Necrotizing pneumonia and septic shock: suspecting CA-MRSA in patients presenting to Canadian emergency departments

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ABSTRACT

We report a case of fatal necrotizing pneumonia and sepsis caused by community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) in an otherwise well, 48-year-old Canadian man with type 2 diabetes mellitus who had travelled to Texas. Despite therapy that included intravenous antibiotics, intravenous immune globulin and other supportive measures, the patient succumbed to his illness. Recently, CA-MRSA pneumonia has been reported in several countries. The virulence of this organism may in part be related to its ability to produce toxins, such as Panton-Valentine leukocidin. As rates of CA-MRSA increase worldwide, physicians should be aware of the potential for MRSA to cause life-threatening infections in patients presenting to Canadian emergency departments (EDs). Necrotizing pneumonia caused by MRSA must be considered in the differential diagnosis of acute, severe respiratory illness. Early recognition of this syndrome in the ED may help physicians initiate appropriate antibiotic therapy in a timely manner.

Key words: necrotizing pneumonia, MRSA, community-acquired MRSA, Canada

RÉSUMÉ

Nous présentons un cas de septicémie et pneumonie nécrosante mortelles causées par *Staphylococcus aureus* résistant à la méthicilline d'origine communautaire (SARM-OC) chez un Canadien de 48 ans autrement bien portant mais atteint de diabète de type 2, en voyage au Texas. Malgré une thérapie à base d'antibiotiques intraveineux, d'immunoglobulines intraveineuses et d'autres mesures de soutien, le patient a succombé à la maladie. Plusieurs pays ont récemment fait état de cas de pneumonie causés par le SARM-OC. La virulence de cet organisme est sans doute en partie liée à sa capacité de produire des toxines, comme la leucocidine de Panton-Valentine. À mesure que les taux de SARM-OC augmentent dans le monde, les médecins devraient savoir que le SARM peut causer des infections mortelles chez des patients se présentant à l'urgence au Canada. La possibilité de pneumonie nécrosante causée par le SARM doit être prise en compte dans tout diagnostic différentiel d'une maladie respiratoire aiguë grave. Le dépistage hâtif de ce syndrome à l'urgence pourrait aider les médecins à administrer rapidement l'antibiothérapie appropriée.

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Introduction

Staphylococcus aureus (S. aureus) infections, including methicillin-resistant *Staphylococcus aureus* (MRSA), occur primarily in the skin and soft tissue. However, a new strain of MRSA is emerging; one that is associated, not only with an increased risk of severe soft tissue infections, but also with necrotizing pneumonia. Emergency physicians in Canada need to be aware that this pathogen is becoming increasingly prevalent. Early recognition and appropriate treatment of severe necrotizing pneumonia and sepsis caused by this strain of MRSA may improve patient outcomes.

Case report

A 48-year-old man with diet-controlled type 2 diabetes mellitus presented to the emergency department (ED) with hypoxic respiratory failure after a spending 4 days in Texas and 8 days in Costa Rica.

While in Costa Rica the patient was hospitalized overnight for hyperglycemia. About 2 days after hospital discharge he developed fever, chills and a nonproductive cough. He returned to Dallas, where he stayed for an additional 4 days. On his last evening there, the patient sought medical attention for fever and cough at a local clinic, where he was diagnosed with bronchitis. The next day, his clinical condition deteriorated en route to Toronto and the patient was taken by ambulance from the aircraft to the closest Toronto ED.

On presentation to the first hospital ED, he had a temperature of 38.0°C and an oxygen saturation of 76% on room air. Arterial blood gases revealed a pH of 7.42, a P_{AO_2} of 42 mm Hg and P_{CO_2} of 35 mm Hg. His clinical exam revealed bibasilar crackles and a chest x-ray showed bilateral pulmonary infiltrates, worse on the right than on the left (Fig. 1). He had a leukocyte count of 4.7×10^9/L and a creatinine of 158 μmol/L. The patient failed to respond adequately to oxygen supplementation and was intubated within a short time of his arrival. His initial antibiotic was levofloxacin 500 mg. Within hours, he became hypotensive, requiring inotropic support and was transferred to our institution for ongoing care.

