Endogenous Group A Streptococcal Endophthalmitis in a Healthy 42-Year-Old Man: A Case Report

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Perm J 2018;22:17-081

E-pub: 06/28/2018

https://doi.org/10.7812/TPP/17-081

ABSTRACT

Introduction: Endogenous endophthalmitis is a rare condition that is caused by hematogenous spread of bacteria or fungi and is usually seen in patients with predisposed medical conditions. We are reporting an unusual case of group A streptococcal infection causing endogenous endophthalmitis and septic arthritis in a healthy 42-year-old man.

Case Presentation: A previously healthy 42-year-old man presented to the Emergency Department with chills, fever, left wrist pain, left eye pain, and vision loss. Owing to the acute onset of the septic arthritis and the patient's bandemia, the Ophthalmology Department was consulted for suspicion of endophthalmitis. Blood cultures, left wrist synovial fluid cultures, and vitreous cultures grew group A streptococcus. An incision and drainage of the left wrist was performed, and intravitreal injection of vancomycin was given. The patient's vision was responsive only to light on discharge from the hospital. The patient underwent a left eye evisceration 2 months later.

Discussion: Endophthalmitis provides a difficult diagnostic and therapeutic challenge. However, even with prompt treatment, visual outcomes may be poor.

INTRODUCTION

Endophthalmitis is a rare and devastating disease. In clinical practice, endophthalmitis is defined as an intraocular bacterial or fungal infection. Endophthalmitis is categorized into 2 different types, exogenous and endogenous. Exogenous endophthalmitis occurs when bacterial or fungal organisms are introduced after ocular surgery, from retained foreign bodies, or from lacerating trauma. Endogenous endophthalmitis occurs when organisms reach the eye from crossing the blood-ocular barrier from the blood stream and accounts for 2% to 8% of all cases of endophthalmitis.[1,2] Endogenous endophthalmitis typically affects patients with medical conditions such as diabetes, intravenous drug use, HIV infection, malignant tumor, or other autoimmune diseases.[1] One review[1] showed that 207 (60%) of 342 patients had a medical condition that predisposed them to infection, and another source[2] reported 90% of patients had a condition that predisposed them to infection. There have been other case reports in which healthy patients have developed endophthalmitis from *Staphylococcus epidermidis*,[3,4] *Listeria monocytogenes*,[5] *Aspergillus*,[6] and *Pseudomonas*.[7]

Some of the causative agents in bacterial endogenous endophthalmitis include *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Neisseria meningitides*, and other *Streptococcus* species.[1] Some typical sources of infection include liver abscesses, lung and soft tissue infections, endocarditis, meningitis, and septic arthritis.[1]

CASE PRESENTATION

Presenting Concerns

A 42-year-old Asian man presented to the Emergency Department with chills, fever, left wrist pain, left eye pain, and vision loss. The patient reported that he developed chills 2 days before presentation. One day before presentation he started developing body aches and left wrist pain. Later that day, his left eye became erythematous and started developing vision loss. Systems review revealed no weight loss, nausea, or lesions of the mouth or genitalia. There was no history of diabetes, malignant tumor, autoimmune disease, immune compromise, recent travel, recent surgery, or intravenous drug use.

Examination of his left eye revealed an erythematous conjunctiva and cloudy pupil. The visual acuity in the left eye was hand motion. The left wrist was also erythematous and swollen. Laboratory testing was significant for a white blood cell count of 14,900 (74% neutrophils, 19% bands) and a lactate of 3.7 mmol/L. The patient's family history was significant for polymyalgia rheumatica and gout in his father and breast and colon cancer in his mother (diagnosed at age 67 years).

Gram stain of the patient's left wrist revealed gram-positive cocci and many white blood cells. Because of the acute onset of ocular complications in the context of sepsis, the Ophthalmology Department was consulted on suspicion of endophthalmitis.

