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GRAND ROUNDS

Red eye, blurry vision, and cough

The 48-year-old patient also has chills and a low-grade fever. How would you proceed with his care?

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A 48-year-old Caucasian man comes to your office with redness and blurring of vision in his right eye that started the day before. For 3 weeks, he has had a productive cough with sputum, chills, and low-grade fever. Conjunctival injection is obvious. The view through the cornea is hazy, and there is a creamy white, layered settlement in the anterior chamber (**FIGURE 1**).

Q What do you suspect may be causing his ailment?

A

FIGURE 1
Blurry vision in right eye

The patient has a layer of pus (hypopyon) in the anterior chamber of his right eye; the cornea is also cloudy.

Additional medical history

- The patient's medical history reveals nothing significant.
- He has sustained no recent trauma to the eye.

Surgical history

- The patient had surgery to repair an umbilical hernia, and orthopedic surgery on his left elbow and ankle.

Family history

- His mother has chronic obstructive airway disease; his father has hypertension.

Social history

- The patient used cocaine about 20 years ago.
- He has abused alcohol, and is currently participating in an outpatient alcohol rehabilitation program.
- He is unemployed.

Review of systems

- Findings from other systems are unremarkable.

Physical examination

- The patient is alert and oriented.
- Temperature is 38.6°C (101.5°F), heart rate is 103 bpm, respiratory rate 20, blood pressure 114/57 mm Hg.
- Oxygen saturation is 95% on room air.
- Lungs: normal air entry bilaterally with a few crackles in right upper lung field.
- Heart: regular heart sounds, diastolic murmur in left lower sternal border.
- Abdomen: soft, nontender, nondistended, no organomegaly, and normal bowel sounds.
- Extremities show no significant edema.

CONTINUED

FIGURES 1 AND 2 COURTESY OF EGAMBARAM SENTHILVEL, MD

Patients with endogenous endophthalmitis exhibit several ocular symptoms: decreased vision, redness, floaters, headache, and eye discharge.

Q What are your next steps?

A

You request an immediate ophthalmology consultation, which confirms that visual acuity in the right eye is limited to light perception. The patient's left eye exam is normal. In the slit-lamp examination of the right eye, the vitreous view is obscured by hypopyon and corneal haziness. Hypopyon signals inflammation of the anterior uvea and iris. Hypopyon can occur with such noninfectious problems as corneal ulcer, Behçet's disease, systemic lupus erythematosus, sarcoidosis, and lymphoma/leukemia; and with endophthalmitis or panophthalmitis due to bacterial or fungal infection.

Based on the patient's clinical presentation, you diagnose endogenous endophthalmitis, start treatment empirically with intravenous (IV) vancomycin, ceftriaxone, and moxifloxacin, and hospitalize him for further workup.

Endophthalmitis: A medical emergency

Endophthalmitis is a bacterial or fungal infection of the vitreous or aqueous humor of the eye.

The *exogenous* form occurs with direct inoculation of an organism into the anterior chamber, following penetrating or blunt trauma to the eye, insertion of a foreign body, rupture of the conjunctival bleb, cataract surgery (usually within 1 week of surgery), or intraocular lens implantation.

Endogenous endophthalmitis results from microbial seeding of the vitreous or aqueous humor during bacterial or fungal septicemia. The endogenous form accounts for just 2% to 16% of all cases of endophthalmitis.[1–3] It is also known as metastatic endophthalmitis. Most of these infections arise suddenly, and it is a vision-threatening condition that should be managed as an ophthalmologic emergency.

Q What additional tests would you order?

A

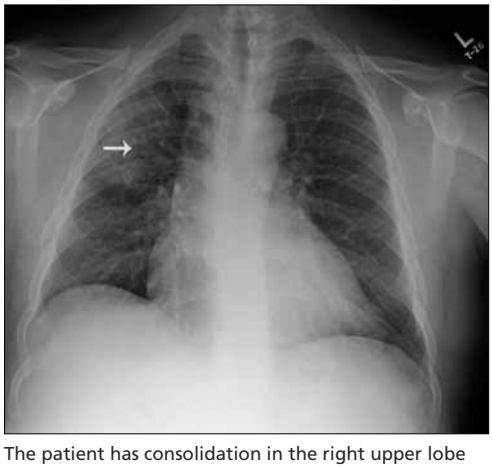
- The white blood cell count is 22,000/mcL; hemoglobin, 15.3 g/dL; hematocrit, 45.4%; platelets, 158,000/mcL; neutrophils, 8800/mcL; and bands of 10%.
- Basal metabolic panel is normal.
- Electrocardiogram is normal.
- Chest x-ray film shows right upper lobe infiltrate with minimal pleural effusion (**FIGURE 2**).