On arrival, the patient had a blood pressure of 90/60 mm Hg and a heart rate of 180 beats per minute on dopamine; he was febrile at 38.8ºC. The patient was sedated, paralyzed, ventilated and started on ceftriaxone and azithromycin.

Past medical history revealed hypertension, diet-controlled type 2 diabetes mellitus, coronary artery spasm, depression and a congenital single kidney. He was a former smoker, with a 20-pack-year history and no known lung disease. His medications included hydrochlorothiazide, amlodipine, nitroglycerin, naproxen and paroxetine.

Repeat laboratory investigations revealed a leukocyte count of 5.7×10^9/L (no eosinophilia), a sodium level of 129 mmol/L, a mild elevation of the transaminases (with an aspartate aminotransferase of 112 U/L and an alanine aminotransferase of 48 U/L), an elevated lactate dehydrogenase of 404 U/L, a creatine kinase of 5180 U/L with negative troponins and a lactate of 2.6 mmol/L.

Bronchoscopy was performed on day 2, showing copious non-purulent, serosanguinous secretions and a friable airway. Sputum cultures taken from both hospitals were reported as growing MRSA. Vancomycin and intravenous immunoglobulin were added to the patient's therapy.

On day 3, the patient required dialysis and developed disseminated intravascular coagulation. He had ongoing fever, with a maximum temperature of 40.6°C; and his leukocyte count dropped to a minimum of 3.1×10^9/L. On day 4 he developed rapid atrial fibrillation requiring cardioversion and amiodarone. The patient had persistent hypoxia and hypercapnea, and remained hypotensive despite increasing doses of inotropes. He died just over 72 hours after his admission to hospital.

Post mortem examination revealed extensive bilateral necrotizing pneumonia, with large lung abscesses.

The isolate was sensitive to vancomycin, trimethoprim–sulfamethoxazole (TMP–SMX), tetracycline, ciprofloxacin, gentamicin, mupirocin, clindamycin and rifampin, but resistant to erythromycin. DNA fingerprint analysis using pulsed-field gel electrophoresis and multilo-

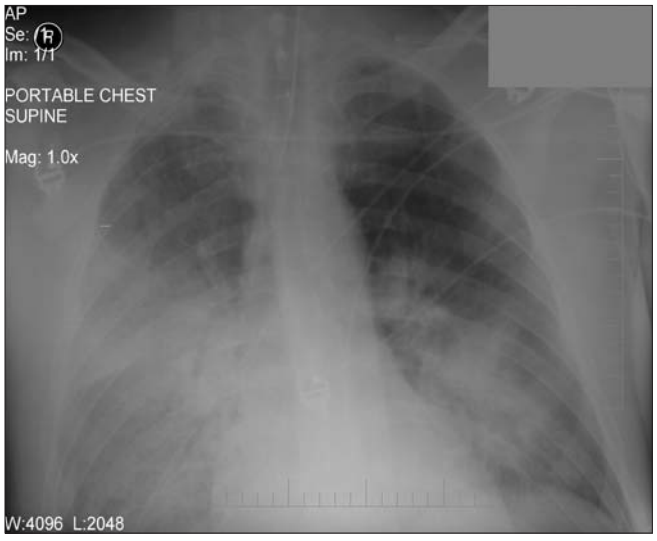

Fig. 1. Chest x-ray demonstrating bilateral pulmonary infiltrates.

cus sequence typing, which was conducted at the National Microbiology Laboratory,[1] found that the isolate was related to CMRSA10 (which is also called USA300), a new epidemic strain observed in Canadian hospitals (unpublished observations, Canadian Nosocomial Infection Surveillance Program).[2,3] As with other CMRSA10–USA300 isolates, this isolate fell within sequence type 8 on multilocus sequence typing and contained SCCmec type IVa as well as the genes lukF-PV and lukS-PV encoding Panton-Valentine leukocidin (PVL).[4]

Discussion

Previously known as a hospital pathogen, MRSA is now emerging independently as a community pathogen. The new strains of MRSA causing community-acquired infections, called community-associated MRSA (CA-MRSA), are genetically very different from hospital strains of MRSA. They appear to cause illness in very different populations.[5,6] Most CA-MRSA infections are caused by 1 of 2 clones, called CMRSA10 (USA300) and CMRSA7 (USA400). Infections owing to these clones are emerging around the world at somewhat different rates in differing locales. The greatest incidence of disease in North America has been in Texas and southern California, where staphylococcal infections are now most commonly due to MRSA.[7] In Canada, CA-MRSA is most common in southern Alberta and southwestern British Columbia, but is increasingly being reported in other provinces.