Therapeutic Intervention and Treatment

The patient received 500 mg of acetazolamide in the Emergency Department because it was thought that he may have had acute narrow-angle glaucoma. An orthopedist performed an incision and drainage of the left wrist. An ophthalmologist performed a vitreous tap and intravitreal injection of vancomycin (1 mg in 0.1 cc normal saline dilution) in the patient's left eye. The patient also received a second intravitreal injection of vancomycin 2 days later and was given prednisolone eye drops. Within 24 hours of admission, the patient was started on 2 g of intravenous ceftriaxone twice per day and 1750 mg of intravenous vancomycin once per day. Vancomycin was discontinued after culture results were analyzed, and 900 mg of clindamycin 3 times per day was added. The patient

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was discharged from the hospital with a peripherally inserted central catheter and continued on 2 g of ceftriaxone twice per day for 3 more weeks.

Follow-Up and Outcomes

An extensive evaluation included transesophageal echocardiography to rule out endocarditis; it was negative. A computed tomography scan of the chest and abdomen/pelvis looking for occult malignant tumor was negative, and chest radiograph revealed only a left lung base infiltrate. Blood cultures grew group A streptococcus, left wrist synovial fluid aspirate grew group A streptococcus, and vitreous cultures from the left eye grew group A streptococcus. The HIV antibody was nonreactive.

On the second day of hospitalization, examination revealed worsening left eye vision that was responsive only to light; however, further examinations were stable. On the third day of hospitalization, a second intravitreal injection of vancomycin was performed. On the fifth day of hospitalization, there was increasing erythema and swelling on the left arm. A follow-up computed tomography scan of the left upper extremity revealed mild edema in the muscles within the distal anterior aspect of the forearm and small air bubbles in the subcutaneous tissues posterior to the carpal bones. A second incision and drainage was performed. The patient's eye, 7 days after admission, is shown in Figure 1. When the patient was discharged on day 10, his left eye was responsive only to light.

Two months later, because of the severity of the illness, it was recommended by the retina service that the patient undergo evisceration of the left eye, which he elected to do. Figure 2 shows a timeline of the case.

DISCUSSION

Endophthalmitis provides a difficult diagnostic and therapeutic challenge. Misdiagnosis of endogenous endophthalmitis is common. One review[1] noted that 89 (26%) of 342 patients were misdiagnosed. Misdiagnoses may also be underreported in literature.[1,8] In one case series,[8] 63% of the cases were initially misdiagnosed. It may be diagnosed as conjunctivitis early in the disease process, whereas later presentation with severe inflammation and high intraocular pressure may lead to a diagnosis of acute narrow-angle glaucoma if the overall clinical picture is not considered.[8] When our patient arrived in the Emergency Department, he was initially thought to have acute narrow-angle glaucoma and was given acetazolamide. A few hours later, the admitting physician had a high suspicion for endophthalmitis because of the acute ocular disease in the setting of sepsis. Even with prompt intravitreal injection of vancomycin within 1 day of visual symptoms, the visual prognosis was ultimately poor.

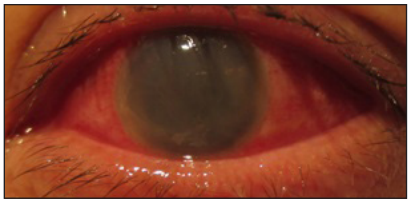

Figure 1. The patient's left eye, seven days after admission.

