

Meningitis Due to Hematogenous Dissemination of Community-Associated Methicillin-Resistant *Staphylococcus aureus* (MRSA) in a Patient With AIDS

Shilpa Sayana, MD, MPH, and Homayoon Khanlou, MD

Meningitis due to methicillin-resistant *Staphylococcus aureus* is a rare clinical presentation but has been well documented in postneurosurgical patients. To our knowledge, no case of methicillin-resistant *Staphylococcus aureus* meningitis has been previously reported in a nonneurosurgical patient with AIDS. In this case report we describe a person with AIDS who had no history of a neurosurgical procedure, shunt devices, head

trauma, or recent hospitalization that presented with methicillin-resistant *Staphylococcus aureus* meningitis. The infection was successfully treated. Methicillin-resistant *Staphylococcus aureus* should be considered in the differential of meningitis in people with AIDS.

Keywords: AIDS; community-acquired; MRSA; meningitis

S *taphylococcus(s) aureus* is a rare cause of meningitis accounting for 7% to 8% of acute bacterial meningitis,¹ and is a common cause of bacterial infections in patients infected with human immunodeficiency virus (HIV).² Human immunodeficiency virus-positive patients are at increased risk for hematogenous or spontaneous *S aureus* meningitis given their chronic immunocompromised state.³ Methicillin-resistant *S aureus* (MRSA) is an even more isolated occurrence usually associated with postneurosurgery or indwelling devices in the central nervous system. All the reported cases of MRSA meningitis have been described in these 2 situations. To our knowledge, this is the first reported case of spontaneous occurring MRSA meningitis in a patient with AIDS.

From the Department of Medicine, AIDS Healthcare Foundation, Los Angeles, California.

Address correspondence to: Shilpa Sayana, AIDS Healthcare Foundation, 6255 W. Sunset Blvd, 21st floor, Los Angeles, CA 90028; e-mail: shilpa.sayana@aidshhealth.org.

Report of Case

A 35-year-old homosexual man living with AIDS, CD4 count of 84 cells/mm³ and viral load of 245 000 copies/μL, was evaluated in the emergency room, complaining of severe headaches, confusion, malaise, and fevers. He was alert but confused, oriented only to person. His temperature was 102°F, pulse rate was 94, respirations, blood pressure, and oxygen saturation were normal. Physical exam was normal except for nuchal rigidity, a left abducens nerve palsy, and multiple injection site cellulites on his shins and arms.

His medical history was significant for heroin abuse, iron deficiency anemia, and AIDS (not on antiretroviral therapy secondary to his social situation), without a history of any opportunistic infections to date. His prescribed outpatient medications were methadone, iron sulfate, Bactrim DS, and Zithromax 1200 mg every week; however, the patient admitted to only taking methadone.

On initial evaluation, his laboratory values disclosed a leukocyte count of 23.1 k/UL with 69%

neutrophils and 20% bands. The hemoglobin and platelets were normal. Most of his chemistry panel was within normal limits except for hyponatremia of 129 mmol/L. On analysis, the cerebrospinal fluid (CSF) was found to be cloudy with 2635 white blood cells (WBCs), 92% neutrophils, 8% monocytes, 575 red blood cells (RBCs), 56 mg/dL glucose, and 185.2 mg/dL protein. Given the highly abnormal CSF results and the possibility of a lab error, the lumbar puncture was repeated 1 hour after the initial one, and the fluid persisted to be cloudy with 2575 WBC, 99% neutrophils, 1% monocytes, and 440 RBCs. Gram stain revealed gram-positive cocci in clusters.

The patient was initially treated with intravenous (IV) ceftriaxone, vancomycin, high dose ampicillin, acyclovir, and dexamethasone for the first 48 hours. At hospital day 5, his initial set of blood cultures and CSF grew only MRSA that was resistant to oxacillin [minimum inhibitory concentration (MIC) of 4] and sensitive to vancomycin (MIC of 1), tetracycline (MIC of 1), gentamicin (MIC of 0.5), and clindamycin (MIC of 0.25) per the antibiogram. After the results of CSF were available, his antibiotic regimen was adjusted. Vancomycin was continued and maintained to have a trough level >15 mg/dL and IV bac-trim was added. Cerebrospinal fluid was negative for India ink stain, acid-fast bacillus (AFB) culture, viral culture, group B streptococcus, and Herpes simplex virus types 1 and 2. Urinalysis revealed mild proteinuria, 1 WBC, 5 RBC, and the urine culture was negative. A transthoracic echocardiogram was obtained, which revealed no vegetations. A computed tomography (CT) scan of the orbits and brain was normal. However, magnetic resonance imaging (MRI) with gadolinium disclosed mild meningeal enhancement near the left cerebellar pontine angle with no intraparenchymal mass or midline shift.

The patients' clinical status improved with IV antibiotics. He was also restarted on antiretroviral therapy. On hospital day 14, he underwent a repeat lumbar puncture, which revealed WBC of 275 with 1% neutrophils and 99% monocytes, RBC of 200, 56 mg/dL glucose, and 81 mg/dL protein. Gram stain and culture were negative. He received 10 more days of IV vancomycin and was discharged with oral bac-trim to follow-up at the outpatient clinic. At 3 months posthospitalization, the patient was doing well with a resolution of the left abducens nerve palsy.

