58-Year-Old Man With Fever and Right Eye Pain

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A 58-year-old man presented to his primary care physician with subjective fevers of 4 days’ duration. His physician diagnosed a viral syndrome and prescribed acetaminophen. One day later, the patient returned complaining of acute-onset right eye pain, blurred vision, confusion, and pain in the left great toe. He did not wear contact lenses and had had no eye injury, headache, recent dental work, or symptoms involving the gastrointestinal or genitourinary tract. His peripheral leukocyte count was elevated to $19 \times 10^9 /L$ (reference range, $3.5-10.5 \times 10^9 /L$). Blood cultures were obtained. Endophthalmitis was diagnosed, and 1 g of ceftriaxone was administered intramuscularly. The patient was then transferred to our institution for further care.

The patient’s medical history was notable only for hypertension, which was being treated with trandolapril. On physical examination, he was febrile (temperature, 38.6°C) and hypertensive (blood pressure, 156/84 mm Hg) with a pulse rate of 85/min. The patient no longer appeared confused and was alert and oriented to person, place, and time. Examination of his head and neck revealed only right eye chemosis and markedly decreased visual acuity (counting fingers at 6 in). His left great toe was erythematous, swollen, and painful with movement. Results of the remainder of the complete multisystem examination were unremarkable.

1. Which one of the following would be the most appropriate next step in the management of this patient in the emergency department?
   a. Emergent ophthalmology consultation
   b. Intravenous antibiotic therapy
   c. Antibiotic eyedrops
   d. Topical corticosteroids
   e. Blood cultures

Endophthalmitis is a vision-threatening infection of the vitreous and/or aqueous humor. Therefore, ophthalmology consultation should be obtained immediately to confirm the diagnosis and assist with management. The optimal treatment of endogenous endophthalmitis is not well defined because of a lack of randomized controlled trials. Topical and systemic antibiotics often do not reach therapeutic levels within the vitreous humor. Consequently, standard care usually consists of vitreal aspiration and/or vitrectomy followed by intravitreal antibiotic therapy. The benefits of topical and intravitreal corticosteroids are unproved. Although blood cultures should be obtained before antibiotic therapy is initiated, this patient’s blood had already been withdrawn for culture by his local primary care physician before initiation of treatment with intramuscular ceftriaxone.

The patient was evaluated in the emergency department by an ophthalmologist who obtained a vitreal aspirate for culture. Topical corticosteroids and antibiotics were applied to the eye. Additionally, vancomycin (1 mg), ceftazidime (2.25 mg), and dexamethasone (0.4 mg) were administered intravitreally. Finally, communication with the patient’s local physician revealed that previously obtained blood cultures were growing group B streptococci in 2 of 4 dishes.

2. Which one of the following tests should be performed next to evaluate the cause of this patient’s bacteremia?
   a. Urine culture
   b. Magnetic resonance imaging (MRI) of the head
   c. MRI of the left foot
   d. Transesophageal echocardiography
   e. Indium-labeled white blood cell scan

Because this patient had no symptoms suggestive of a genitourinary source of infection, a urine culture is unlikely to yield a cause. Although head MRI would be useful in assessing for brain abscess or septic emboli, this patient had no headache or meningeal signs, and he was not confused on presentation to our institution. Hence, this test probably would not identify a cause of the bacteremia. Left foot MRI would effectively exclude abscess or osteomyelitis as a cause of the patient’s left great toe inflammation, but the toe would not be the most likely source of bacteremia. Endogenous (metastatic) endophthalmitis results from bacteremia, and endocarditis is the most common cause of bacteremia in patients with endogenous endophthalmitis (40%), followed by urinary tract infections, abdominal abscesses, meningitis, and indwelling catheters. Especially given this patient’s peripheral findings (endophthalmitis and inflamed toe), which possibly resulted from cardiac emboli, transesophageal echocardiography was...
considered the test of choice. An indium-labeled white blood cell scan can be useful in determining sources of infection, but it is generally reserved for situations in which other investigations are unrevealing.

