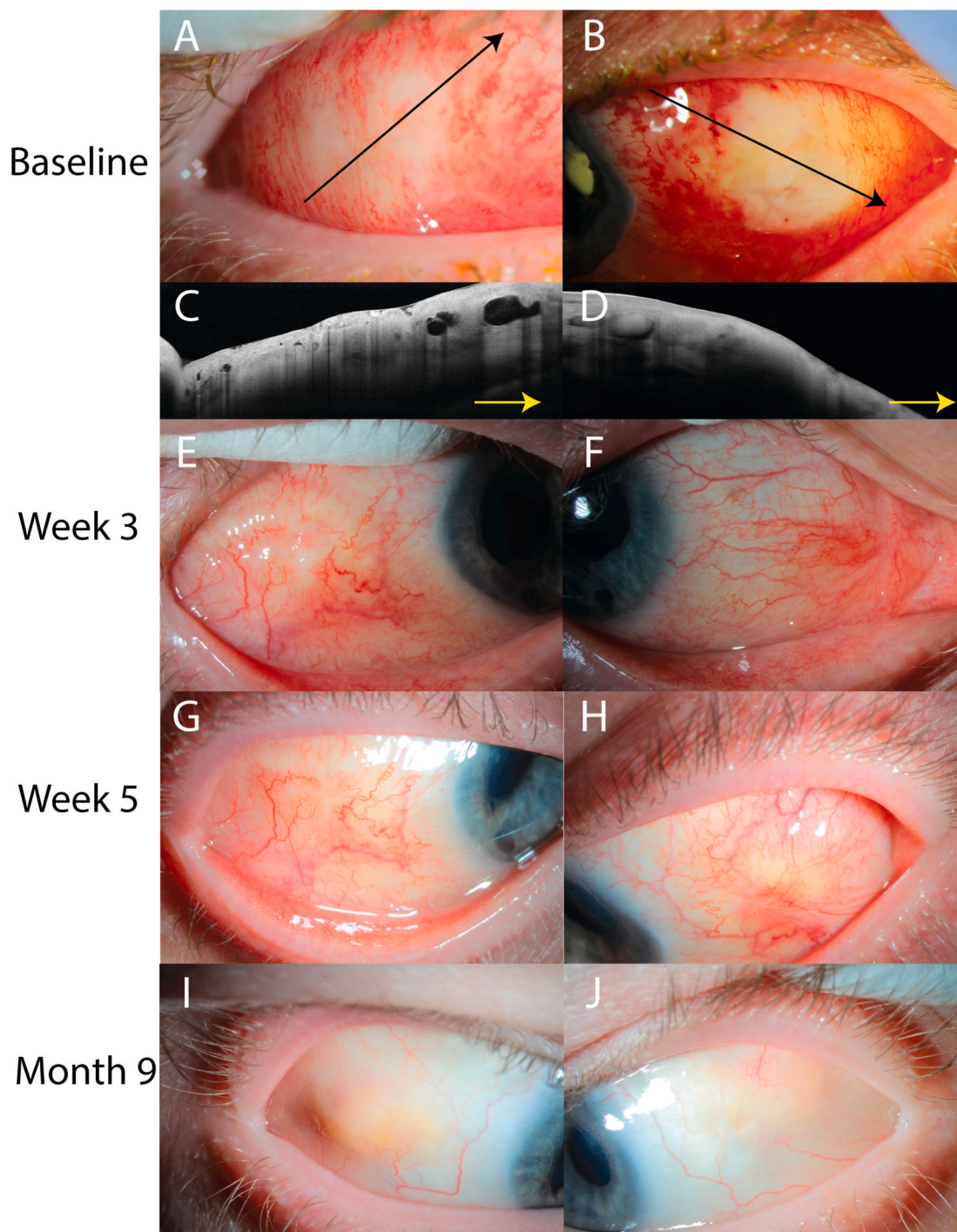
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patient's exam remained unchanged. He was started on 50mg oral prednisone. One week later, fungal culture with staining by lactophenol cotton blue of the left eyes revealed tuberculate macroconidium consistent with *H. capsulatum*, which was confirmed by DNA accuprobe (Hologic, Marlborough, MA). He was initiated on oral itraconazole 200 mg twice daily and fortified topical amphotericin B 0.15% four times daily with a rapid taper of oral prednisone. Chest X-ray was negative for intra-pulmonary nodules suggestive of active pulmonary histoplasmosis. Complete evaluation by an infectious disease specialist was unconvincing for associated disseminated systemic disease. Three days later

his right eye grew *H. capsulatum*. The patient was treated with topical amphotericin for two months until the subconjunctival purulence resolved (Fig. 1E-H). The patient is maintained on a six-month course of itraconazole guided by an infectious disease specialist. On most recent follow-up, nine months after presenting with subconjunctival purulence, the patient had a BCVA of 20/30 OD and 20/80 OS without evidence of active scleritis (Fig. 1I-J). Visual acuity of the left eye was limited by cystoid macular edema secondary to HLA-B27 iritis.