Group A streptococcus, also known as *Streptococcus pyogenes*, is a gram-positive, epithelial-surface-colonizing cocci[9] and is not typically associated with endophthalmitis. It was the causative agent in 2 of the 342 cases in one review[1] of cases from 1986 to 2012 and 0 of the 27 cases of another review[10] of cases from 1982 to 2000. Table 1 provides a list of causative bacterial organisms, adapted from the review article by Jackson et al.[1]

Group A streptococcus causes a diverse range of diseases such as pharyngitis, impetigo, cellulitis, scarlet fever, pneumonia, toxic shock syndrome, necrotizing fasciitis, septic arthritis, endocarditis, and rheumatic fever.[9] It has many virulence factors, is able to migrate to normally sterile areas such as the bloodstream and tissues,[9] and as in our case is able to cause

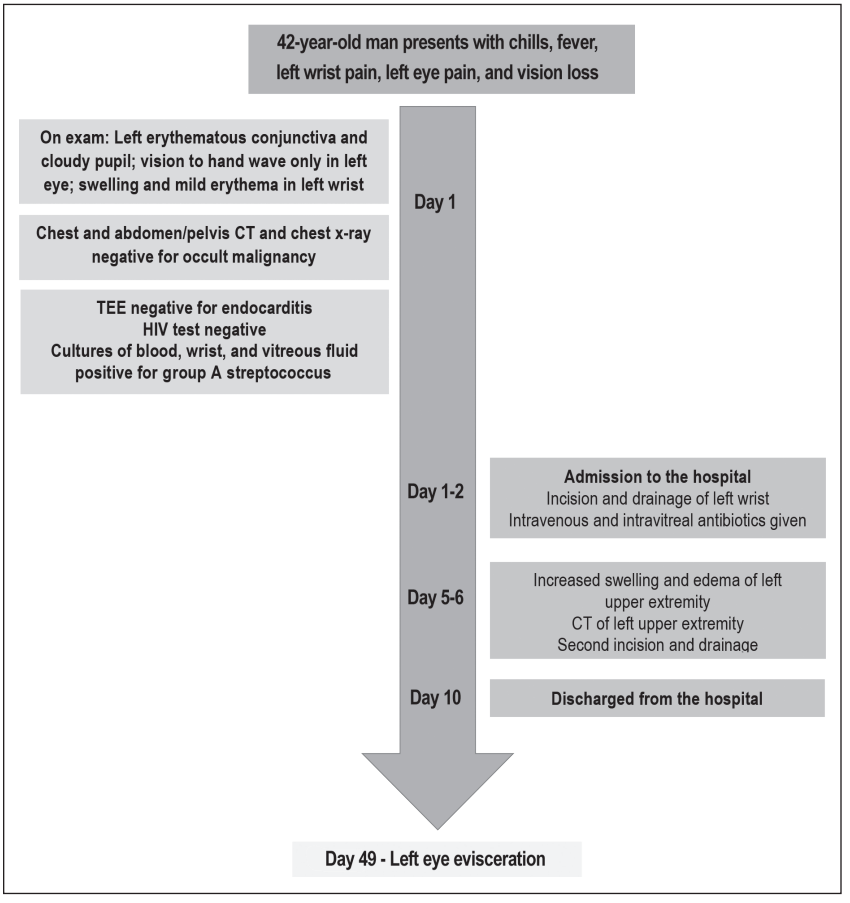

Figure 2. Timeline of the case.

CT = computed tomography; exam = physical examination; TEE = transesophageal echocardiography.

bacteremia and subsequent endophthalmitis and septic arthritis. Group A streptococcus infection can lead to Sydenham chorea and has been associated with pediatric autoimmune neuropsychiatric disorders with streptococcal infections; one mechanism proposed is associated with antibody cross-reaction with neuronal brain tissue.[9] The mechanisms underlying invasive group A streptococcus disease remain the subject of intense research.[9]

Table 1. Causative bacteria for 342 patients diagnosed with endogenous endophthalmitis[a]

Bacterial organism[b]	N (%)
Gram-positive organisms	
Staphylococcus aureus	33 (10)
Streptococcus pneumoniae	17 (5)
Other streptococcal species[c]	44 (13)
Nocardia species	12 (4)
Listeria monocytogenes	12 (4)
Bacillus cereus	8 (2)
Other[d]	16 (5)
Gram-negative organisms	
Klebsiella pneumoniae	93 (27)
Escherichia coli	23 (7)
Pseudomonas aeruginosa	20 (6)
Neisseria meningitidis	18 (5)
Serratia species	7 (2)
Salmonella species	3 (1)
Other[e]	24 (7)