Because transesophageal echocardiography showed no evidence of infective endocarditis, additional tests were performed. Results of urine culture and foot MRI were both negative. Head MRI showed acute infarcts within the superior cerebellar vermis and left frontal lobe consistent with an embolic etiology. Because no primary source of infection was identified, an indium-labeled white blood cell scan was performed, which revealed only left great toe soft tissue inflammation and no evidence of inflammation elsewhere.

3. Which one of the following should not be included in this patient’s differential diagnosis?
   a. Bacteremia
   b. Systemic inflammatory response syndrome (SIRS)
   c. Sepsis
   d. Possible endocarditis
   e. Septic arthritis

In 1992, an American College of Chest Physicians and Society of Critical Care Medicine consensus panel defined bacteremia, SIRS, sepsis, severe sepsis, and septic shock. Bacteremia is defined by the presence of viable bacteria in the blood. Systemic inflammatory response syndrome is a widespread inflammatory response characterized by the presence of 2 or more of the following: temperature higher than 38°C or lower than 36°C, heart rate greater than 90 beats/min, respiratory rate greater than 20/min or PaCO₂ lower than 32 mm Hg, and white blood cell count higher than 12 × 10⁹/L. Sepsis is a systemic response to infection. Thus, in sepsis, SIRS is present along with documented infection.

Our patient met the criteria for bacteremia, SIRS, and sepsis. However, he also had possible endocarditis because he had 3 of the minor modified Duke criteria: temperature higher than 38°C, evidence of arterial emboli, and positive blood cultures on 1 occasion. Identifying the specific diagnosis of possible endocarditis (as opposed to bacteremia and sepsis) is crucial because the diagnosis determines the choice and duration of antibiotic therapy. Our patient did not meet criteria for definite endocarditis, which requires the presence of either 1 major criterion and 3 minor criteria or the presence of 5 minor criteria. Although the patient had an inflamed toe, septic arthritis would not be the best diagnosis because it would fail to incorporate and explain the other evidence of arterial embolization.

The patient was admitted to our hospital, and antimicrobial therapy was initiated to treat the group B streptococcal bacteremia.

4. Which one of the following is the most appropriate antimicrobial regimen for this patient?
   a. Vancomycin hydrochloride for 4 to 6 weeks
   b. Gentamicin sulfate for 2 weeks combined with either aqueous crystalline penicillin G or ceftriaxone sodium for 4 to 6 weeks
   c. Aqueous crystalline penicillin G for 4 to 6 weeks
   d. Ceftriaxone sodium for 4 to 6 weeks
   e. Gentamicin sulfate for 2 weeks

Vancomycin therapy should be administered only to patients who are unable to tolerate β-lactam therapy, so it would not be indicated for this patient. Infective endocarditis caused by group B streptococcus is uncommon. In general, group B streptococci are slightly more resistant to penicillin than are group A streptococci. Nevertheless, treatment with either penicillin or ceftriaxone would be acceptable. Some experts recommend adding gentamicin to a penicillin or cephalexin for at least the first 2 weeks of a 4- to 6-week course of antimicrobial treatment. Therefore, gentamicin for 2 weeks combined with either aqueous penicillin G or ceftriaxone for 4 to 6 weeks would be the most appropriate regimen for this patient. Monotherapy with either penicillin or ceftriaxone would be reasonable but, as noted above, may be less effective than combination therapy with gentamicin, which provides synergistic killing. Monotherapy with gentamicin is not advised. Our patient was treated with a continuous infusion of penicillin (24 million U/d) and 75 mg of gentamicin intravenously every 8 hours.

5. Which one of the following would be the recommended long-term antibiotic regimen for this patient?
   a. 4 to 6 weeks of oral cephalexin as an outpatient
   b. 4 to 6 weeks of intravenous aqueous crystalline penicillin G in the hospital
   c. 4 to 6 weeks of intravenous ceftriaxone sodium in the hospital
   d. 4 to 6 weeks of intravenous aqueous crystalline penicillin G as an outpatient
   e. 4 to 6 weeks of intravenous ceftriaxone sodium as an outpatient

Oral antibiotics would be a poor choice for this patient because antimicrobial agents are often suboptimally absorbed by the gastrointestinal tract and are generally not recommended for the treatment of endocarditis. Hospital length of stay for patients with endocarditis has declined in recent years. Outpatient parenteral antibiotics are safe and cost-effective in the following circumstances: a reliable home support system and access to a hospital, regular visits and monitoring for complications by a home infusion nurse, and regular outpatient visits (ie, weekly) with an experienced physician throughout the patient’s course of outpatient therapy.
parenteral antibiotic therapy.