Expanding the investigation

You consult an infectious disease specialist, who recommends continuing the antibiotics you've prescribed until blood culture results are available. Subsequent results are positive for *Streptococcus pneumoniae* with pansensitivity. The patient also undergoes transthoracic echocardiography, revealing a 9-mm mass on the aortic valve with associated severe aortic valve regurgitation and mild mitral valve regurgitation. The patient is transferred to the coronary care unit within 12 hours of his admission.

Surgery is scheduled immediately. A preoperative transesophageal echocardiogram

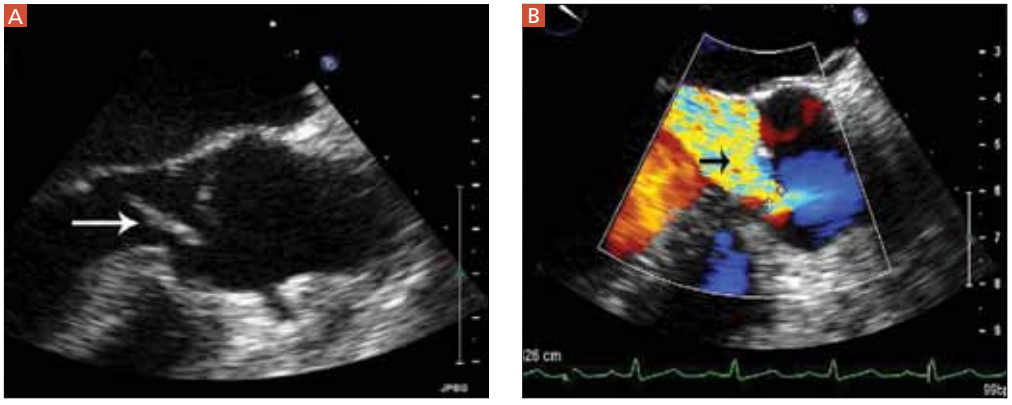
FIGURE 2
Posterior-anterior chest x-ray



The patient has consolidation in the right upper lobe with minimal pleural effusion on the right side.

FIGURE 3

Aortic valve vegetation, regurgitation



IMAGES COURTESY OF ROBERT S. FINKELHOR, MD

Transesophageal echocardiography image shows a vegetation on the coronary cusp of the aortic valve (**A**) and significant aortic valve regurgitation (**B**).

(**FIGURE 3**) confirms earlier findings and additionally reveals a small mitral valve vegetation. At surgery, the aortic valve is resected and replaced; a perivalvular abscess is drained.

Given culture results of *S pneumoniae* with pansensitivity, IV vancomycin is discontinued postoperatively, and IV ceftriaxone and oral moxifloxacin are continued for 6 weeks and 2 weeks, respectively. The ophthalmologist had also injected vancomycin into the vitreous; vitreous culture was not performed. At 6 weeks follow-up, the patient is blind in his right eye. He has also developed sensorineural hearing loss in his left ear, and has finished a course of steroids prescribed by an ear-nose-and-throat specialist.

What we know about endogenous endophthalmitis

A patient with endogenous endophthalmitis usually exhibits several ocular symptoms: decreased vision, redness, floaters, headache, and eye discharge.[2,4] Systemic symptoms often occur 3 to 7 days after the onset of ocular symptoms; only half of all cases report prior systemic symptoms.

Associated conditions to consider

Endogenous endophthalmitis has been associated with long-standing medical conditions such as diabetes mellitus and chronic renal failure.[4–6] In 40% of cases, endocarditis is the source of bacteremia.[2,4] Other possible sources are meningitis, urinary tract infection, intra-abdominal abscess, cellulitis, IV drug abuse, and septic arthritis;[7] invasive medical procedures such as gastrointestinal endoscopy;[8] and abdominal surgery.[4,9] According to our literature review, only 6 cases have been reported with pneumonia as the primary source of bacteremia.[4,5,10]

Likely causative organisms

Endophthalmitis is a clinical diagnosis confirmed by positive culture results on aqueous or vitreous samples. However, a negative result does not exclude the diagnosis. As per Okada et al,[4] causative organisms were isolated from either vitreous or blood samples in 96% of their cases.

Fungal organisms account for more than 50% of all cases of endogenous endophthalmitis (**TABLE**). *Candida albicans* is, by far, the most frequent cause of fungal endophthalmitis, and aspergillosis is the second most common cause.

Bacterial endogenous endophthalmitis most often occurs with gram-positive organisms. However, an East Asian study by Wong et al[11] showed gram-negative organisms in 70% of cases, with *Klebsiella pneumoniae* alone being responsible in 60% of the cases. Endophthalmitis caused by *S pneumoniae* usually has a poor prognosis.[12]

Ultrasound imaging of the eye (B-scan) usually shows increased echogenicity of the vitreous due to inflammation—a useful diagnostic indicator when the view of the vitreous

Endogenous endophthalmitis has been associated with long-standing medical conditions such as diabetes and chronic renal failure.

