Occult Fungal Scleritis

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Key Words

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Abstract

Purpose: To heighten awareness of occult fungal scleritis.
Method: Case report and review of the literature. **Results:** A 73-year-old woman with diabetes mellitus was diagnosed for 3 months with immune-mediated scleritis and subsequently treated with corticosteroids. On referral, the patient had a scleral nodule with contiguous corneal infiltrate and hypopyon. Culture grew *Fusarium* species not further classified. The infection could not be controlled with antifungal therapy, and the eye was removed. No exogenous or endogenous source for the infection could be identified by clinical history or examination. **Conclusion:** Fungal scleritis can develop in persons without a history of foreign body injury, minor trauma, or evidence of endogenous fungemia. A high index of suspicion for infectious scleritis must be maintained in persons with presumed immune-mediated scleritis who fail to respond to conventional therapy, particularly if they present with decreased visual acuity. © 2016 S. Karger AG, Basel

Introduction

Establishing an accurate diagnosis of infectious scleritis can be challenging. In the largest published case series of infectious scleritis, the average time between onset of symptoms and diagnosis was 12 days, with nearly a quarter of cases taking 1 month or longer [1]. Of those eyes correctly diagnosed, almost 50% lost functional vision. In the vast majority of cases, infectious scleritis follows accidental or surgical trauma, and rarely can be attributed to hematogenous spread [2–5]. We describe a patient with delayed diagnosis of *Fusarium* scleritis who had no clear identifiable source for her infection.

Case Report

A 73-year-old woman with type I diabetes mellitus was referred for evaluation of unilateral scleritis and uveitis. Her past ocular history was significant for proliferative diabetic retinopathy, for which she received panretinal photocoagulation in both eyes 6 years previously, and cataract extraction with intraocular lens placement 5 years ago. Her current affliction started 4 months earlier with left eye pain and blurred vision. The patient denied using

contact lenses and there was no history of injury prior to the onset of symptoms. Her referring retina specialist reported a visual acuity of 20/50 in the affected eye. Pertinent findings consisted of 1+ corneal edema, mild conjunctival injection, and a new vitreous hemorrhage. She was treated with prednisolone acetate 1% once daily. The vitreous hemorrhage was observed. Intermittent left eye pain continued for 7 weeks, accompanied by severe left-sided headache and left temporal pain. Her ocular examination was unchanged. The erythrocyte sedimentation rate was 10 mm/h. A neurologist consultant diagnosed trigeminal neuralgia and placed her on gabapentin and oxycodone with minimal relief. A month later, a subtenon injection of triamcinolone acetonide was given. The eye pain and redness worsened. Then a cornea specialist evaluated the patient and diagnosed her with uveitis and referred her for a second opinion because of a hypopyon. There was concern for an autoimmune etiology and thus oral prednisone was started. A comprehensive rheumatologic workup was undertaken, but the results were unrevealing. Her blood sugar on prednisone remained adequately controlled, but there were periods of poor glycemic control in the past with hemoglobin A1c as high as 9.3%. As her ocular condition further deteriorated, she was referred for another opinion.

On presentation to Morsani College of Medicine, her best-corrected visual acuity in her left eye was 20/400. No afferent pupillary defect was present and her intraocular pressure was within normal limits. Pertinent ocular findings included a temporal scleral nodule with an associated crescent-shaped peripheral corneal infiltrate, which had previously been diagnosed as a pterygium (fig. 1). A small hypopyon was present. The scleral nodule was thick and soft when balloted with cotton tip applicator. No corneal wound from her previous cataract surgery was visualized. Dilated examination revealed asteroid hyalosis and peripheral photocoagulation scars from previously treated proliferative diabetic retinopathy. The vitreous hemorrhage had largely absorbed and settled inferiorly. Anterior segment optic coherence tomography revealed mild hyperreflectivity of stroma and endothelium (fig. 1, inset). Examination of the right eye showed signs of proliferative diabetic retinopathy and old photocoagulation scars, and was otherwise non-contributory.

The patient consented to a scleral biopsy, which was performed the same day. In the operating room, a small creamy discharge was noted after conjunctival incision over the nodule. Three days later, scleral cultures grew nine colonies of mold, which were later identified as *Fusarium* species, sensitive to amphotericin B and voriconazole. The overlying conjunctival biopsy revealed nonspecific chronic inflammation; histochemical stains for fungus were negative.

With input from an infectious disease consultant, the patient was treated with topical natamycin 5% every 2 h, topical voriconazole 1% every 4 h, and topical amphotericin B 0.05% every hour. Oral voriconazole and intravenous amphotericin B liposome were also given. Five days after her initial biopsy, due to an enlarging corneal infiltrate, the patient was taken back to the operating room for corneal debridement and cryotherapy of the corneal infiltrate. An intrastromal corneal injection of 0.50 ml of voriconazole (50 µg/ml) was given and the remaining subtenon Kenalog was removed. An additional intrastromal injection of voriconazole was given 4 days later. Despite treatment, the corneal infiltrate continued to enlarge, while the vision deteriorated and the eye pain worsened. Two weeks later, an afferent pupillary defect and limited abduction were detected. Surgical enucleation was recommended.

