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Invasive CA-MRSA in northwestern Ontario: a 2-year prospective study

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Introduction: Northwestern Ontario has a documented high rate of skin and soft-tissue infections due to community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA). Recently, invasive illness from this common pathogen has become a serious clinical problem in the region. We sought to better understand this trend of invasive CA-MRSA.
Methods: We prospectively studied cases of positive CA-MRSA bacteremia in 2012 and 2013. We examined genetic typing, comorbidities and outcomes.
Results: Twenty-three cases of CA-MRSA bacteremia were treated during the 2-year study period. Intravenous drug use accounted for only 17% of cases. One death and 2 cases of endocarditis occurred.
Conclusion: High rates of CA-MRSA in skin and soft-tissue infections, combined with poor living conditions and poor access to potable water, may account for most of these cases of CA-MRSA bacteremia. Social determinants of health are relevant when common resistant bacterial isolates become associated with life-threatening illness.

Introduction : La région du Nord-Ouest de l'Ontario présente un taux élevé et documenté d'infections de la peau et des tissus mous causées par une souche de *Staphylococcus aureus* méthycillinorésistante d'origine communautaire (SARM-C). La maladie invasive causée par cet agent pathogène commun est récemment devenue un problème clinique grave dans la région. Nous avons voulu mieux comprendre cette tendance du SARM-C invasif.
Méthodes : Nous avons étudié de manière prospective des cas de bactériémie positive à SARM C en 2012 et 2013. Nous avons analysé le typage génétique, les comorbidités et l'issue des infections.
Résultats : Vingt-trois cas de bactériémie à SARM-C ont été traités au cours de la période de 2 ans. L'utilisation de drogues injectables a pu être incriminée dans seulement 17 % de cas. On a enregistré 1 décès et 2 cas d'endocardite.
Conclusion : Des taux élevés de SARM-C dans les infections de la peau et des tissus mous alliées à de piètres conditions de vie et à un accès limité à de l'eau potable pourraient expliquer la plupart de ces cas de bactériémie à SARM-C. Il faut tenir compte des déterminants sociaux de la santé lorsque des isolats bactériens communs et résistants deviennent associés à des maladies gravissimes.

INTRODUCTION

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is generally acknowledged to be increasing in community and hospital settings.[1–4] It typically is associated with skin or soft-tissue infections. Northwestern Ontario, home to many remote First Nations communities, has recently documented one of the highest rates of CA-MRSA in Canada; 56% of all *S. aureus* isolates were found to be CA-MRSA.[1] The region has also experienced a recent rise in invasive illness, including bacteremia, caused by CA-MRSA. The purpose of this study was to document this trend of invasive CA-MRSA and identify the related strains in our catchment area of 28 000 people, most of whom are living

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on remote reserves and served by the Sioux Lookout Meno Ya Win Health Centre.[5]

METHODS

We prospectively gathered clinical information regarding cases of sepsis and pneumonia from CA-MRSA infections during 2012 and 2013. We identified 23 cases over this 2-year period. Type and source of infection, demographics, comorbidities, treatment and outcomes were compiled for this study. We sent bacteremic CA-MRSA isolates for genetic and Panton–Valentine leukocidin (PVL) testing. The study was approved by the Sioux Lookout Meno Ya Win Health Centre Research Review and Ethics Committee.

RESULTS

Among the approximately 100 annual positive blood cultures in our region, 8 cases of CA-MRSA bacteremia were diagnosed in 2012, and 15 cases were diagnosed in 2013. One death involving sepsis with renal failure was ascribed to a CA-MRSA infection (Table 1).

Osteoarticular infections accounted for 26% of the cases of bacteremia, followed by respiratory and abdominal sources (i.e., pancreatitis, cholecystitis, pyelonephritis) at 22% each. Two cases of endocarditis were diagnosed (Table 2). Only 4 known intravenous drug users were among the 23 cases. About half of infected patients had type 2 diabetes mellitus (Table 1).

Sixteen of the 23 cases of MRSA bacteremia were genetically typed. Canadian epidemic strain MRSA (CMRSA) 10 and 7 were the common pathogens in 8 and 6 cases of the 16 known strains, respectively. Nine of these 16 strains tested positive for PVL. All CA-MRSA isolates were identified by their antibiotic susceptibilities, as well as genetic typing where available (16/23) (Table 3).

In addition to the 23 cases of CA-MRSA bacteremia reported here, there were 14 other patients with CA-MRSA invasive infections. During the study period, 8 urine, 4 sputum and 2 synovial fluid infections occurred.

DISCUSSION

Invasive MRSA has long been noted as a serious health care issue. In the past, health care–associated (HA)–MRSA was implicated in serious and invasive infections, and CA-MRSA infections were generally non–life-threatening soft-tissue infections. Bacteremia from CA-MRSA was a rare event.