These new clones of MRSA carry virulence genes, including PVL, making infections substantially more severe than usual for *S. aureus*. Thus infections may occur in healthy adults and children. Most patients with CA-MRSA have no history of hospitalization or contact with the health care system.[8] Although most infections are suppurative soft tissue infections, necrotizing pneumonia can also occur. CA-MRSA infections are more common in several distinct population groups, such as aboriginals, military personnel, inmates at correctional facilities, competitive sports participants, injection drug users and the homeless. The common risks among these groups include living in crowded and sometimes unhygienic conditions, frequent skin to skin contact and frequent compromise of skin integrity.[3] However, CA-MRSA infections are increasingly occurring in people with none of these risk factors.

The clinical characteristics for patients with CA-MRSA necrotizing pneumonia include an influenza-like prodrome, viral co-infection, leucopenia and hemoptysis.[9–11] Most cases have presented with radiologic abnormalities, including unilateral or bilateral infiltrates, pneumatoceles and abscesses.[9–15] Disease is both severe and rapidly progressive.

Therapeutic options for severe CA-MRSA infections are limited to vancomycin and linezolid.[16,17] However, the high cost of linezolid makes it an impractical option for empiric treatment in the ED. In less severe infections, clindamycin, TMP–SMX and doxycycline are potential options. The majority of strains remain susceptible to TMP–SMX, but more than 30% of isolates are resistant to clindamycin and doxycycline. Fluoroquinolones are not recommended because resistance to these agents develops rapidly.[17]

Current guidelines for the treatment of community-acquired pneumonia do not include a regimen that would empirically cover MRSA.[18,19] In our patient's case, his travel history to Texas was the only epidemiologic clue to suggest MRSA. The clinical clues at presentation included the prodrome, the severity and the radiologic findings; leucopenia was a late finding (day 3). None of these clues are specific. As with most other cases, this patient's sputum yielded MRSA; however, such results do not help with the prompt provision of adequate antibiotic therapy in the ED. Emergency physicians across Canada should be routinely sending cultures from healthy patients with suppurative skin infections so that they can identify when CA-MRSA appears in their community as well as monitor its changing prevalence. Once CA-MRSA's presence in a community is establish, vancomycin should be considered as part of empiric therapy for patients presenting with life-threatening pneumonia.

Competing interests: None declared.

References

1. Mulvey M, Chui L, Ismail J, et al. Development of a Canadian standardized protocol for subtyping methicillin-resistant *Staphylococcus aureus* using pulsed-field gel electrophoresis. J Clin Microbiol 2001;39:3481-5.
2. McDougal L, Steward C, Killgore G, et al. Pulsed-field gel electrophoresis typing of oxacillin-resistant *Staphylococcus aureus* isolates from the United States: establishing a national database. J Clin Microbiol 2003;41:5113-20.
3. Weber JT. Community-associated methicillin-resisitant *Staphylococcus aureus*. Clin Infect Dis 2005;41:S269-72.
4. Enright M, Day N, Davies C, et al. Multilocus sequence typing for characterization of methicillin-resistant and methicillin-susceptible clones of *Staphylococcus aureus.* J Clin Microbiol 2000;38:1008-15.
5. Naimi T, LeDell K, Como-Sabetti K, et al. Comparison of community and health care associated methicillin-resistant *Staphylococcus aureus* infection. JAMA 2003;290:2976-84.
6. Carleton H, Diep BA, Charlebois E, et al. Community-adapted methicillin-resistant *Staphylococcus aureus* (MRSA): population dynamics of an expanding community reservoir of MRSA. J Infect Dis 2004;190:1730-8.
7. Moran GJ, Krishnadasan A, Gorwitz RJ, et al. Methicillin-