**Fig. 1.** External photos of the A) right and B) left eye at initial presentation demonstrating temporal sub-conjunctival abscesses and surrounding injection. OCT b-scans through the purulent abscesses of C) right and D) left eye with scleral thickening and hypochoic cysts. External photos at week 3 (E-F), week 5 (G-H), and month 9 (I-J) after initial presentation of right and left eyes demonstrate resolution of scleritis of both eyes.

### 3. Discussion

Infection is an uncommon cause of scleritis, accounting for only 5–10% of cases.<sup>8</sup> Among the infectious etiologies, the most common cause is *Pseudomonas aeruginosa*, with mycotic etiologies ranging from 5 to 38% of infectious cases.<sup>8</sup> If a fungal organisms are suspected, cultures should be kept for longer regardless of persistently negative bacterial cultures. Fungal cultures at our institution are kept for 28 days minimum. A review of the literature reveals that there are only two case reports of *H. capsulatum* scleritis.<sup>6,7</sup> In both reported cases, unilateral scleritis was described.

In one case, a 47-year-old woman on methotrexate, azathioprine, and oral prednisone for rheumatoid arthritis and dermatomyositis presented with red eye and decreased visual acuity. Exam revealed a purulent and necrotic scleral lesion and she was diagnosed with *H. capsulatum* scleritis via fungal cultures and PCR.<sup>7</sup> The patient demonstrated marked improvement after 8 days of oral itraconazole. The second case described a 77-year-old man who developed a painless yellow scleral lesion one month after uncomplicated cataract surgery.<sup>6</sup> Notably, he had received a periocular triamcinolone injection for idiopathic vitritis eight months prior to developing scleritis.<sup>6</sup> Similar to the present case, this patient was treated with oral itraconazole and topical amphotericin B 0.15%, but ultimately required surgical debridement due to non-response with extension of the necrosis through Tenon's capsule and the lateral rectus muscle.

Our case is unique given the bilateral presentation in a patient who underwent cataract surgery months earlier. Our patient was chronically immunosuppressed on secukinumab, a human monoclonal antibody which inhibits IL-17A and is FDA approved for the treatment of ankylosing spondylitis.<sup>9</sup> He also received peri-operative intravitreal triamcinolone in both eyes, as well as post-operative topical and oral steroids to treat his exuberant post-operative inflammation. We hypothesize that the combination of systemic immunosuppression in combination with long-acting local steroids allowed the opportunistic *H. capsulatum* to thrive in the locally immunosuppressed sclera. The patient has no prior history of *H. capsulatum* infection, and as such, it is difficult to know if this represents de novo infection versus latent reactivation. Beyond a chest x-ray, no further systemic work-up was pursued as guided by our infectious disease specialist as the patient did not exhibit signs or symptom of disseminated disease. Nonetheless, systemic histoplasmosis has been associated with immunomodulatory therapy in the uveitic population.<sup>10</sup> Starr et al. examined patients on systemic immunosuppression for noninfectious uveitis and the development of disseminated or pulmonary histoplasmosis. They found this population to be at higher risk of developing *Histoplasma* infections, with nine reported cases of disseminated or pulmonary disease that recovered after systemic antifungals.

Ophthalmologists must be aware that scleritis is a rare manifestation of systemic *Histoplasma capsulatum* infection and that immunomodulatory therapy appears to be a risk factor for *H. capsulatum* infection. Additionally, cataract surgery in uveitic patients brings with it a set of unique challenges. The high rates of postoperative inflammation mandates aggressive peri-operative control of inflammation, often achieved with a combination of systemic immune suppression and local steroid therapy.<sup>11</sup> The use of aggressive immunosuppression increases the risk of local infection with both typical and atypical microbes. This report emphasizes the need for careful monitoring of post-operative uveitis patients especially those who are actively managed with systemic and local immunosuppressive therapy.

#### Patient consent

Consent to publish the case report was not obtained. This report does

not contain any personal information that could lead to the identification of the patient.

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#### Authorship

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#### Declaration of competing interest

None exist for any of the authors.

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