TABLE

Endogenous endophthalmitis: Which organisms to suspect, and when[4,9,11,15]

Organism	Sources of infection
Gram-positive	
Staphylococcus aureus	Endocarditis, skin infections
Streptococcus pneumoniae	Endocarditis, pneumonia, meningitis
Streptococcus milleri	Endocarditis, liver abscess
Group B *Streptococcus*	Endocarditis
Clostridium species	GI tract abscess, procedures, carcinomas
Bacillus cereus	IV drug use
Gram-negative	
Pseudomonas aeruginosa	Abdominal abscess
Neisseria meningitides	Meningitis
Escherichia coli	Urinary tract or hepatobiliary system
Klebsiella pneumoniae	Urinary tract or hepatobiliary system
Fungal	
Candida albicans	Immunosuppression, diabetes mellitus, GI surgery, hyperalimentation
Aspergillosis	IV drug use, cardiac surgery, organ transplant

GI, gastrointestinal; IV, intravenous

Vancomycin plus ceftazidime or fluoroquinolones are commonly used empirically for all forms of endophthalmitis until vitreous culture results are available.

is obscured by anterior chamber abnormalities. (This test was unavailable for our case.)

Doing the most to preserve vision

Preserving a patient's vision depends on prompt identification of the causative organism with blood and intravitreal cultures, and on appropriate therapy, including IV and intravitreal administration of antibiotics. Vitreal surgery is also a consideration. No randomized control trial has studied endogenous endophthalmitis management, due to the small number of cases worldwide. In managing endogenous endophthalmitis, most experts follow the outcome of the Endophthalmitis Vitrectomy Study (EVS),[13] in which immediate vitrectomy and IV antibiotics were used to treat postoperative bacterial endophthalmitis.

Notable points from EVS, and a caveat. EVS enrolled 420 patients who had clinical evidence of endophthalmitis 6 weeks after cataract surgery or secondary to intraocular lens implantation, randomly assigning them in a 2×2 factorial design to study groups: vitrectomy vs vitreous tap, and systemic antibiotics vs no systemic antibiotics. All patients received intravitreal antibiotics. The systemic antibiotics used were ceftazidime and amikacin. There was no difference in final visual acuity between the vitrectomy and vitreous tap groups, except in patients who presented with the worst vision (light perception only). For these patients, vitrectomy significantly decreased the chance of severe visual loss to 20%, vs 47% in the vitreous tap group. The EVS also concluded that omitting systemic antibiotics does not compromise outcomes, and can reduce toxic effects, cost, and length of hospital stay.

An important qualifier of the EVS report is that the study enrolled patients with *exogenous* endophthalmitis; no patients with *endogenous* endophthalmitis were included. Moreover, systemic antibiotics used in EVS mainly covered gram-negative agents, even

though gram-positive cocci were responsible for 94% of the cases.

Considerations in antibiotic selection. Vancomycin plus ceftazidime or fluoroquinolones are commonly used empirically for all forms of endophthalmitis until vitreous culture results are available. Fourth-generation fluoroquinolones (moxifloxacin and gatifloxacin) have increased potency against gram-positive bacteria compared with levofloxacin, while maintaining similar potency against gram-negative bacteria. Moxifloxacin has significantly greater ocular penetration and better gram-positive potency than gatifloxacin.[14]

Patients with endogenous endophthalmitis receive long-term IV antibiotics to treat the focus of systemic infection. As noted earlier, this patient completed a 6-week course of IV ceftriaxone and 2 weeks of oral moxifloxacin.

Even prompt action may not be enough

Red eye is common in outpatient settings. Endogenous endophthalmitis may be an uncommon cause of red eye, but you should consider it when a patient also has blurry vision and systemic symptoms. In this instance, it was an unusual complication of community-acquired pneumonia, which is also commonly seen in primary care. Treatment necessarily includes systemic and intravitreal antibiotics with or without vitrectomy. Immediate ophthalmologic referral is critical to preserving vision.

The patient in this case had a repeat transesophageal echocardiogram at 2 months, and it showed a rupture in the mitral valve from the small vegetation, with worsening of regurgitation. The cardiothoracic surgeon attempted repair of the mitral valve, but ended up having to replace it. The infectious disease team recommended a 6-week course of vancomycin, which the patient finished.

The sensorineural hearing loss in the patient's left ear was profound and did not improve after a course of oral prednisone. Magnetic resonance imaging showed labyrinthitis secondary to septic emboli. He received 2 transtympanic injections of dexamethasone, but his hearing still did not improve. The otolaryngology staff has discussed the possibility of a bone-anchored hearing aid. At a recent visit to the eye clinic, the patient had no light perception in the affected eye, despite an absence of active infection. Enucleation of the eye is being discussed. JFP

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Our patient's hearing loss in his left ear was profound, and despite an absence of active infection, he had no light perception in the affected eye.

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