Aqueous crystalline penicillin G is not a good choice for outpatient therapy because it is administered either 6 times daily or as a continuous infusion. Ceftriaxone sodium would be the most appropriate choice for this patient because it is administered once daily and the infecting organism in our patient was ceftriaxone sensitive.

The group B streptococcus isolated from our patient was later identified as *Streptococcus agalactiae*. On the basis of susceptibility testing, penicillin and gentamicin were discontinued, and intravenous ceftriaxone sodium therapy was initiated. Repeated transthoracic echocardiography yielded negative findings 1 week after initiation of antibiotic therapy. The patient gradually improved, and his fever resolved after several days of parenteral antibiotic therapy. On hospital day 10, he was discharged to complete 6 weeks of outpatient treatment with intravenous ceftriaxone sodium infusion. Transthoracic echocardiography 3 weeks after discharge showed normal findings, and the patient remained afebrile. Four weeks after discharge, the patient’s ophthalmologist performed a vitrectomy, scleral buckling, endolaser application, and silicone oil injection to the right eye. Two months after the initial diagnosis of endophthalmitis, the patient’s vision was much improved.

**DISCUSSION**

Endogenous bacterial endophthalmitis (EBE), also called metastatic endophthalmitis, is a rare condition that results from circulating organisms entering the eye’s internal space through the blood-ocular barrier. Endogenous bacterial endophthalmitis accounts for 2% to 8% of cases of endophthalmitis. The most common infectious sources in EBE are heart valves, meninges, skin, and both urinary and hepatobiliary tracts. The disease usually occurs in immunocompromised patients. Specific risk factors include chronic diseases (eg, diabetes mellitus, renal failure, malignancy, acquired immunodeficiency syndrome), immunosuppressive therapy, invasive surgery, intravenous drug abuse, and indwelling catheters. Causative microorganisms vary with geographic distribution. In the Western Hemisphere, gram-positive cocci (especially *Staphylococcus aureus* and *Streptococcus pneumoniae*) are frequent. In the Eastern Hemisphere, gram-negative bacilli (particularly *Klebsiella pneumoniae* and *Escherichia coli*) are common.

Endophthalmitis is a clinical diagnosis that is confirmed by positive cultures of aspirated vitreous or aqueous humor. Characteristic symptoms are eye pain, blurred vision, and floaters. Typical physical findings are discharge, blepharitis, chemosis, hypopyon, elevated intraocular pressure, and poorly visualized fundi due to intraocular inflammation.

The management of EBE remains uncertain given the absence of randomized controlled trials. Nonetheless, widely accepted treatments include vitreous aspiration and vitrectomy, intravitreal antibiotics (eg, 1 mg of vancomycin plus either 0.4 mg of amikacin or 2.25 mg of ceftazidine), intravitreal corticosteroids (eg, 0.4 mg of dexamethasone), systemic antibiotics, topical antibiotics, and topical corticosteroids. Unfortunately, the prognosis for patients with EBE is poor; studies show that 60% of patients have an ultimate visual acuity of hand motion at best, and 25% to 29% of patients eventually require enucleation.

Group B streptococci are encapsulated microorganisms found as commensals in the upper respiratory tract, skin, colorectum, and vagina. They frequently cause neonatal sepsis and high mortality (30%-50%) during the initial hours of life. In adults, group B streptococci cause pharyngitis, cellulitis, meningitis, and pneumonia. The 48-hour mortality in patients with group B streptococcal bacteremia is high, often reaching 39%. Group B streptococcus endogenous endophthalmitis, a rare and devastating disease, is usually associated with septic arthritis and often results in visual loss.

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**REFERENCES**


Correct answers: 1. a, 2. d, 3. e, 4. b, 5. e.