A case of spontaneous methicillin-resistant *Staphylococcus aureus* meningitis in a health care worker

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Meningitis caused by *Staphylococcus aureus* is an unusual illness that is often associated with bacteremia, contiguous infection and/or a post-neurosurgical state. Until recently, most cases were caused by methicillin-susceptible strains, but there are a few reports of methicillin-resistant *S aureus* strains causing meningitis. A new case of meningitis caused by methicillin-resistant *S aureus* in a neonatal intensive care nurse who did not have bacteremia or neurosurgery is reported. The patient made a full recovery after treatment with vancomycin and rifampin.

Key Words: *Meningitis; MRSA; Rifampin;* Staphylococcus aureus; *Vancomycin*

Un cas de méningite à *Staphylococcus aureus* spontanée méthicillinorésistante chez une travailleuse de la santé

La méningite causée par le *Staphylococcus aureus* est une maladie inhabituelle souvent associée à une bactériémie, à une infection contiguë ou à un état postneurochirurgical. Jusqu'à récemment, la plupart des cas étaient imputables à des souches susceptibles à la méthicilline, mais il existe quelques observations de souches de *S aureus* méthicillinorésistantes provoquant la méningite. Un nouveau cas de méningite causé par le *S aureus* méthicillonéristant s'est déclaré chez une infirmière de soins intensifs néonatals qui ne souffrait pas de bactériémie et n'avait pas subi de neurochirurgie. La patiente s'est complètement rétablie après un traitement à la vancomycine et à la rifampine.

Staphylococcus aureus has infrequently been described as a cause of meningitis (1,2). The three clinical situations that predispose to the development of *S aureus* meningitis are neurosurgical intervention, contiguous infection and *S aureus* bacteremia (3-8). Until recently, most cases have been caused by methicillin-susceptible *S aureus* strains. There are now an increasing number of reports (3,4) of severe infections attributed to methicillin-resistant strains of *S aureus* (MRSA). We report a case of MRSA meningitis in a previously healthy nurse who was not bacteremic at the time of presentation and had not undergone neurosurgery.

CASE PRESENTATION

A 24-year-old woman was seen in the emergency room with severe headache and nausea. The patient stated that her headache began four days before presentation and that it had progressively increased in intensity. This severe, generalized headache was associated with neck stiffness, fever and chills. The patient's past medical history included hypothyroidism secondary to radioablation for Grave's disease and migraine headaches. She had suffered minor head trauma four years earlier for which she had not required hospitalization or treatment. The patient worked as a neonatal intensive care unit nurse (NICU). She claimed that she had not cared for any babies with known or suspected infection in the recent past and she was also unaware of any infected babies in her unit in the recent past.

On examination, she was alert but in distress, with a temperature of 38.5°C, blood pressure 147/72 mmHg, pulse of 96 beats/min and a respiration rate of 18 breaths/min. The patient was found to have a stiff neck and a grade 1/6 systolic ejection murmur. The rest of the physical examination was unremarkable. A computed tomography scan of the patient's head, sinuses and facial bones revealed no evidence of bleeding, fracture, mass effect or infarct. A small air-fluid level and some mucosal thickening were noted in the left maxillary sinus. These results were not considered to be clinically significant by both radiology and otolaryngology. Two sets of blood cultures were drawn and a lumbar puncture (LP) was performed. Microscopic analysis of the LP revealed over 100 leukocytes per low-power field, but no microorganisms were visualized on Gram stain. The patient was started on intravenous (IV) ceftriaxone 2 g every 12 h and IV ampicillin 1 g every 4 h. The cerebrospinal fluid (CSF) biochemical and cellular components are detailed in Table 1.

The following day, her preliminary CSF culture showed 2+ growth of *S aureus* on the Columbia blood and chocolate agar primary plates. Vancomycin IV (1 g every 12 h) was added to her antibiotic regimen. The final CSF culture revealed MRSA, which was subsequently confirmed at the National

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Laboratory of Public Health of Quebec. The organism was resistant to penicillin, oxacillin, erythromycin, clindamycin and ciprofloxacin, and susceptible to vancomycin, rifampin, tetracycline and trimethoprim/sulfamethoxazole.

The patient's antibiotic regimen was modified to 1 g of vancomycin IV every 12 h and 600 mg of oral rifampin daily. The blood cultures taken before starting antibiotics remained negative. The patient improved steadily throughout the remainder of her admission and she became afebrile after her third day in hospital. She received a total of 10 days of IV vancomycin and a repeat LP was performed on her final hospital day (Table 1). Cultures of the CSF were negative.

During her stay in hospital the patient was investigated for a possible focus of her infection. Both sets of blood cultures and a urine culture were negative. A transthoracic echocardiogram was performed and no abnormalities were demonstrated. A screening nasal swab on admission was negative for MRSA. Bone and gallium nuclear scans showed no evidence of focal abnormal uptake and the patient's chest x-ray was normal. The patient denied ever taking care of a baby with MRSA and had not received recent antibiotic therapy.

The infection control officer at her institution was contacted for more information on local prevalence of MRSA. The last known case of MRSA in the NICU had occurred two years previously. In the six months before the onset of illness, there had been seven children admitted to her institution with MRSA. They were admitted to five different wards and all were placed on isolation from admission and had very short hospital stays (two to seven days). Two of these children had community-acquired strains and the other five were known MRSA carriers. It is the policy of that institution to screen all ward patients whenever a new case of MRSA is identified, as well as to screen all newborns admitted to the NICU. The infection control officer was unaware of any cases of MRSA in the NICU at the time of this patient's illness.