Discussion

Methicillin-resistant *S aureus* infections are a common cause of mortality and accounted for 18 650 deaths in 2005.⁴ *S aureus* meningitis can occur by the either 2 mechanisms; postoperative meningitis, associated with neurosurgical procedures, shunt devices, or head trauma, and hematogenous or spontaneous meningitis, secondary to staphylococcal infection outside the central nervous system.³ Spontaneous meningitis has been described as a community-acquired infection seen in older people who have severe underlying conditions such as cardiovascular disease, diabetes, IV drug use, alcoholism, and HIV infection.³ The first documented case of spontaneous *S aureus* [methicillin-sensitive *S aureus* (MSSA)] meningitis in a patient living with AIDS was reported in 1998.⁵

In recent years there has been an increase in MRSA infections in adult *S aureus* meningitis.⁶ HIV infection is a risk factor for MRSA infection; in a retrospective study of 3455 patients living with HIV, the incidence of MRSA infection was nearly 5 per 100 patient-years; the incidence of MRSA infection had increased 6-fold between 2000 and 2003.⁷ The primary sites of these infections were the skin and the soft tissues (83%). Risk factors included advanced immunosuppression (CD4 count <50 cells/mm³), high plasma HIV RNA (>100 000 copies/ μ L), and lack of antiretroviral therapy. In a study from 2005, the annual incidence of MRSA among 425 patients living with HIV was 40 cases/1000 person-years compared to 741 cases/325 000 (or 2.28/1000) among HIV-negative persons (18-fold higher rate).⁸ All HIV-infected patients developed soft-tissue infections, 16% required hospitalization, 67% had a positive nares culture, 0% were taking septa prophylaxis, and 56% were on antiretroviral therapy. In addition, in 1 study, trimethoprim-sulfamethoxazole seems to be protective against MRSA colonization.⁹

Methicillin-resistant *S aureus* appears to be a more disseminated disease in HIV-positive individuals given the level of immunosuppression. All cases of MRSA meningitis described in the literature are seen in patients who were either considered to have hospital acquired meningitis or were postneurosurgical.⁶ However, our patient who presented with MRSA meningitis was not postneurosurgical and did not have a history of hospitalization prior to presentation. By extrapolating from the same mechanisms

that cause meningitis in MSSA, our patient most likely developed hematogenous or spontaneous meningitis due to bacteremia with MRSA. The original source of the MRSA may have been from his skin injection site cellulites. The possibility of endocarditis was entertained for our patient given his bacteremia, however, given the repeatedly normal cardiac examinations, the absence of pyuria with negative blood cultures and a completely normal transthoracic echocardiogram made this diagnosis unlikely. The left abducens palsy was most likely related to irritation of cranial nerve VI from meningeal inflammation near the left cerebellar pontine angle (where the nucleus for the abducens nerve resides) as seen in MRI. In our patient, his nonadherence to his prophylactic medication may have contributed to his vulnerability to MRSA.

Summary

To our knowledge, this report describes the first reported case of spontaneous MRSA meningitis in a nonneurosurgical patient living with AIDS. Given the increased risk of *S aureus* infections and bacteremia² in HIV-positive individuals and the increasing prevalence and virulence of community-acquired MRSA infections, MRSA meningitis should be considered in the differential of bacterial meningitis in patients with AIDS.

References

1. Durand ML, Calderwood SB, Weber DJ, et al. Acute bacterial meningitis in adults. A review of 493 episodes. *N Engl J Med*. 1993;328:21-28.
2. Senthilkumar A, Kumar S, Sheagren JN. Increased incidence of *Staphylococcus aureus* bacteremia in hospitalized patients with acquired immunodeficiency syndrome. *Clin Infect Dis*. 2001;33:1412-1416.
3. Pintado V, Meseguer MA, Fortun J, et al. Clinical study of 44 cases of *Staphylococcus aureus* meningitis. *Eur J Clin Microbiol Infect Dis*. 2002;21:864-868.
4. Klevens RM, Morrison MA, Nadle J, et al. Invasive methicillin-resistant *Staphylococcus aureus* infections in the United States. *JAMA*. 2007;298:1763-1771.
5. Miller LG, Mathisen GE, Chang S. *Staphylococcus aureus* meningitis in a patient with acquired immunodeficiency syndrome. *Mayo Clin Proc*. 1998;73:1083-1084.
6. Chang WN, Lu CH, Wu JJ, et al. *Staphylococcus aureus* meningitis in adults: a clinical comparison of infections caused by methicillin-resistant and methicillin-sensitive strains. *Infection*. 2005;29:245-250.
7. Mathews WC, Caperna JC, Barber RE, et al. Incidence of and risk factors for clinically significant methicillin-resistant *Staphylococcus aureus* infection in a cohort of HIV-infected adults. *J Acquir Immune Defic Syndr*. 2005;40:155-160.
8. Crum-Cianflone NF, Burgi AA, Hale BR. Increasing rates of community-acquired methicillin-resistant *Staphylococcus aureus* infections among HIV-infected persons. *Int J STD AIDS*. 2007;18:521-526.
9. Cenizal MJ, Hardy RD, Anderson M, et al. Prevalence of and risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) nasal colonization in HIV-infected ambulatory patients. *J Acquir Immune Defic Syndr*. 2008;48:567-571.