[a] Adapted and reprinted from Jackson TL, Paraskevopoulos T, Georgalas I. Systematic review of 342 cases of endogenous bacterial endophthalmitis. Surv Ophthalmol 2014 Nov-Dec;59(6):627-35; copyright 2014. DOI: https://doi.org/10.1016/j.survophthal.2014.06.002. With kind permission from Elsevier.[1]

[b] Also included are 6 cases of mixed infections and 6 cases of acid-fast bacilli infections.

[c] Other streptococcal species include: Group B streptococci (20); group G streptococci (9); group C streptococci (3); group A streptococci (2); *Streptococcus milleri* (1); *Streptococcus mitis* (1); Viridans group streptococci (2); *Streptococcus sanguis* (1); *Streptococcus dysgalactiae* (1); *Streptococcus constellatus* (1); *Streptococcus bovis* (1); *Streptococcus anginosus* (1); Streptococcus, species not stated (1).

[d] Other gram-positive species include: *Clostridium septicum* (4); *Staphylococcus epidermidis* (3); *Enterococcus faecalis* (3); *Clostridium perfringens* (2); *Propionibacterium acnes* (2); *Actinomyces israelii* (1); *Bacillus*, species not stated (1).

[e] Other gram-negative species include: *Enterobacter agglomerans* (2); *Kingella kingae* (1); *Aeromonas hydrophila* (2); *Aeromonas sobria* (1); *Ochrobactrum anthropi* (1); *Brucella melitensis* (1); *Haemophilus influenzae* (1); *Tropheryma whipelli* (1); *Actinobacillus actinomyceteincomitans* (1); *Capnocytophaga canimorsus* (1); *Vibrio vulnificus* (1); *Proteus mirabilis* (1); *Moraxella* species (1); *Burkholderia pseudomallei* (1); *Morganella morganii* (1); *Serratia marcescens* (1); *Citrobacter koseri* (1); *Fusobacterium necrophorum* (1); *Stenotrophomonas maltophilia* (1); *Pantoea agglomerans* (1); and *Sphigomonas paucimobilis* (1).

Animal studies have also shown that increased blood-ocular barrier permeability caused by diabetes predisposes subjects to developing endophthalmitis.[11,12] Certain bacterial species such as *S aureus* produce toxins that may help facilitate permeability without a predisposing factor such as diabetes.[12] In the same study, *K pneumoniae* was unable to penetrate the retinal pigment epithelium in healthy mice; however, when mice were introduced to sodium iodate, which induced retinal pigment epithelium degradation, or in mice with streptozotocin-induced diabetes, an incidence of endogenous endophthalmitis was seen.[12] Also, one specific strain of hypervirulent, hypermucoviscous *K pneumoniae* has been associated with increased endophthalmitis incidence compared to other strains.[13] This strain has been associated with increased efficiency to acquire iron and capsule production.[13]

Our case is unusual because our patient was young and had no predisposing factors but went on to develop endogenous endophthalmitis from group A streptococcus. No infectious focus was found in our case. Group A streptococcus species has a diverse range of virulence factors and has been associated with other disorders such as Sydenham chorea and pediatric autoimmune neuropsychiatric disorders with streptococcal infections; however, group A streptococcus is usually not associated with endogenous endophthalmitis.[1,9,10] Unfortunately, even with high clinical suspicion and early treatment, colonization from group A *S pyogenes* led to a poor visual outcome in our case. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

Acknowledgment

Mary Corrado, ELS, provided editorial assistance.

How to Cite this Article

Duong T, Shahbazi S, Lee S. Endogenous group A streptococcal endophthalmitis in a healthy 42-year-old man: A case report. Perm J 2018;22:17-081. DOI: https://doi.org/10.7812/TPP/17-081

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