resistant *S. aureus* infections among patients in the emergency department. N Engl J Med 2006;355:666-74.
8. Gorak E, Yamada S, Brown J. Community-acquired methicillin-resistant *Staphylococcus aureus* in hospitalized adults and children without known risk factors. Clin Infect Dis 1999;29:797-800.
9. Francis J, Doherty M, Lopatin U, et al. Severe community-onset pneumonia in healthy adults caused by methicillin-resistant *Staphylococcus aureus* carrying the Panton-Valentine leukocidin genes. Clin Infect Dis 2005;40:100-7.
10. Frazee BW, Salz TO, Lambert L, et al. Fatal community-associated methicillin-resistant *Staphylococcus aureus* pneumonia in an immunocompetent young adult. Ann Emerg Med 2005;46: 401-4.
11. Gonzalez BE, Hulten KG, Dishop MK, et al. Pulmonary manifestations in children with invasive community-acquired *Staphylococcus aureus* infection. Clin Infect Dis 2005;41:583-90.
12. Janvier J, Elsayed S, Gregson D, et al. Necrotizing pneumonia secondary to community-associated methicillin-resistant *S. aureus* (CA-MRSA) USA300 strain without evidence of antecedent viral respiratory tract infection. [Abstract]. Can J Infect Dis Med Microbiol 2006;17:30.
13. Monaco M, Antonucci R, Palange P, et al. Methicillin-resistant *Staphylococcus aureus* necrotizing pneumonia. Emerg Infect Dis 2005;11:1647-8.
14. Peleg A, Munckhoff W. Fatal necrotising pneumonia due to community acquired methicillin-resistant *Staphylococcus aureus* (MRSA). Med J Aust 2004;181:228-9.
15. Dufour P, Gillet Y, Bes M, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* infections in France: emergence of a single clone that produces Panton-Valentine leukocidin. Clin Infect Dis 2002;35:819-24.
16. Barton M, Hawkes M, Moore D, et al. Guidelines for the prevention and management of community-associated methicillin-resistant *Staphylococcus aureus*: a perspective for Canadian health care practitioners. Can J Infect Dis Med Microbiol 2006; 17(Suppl. C):4C-24C.
17. Nicolle L. Community-acquired MRSA: a practitioner's guide. CMAJ 2006;175:145-6.
18. Mandell LA, Bartlett JG, Dowell SF, et al. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. Clin Infect Dis 2003;37:1405-33.
19. File T, Garau J, Blasi F, et al. Guidelines for empiric antimicrobial prescribing in community-acquired pneumonia. Chest 2004; 125:1888-901.

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Erratum

The placement of the arrows in Figure 1 of Barnett and Medzon's May 2007 case report, "Scrofula as a presentation of tuberculosis and HIV," (*Can J Emerg Med* 2007;9[3]:176-9) shifted in error. We apologize for any inconvenience this may have caused. The correct figure appears below.

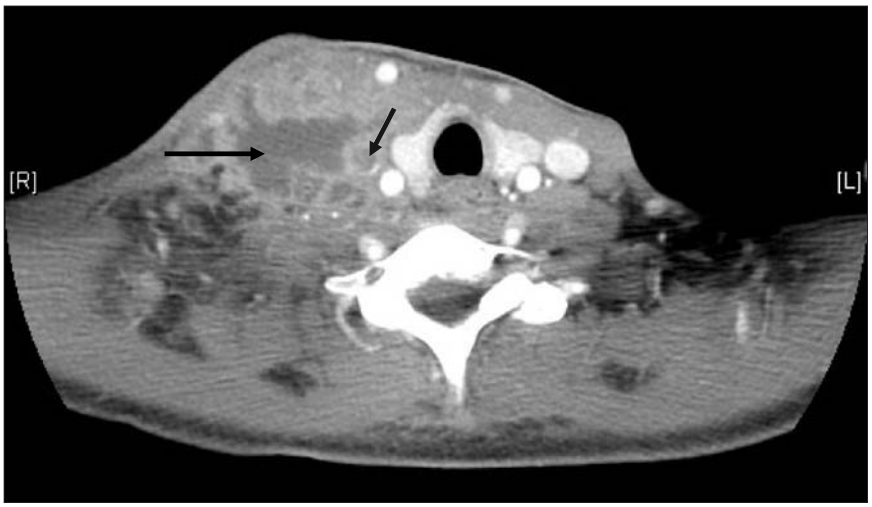

Fig. 1. CT scan of the neck with contrast. The left arrow indicates the multiloculated abscess. The right arrow indicates the right internal jugular vein with a tiny ring of contrast around the occluding thrombus.