Fig. 1. A nonulcerated peripheral corneal infiltrate is adjacent to the scleral nodule. The entire sector of conjunctiva is inflamed. A hypopyon is seen inferiorly in the anterior chamber. **Inset** Anterior segment optic coherence tomography shows hyperreflectivity of the stroma and endothelium. The scleral nodule is noted immediately posterior to the limbus.

Histological examination of the globe revealed scleral ectasia with mixtures of neutrophils and lymphocytes, and extensive scleral necrosis (fig. 2). Septate fungal hyphae 5–9 µm in diameter were found in the peripheral cornea, sclera, and anterior chamber (fig. 3, 4). Fungal hyphae tracked within the sclera posteriorly past the equator. Localized acute and chronic vitritis was present. Anterior orbital connective tissue was chronically inflamed, but without identifiable fungal elements.

Following enucleation, the patient was continued on oral voriconazole for 3 months and recovered uneventfully. She had no evidence of infection elsewhere.

Discussion

Infectious scleritis is almost always preceded by a history of accidental or surgical trauma. Our patient's infection, which ultimately resulted in loss of the eye, could never be linked to any foreign body injury. Given her history of cataract extraction with intraocular lens placement, it is possible that her scleral necrosis was due to surgically induced necrotizing scleritis. However, surgically induced necrotizing scleritis in the setting of cataract procedures is attributed more often to systemic autoimmune disease rather than infection [6]. Rarely, infectious scleritis may be acquired through hematogenous spread [4]. When *Fusarium* causes hematogenous-

Fig. 2. The enucleated eye shows severe scleral thinning (arrow) at the clinical nodule. The lens was dislocated during sectioning. Scleral inflammation and necrosis extends past the equator of globe. The orbital connective tissue contiguous to the inflamed sclera was infiltrated by lymphocytes and histiocytes, and fewer numbers of neutrophils (hematoxylin-eosin, scale bar = 2.75 mm).

ly disseminated disease, it is usually in the context of severe immunosuppression, particularly prolonged neutropenia [7]. Other than diabetes mellitus, our patient was not immunocompromised (no risk factors for HIV, not on chemotherapy, prior corticosteroid use, etc.). While her diabetes mellitus may have caused some degree of immunosuppression, it would not fully elucidate the cause of her infection. Other than rhinocerebral mucormycosis, invasive fungal infections are not more prevalent in persons with diabetes mellitus [8]. Our patient also had no history of recent febrile illness, no history of dialysis, and no identifiably endogenous source of infection (e.g. pulmonary infiltrate, indwelling catheter, etc.).

Could the infection in our patient have been acquired from the subtenon injection of triamcinolone acetonide? Subtenon injections have been reported as the cause of infectious scleritis [9–11], but our patient had symptoms

Fig. 3. Periodic acid-Schiff stain reveals numerous fungal hyphae within the layers of the cornea. Descemet's membrane has been detached. Purulent exudate fills the anterior chamber and the space between Descemet's membrane and the stroma (scale bar = 170 μ m). **Inset** Magnified view of the same area with a closer view of the fungal hyphae in the cornea and the confluent neutrophils within the anterior chamber (scale bar = 75 μ m). DM = Descemet's membrane.

Fig. 4. High-magnification view of the sclera marked with an arrow in figure 2 shows septate fungal hyphae at the junction of necrotic tissue above and scleral collagen below (scale bar = 75 μ m).

and signs of scleral inflammation more than a month before the injection. Furthermore, the patient's first ophthalmologist could not recall using any compounded steroid on the patient.

Could the diagnosis of infectious scleritis have been suspected earlier? Infectious scleritis is often mistaken for autoimmune scleritis due to their similar presentation [5]. However, one potential clue, albeit nonspecific, was the decrease in visual acuity at the time of presentation (i.e. 20/50 in the affected eye). 34–80% of patients with infectious scleritis present with or develop impaired central acuity in contrast to only 3–12% with immune-mediated disease [1, 11–13]. Sainz de la Maza et al. [14] found patients with infectious scleritis have over four times the risk of presenting with or developing reduced vision versus those with other forms of scleritis [14]. Had the connection between vision loss and infectious scleritis been appreciated earlier, it may have prompted timelier biopsy and culture.

Both infectious and autoimmune scleritis can result in a hypopyon, but anecdotal experience would suggest it is more commonly found with infection. Our patient's hypopyon was a relatively late finding, detected 3 months after her scleritis was diagnosed. Had it been noted earlier, an infectious etiology may have been pursued sooner.

Fusarium is the most common fungus causing keratitis in subtropical regions of the world. We are left to conclude that our patient's initial infection originated from conjunctiva or cornea but apparently reached deeper tissues

without causing noteworthy signs or symptoms of surface infection. To avoid catastrophic outcomes, clinicians should maintain a high index of suspicion of infectious scleritis in persons considered to have immune-mediated scleritis who fail to respond to conventional therapy, particularly in the presence of impaired visual acuity. Finally, this case offers another cautionary anecdote beyond scleral perforation against subconjunctival injection of corticosteroids for nonnecrotizing anterior scleritis [15]. Given the devastating consequences of corticosteroids on invasive fungal infection, the diagnosis of immune-mediated nonnecrotizing anterior scleritis must be certain before pursuing periocular administration.

Statement of Ethics

The subject provided consent to publication of this case and its associated images. No IRB approval was required for publication of this case report.

Disclosure Statement

There is no conflict of interest to disclose.

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