Three weeks after stopping the antibiotics, the patient returned to the emergency room complaining of bilateral ear pain and headaches. She had a low grade fever but no neck stiffness. Because of the fear of a possible recurrence of her meningitis another lumbar puncture was performed. There were no abnormalities and the culture remained negative (Table 1). The patient was sent home on no antibiotics and has remained well for more than five months since the last lumbar puncture.

TABLE 1
Cerebrospinal fluid (CSF) results

	Admission	Discharge	21 days post-treatment
Appearance	turbid	clear	clear
RBC ($\times 10^6$/L)	151	750	0
Neutrophils ($\times 10^6$/L)	14,399	0	2
Lymphocytes ($\times 10^6$/L)	100	0	2
CSF glucose (mmol/L)	3.2	3.3	3.3
Serum glucose (mmol/L)	5.0	5.6	5.1
Total protein (g/L)	0.58	0.33	0.32
Normal = 0.2–0.45 g/L			
Gram stain	No organisms seen	No organisms seen	No organisms seen
Culture results	2+ MRSA	No growth	No growth

MRSA Methicillin-resistant Staphylococcus aureus*; RBC Red blood cells*

DISCUSSION

S aureus meningitis is a rare clinical entity. It has been estimated to account for 2% to 10% of cases of bacterial meningitis in adults (1-8). Over 50% of such cases are nosocomial, often due to neurosurgical intervention (3,5,6), while the remaining are 'spontaneous' or community-acquired. Different origins of infection have been associated with the hematogenous spread of *S aureus* to the meninges in community-acquired cases, including bacterial endocarditis, epidural/paraspinal abscess, skin/soft tissue infection, pneumonia, urinary tract infection, sinusitis, otitis media and osteomyelitis (5-8). To our knowledge, all described cases of spontaneous or community-acquired *S aureus* meningitis have been limited to methicillin-sensitive strains of *S aureus* (3-8). While most nosocomial cases have also historically been caused by sensitive strains, a recent report (3) highlights the increasing prevalence of MRSA in hospital-acquired infections. Between 1986 and 2000, 11 of 19 cases of staphylococcal meningitis were due to MRSA strains (all of which occurred after 1995).

In the present report, we describe a 24-year-old woman with culture-proven MRSA meningitis. While our search for a potential focus of infection in this patient remained negative, we are confident that MRSA was in fact the cause of this patient's meningitis. Her initial clinical presentation was consistent with a previously described series of *S aureus* meningitis with fever being present in 84% of patients, headache in 41%, meningeal signs in 62% and altered mental status in 75% (5).

The patient's laboratory investigations, including the results of her LP, were all consistent with the diagnosis of bacterial meningitis. The presence in the CSF of $14{,}499\times10^6$ leukocytes/L (more than 99% neutrophils) and of an elevated total protein with a normal glucose is consistent with findings in *S aureus* meningitis, because 85% of patients have elevated total protein levels, 85% show pleocytosis, and only 30% have decreased CSF glucose levels (5). The negative Gram stain on CSF microscopic examination is not unusual because other groups have only been able to document positive CSF Gram stains in 20% to 59% of cases of MRSA meningitis (5,6,9-12). Finally, it is important to mention that we obtained heavy growth of MRSA into the second streak on the primary plates, making it unlikely that our cultures were the result of sample contamination. As well, the LP was performed by an experienced anesthesiologist.

While our clinical and laboratory data suggest that this patient had 'spontaneous' meningitis, we are unable to explain the origin of her infection. The patient's blood cultures before antibiotic therapy were negative, and our extensive workup in hospital yielded no significant abnormalities explaining the source of her MRSA. We hypothesize that the patient had a transient bacteremia, possibly originating from her sinuses, which seeded the meninges. Given her negative blood cultures and the normal transthoracic echocardiogram, endocarditis was improbable.

After obtaining the results of the CSF culture, we elected to use a combination of vancomycin and rifampin to treat this patient. One critical factor in treating a patient with meningitis is the penetration of a given antibiotic into the CSF.

Although vancomycin is the antimicrobial agent most often used to treat MRSA infections, it is known to have poor CSF penetration (13). However, under conditions of meningeal inflammation, vancomycin levels in the CSF have been shown to increase to moderate degrees (14). We elected to add rifampin to her regimen given the known activity of the drug against MRSA and its ability to cross the blood-brain barrier (15). This antibiotic combination has been used to treat serious *S aureus* infections (16). Recently, there have also been reports of linezolid use to treat infections of the central nervous system and this drug may prove to be an effective therapy in the future for MRSA meningitis (17-20). In our case, the combination of antibiotics was successful, and the patient recovered fully with no sequelae. The normal repeat LP done three weeks after stopping treatment and the long disease-free follow-up period are evidence that her treatment duration was adequate.

Many authors have reported an increased incidence in infections caused by MRSA as a community-acquired pathogen (21,22). However, most patients with community acquired MRSA have a health care associated risk just as our patient did (22). The antimicrobial susceptibility pattern is more consistent with a hospital acquisition. We believe that the present report is an example of a growing trend whereby antibiotic-resistant bacteria such as MRSA can cause serious illness in the community, especially for individuals with exposure to the health care system.

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