In the Canadian Ward Surveillance Study (CANWARD) involving more than 12 Canadian

Table 1. Characteristics of 23 patients with CA-MRSA bacteremia diagnosed in 2012 and 2013

Characteristic	No. (%) of patients*
Age, mean, yr	39.3
Age category, yr	
0–10	1
11–20	3
21–60	15
> 60	5
Comorbidities	
Type 2 diabetes mellitus	11 (48)
Hepatitis B or C, or HIV	0
Intravenous drug use	4 (17)
Investigations	
Echocardiography	11 (48)
Viral serology	9 (39)
Treatment	
Vancomycin	18 (78)
Outcome	
Died	1 (4)
Transferred care	3 (13)
Treated locally	19 (83)

CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*.
*Unless stated otherwise.

Table 2. Diagnoses and sources of infection in 23 patients with CA-MRSA bacteremia

Variable	No. (%) of patients
Diagnosis	
Osteoarticular disease	6 (26)
Respiratory disease	5 (22)
Abdominal organ infection	5 (22)
Endocarditis	2 (9)
Simple bacteremia	3 (13)
Skin or soft-tissue infection	1 (4)
Source of infection	
Central line	1 (4)

CA-MRSA = community associated methicillin-resistant *Staphylococcus aureus*.

Table 3. Genetic typing of 23 cases of CA-MRSA bacteremia

Variable	CMRSA 7	CMRSA 10	Other CMRSA	NA
Genetic typing	6	8	2	7
PVL positive	4	5	0	1

CA-MRSA = community-associated methicillin-resistant *Staphylococcus aureus*; CMRSA = Canadian epidemic strain of MRSA; NA = not available; PVL = Panton–Valentine leukocidin.

hospitals during a 5-year period (2007–2011), only 89 bacteremic isolates of the 8245 positive blood cultures were found to be CA-MRSA,[6,7] for a rate of 1.08% of all positive blood cultures. Our region has about 100 patients with positive blood cultures annually, and CA-MRSA constituted 12% of them during the 2-year study period. In 2012 at the Ottawa Hospital, only 12% of all cases of *S. aureus* bacteremia were CA-MRSA, and a slightly larger percentage was found in the 12 tertiary care hospitals participating in CANWARD in 2011, at 19%.[7] Since 2010, we have encountered an annual doubling of CA-MRSA bacteremia: 2, 4, 8 and 15 cases annually. Of the 19 patients with *S. aureus* bacteremia, 58% (11/19) were CA-MRSA isolates.[1]

In a study done in Calgary from 2000 to 2006, Laupland and colleagues[8] found 2.2 cases of MRSA bacteremia per 100 000 population annually, and most of these were HA-MRSA. Only 11% were CA-MRSA, for an estimated rate of 0.24 per 100 000 population annually. Our incidence of 23 cases in 2 years in a catchment area of 28 000 gives us an annual population rate of 41.1 per 100 000 population, almost 20-fold the rate in Calgary.

Of the 16 cases with genetic typing, we had 8 isolates that were CMRSA 10, the most common Canadian strain and generally the cause of most hospital-related CA-MRSA infections.[6] The second most common genetic type was CMRSA 7, which is the most common strain seen in northern Manitoba and Saskatchewan, our neighbouring provinces.[2,9]

Panton–Valentine leukocidin was initially thought to be universally present in CA-MRSA strains and to be responsible for much of its pathogenesis.[10] Now, only about 85% of CA-MRSA strains are usually positive for this marker, and other genetic attributes may be more closely associated with virulence.[11,12] In our study, 9 of the 16 samples (56%) that were genetically typed were positive for PVL.

Issues with on-reserve housing such as overcrowding, poor sanitation and access to potable water are health risks associated with CA-MRSA infections.[13–16] Our catchment area is made up of remote First Nations populations, which have documented deficiencies in these areas.[17] Seventeen of Ontario's First Nations communities with boil water advisories are in our region.[18] In one community with a population of more than 2000, 90% of the homes are not connected to a water source at all.[19]

We have previously documented high rates of CA-MRSA in our region.[1] Although illicit drug use is a serious issue, these cases do not appear to be primarily related to intravenous drug abuse. We may be seeing a common isolate associated with skin or soft-tissue infections causing a high rate of invasive disease related to other factors. These factors may include the high burden of chronic illness, such as diabetes mellitus and skin disease, combined with overcrowding and limited access to potable water.

Clinicians in our region will need to be alert to concomitant cardiac or osteogenic infections, as well as viral pathogens associated with intravenous drug use (e.g., hepatitis B and C, and HIV) when faced with CA-MRSA bacteremia.

Limitations

The genetic typing was done on an ad hoc basis for CA-MRSA bacteremia isolates, and we were able to document the genetics on only 16 of our 23 samples. Our hospital, like most, could not automatically give us antibiotic susceptibilities on CA-MRSA isolates, and we had to manually determine these. Many similar studies were based in urban settings, where HA- and CA-MRSA values were combined into general MRSA estimates, limiting what studies we could use as comparators.

CONCLUSION

Our population in northwestern Ontario is experiencing a dramatic increase in invasive disease from CA-MRSA infections, particularly bacteremic sepsis, with at least one fatal outcome. The social determinants of health, long identified as problematic, take on greater importance when common, resistant organisms become life-threatening.

Competing interests: None declared.

REFERENCES

1. Muileboom J, Hamilton M, Parent K, et al. Community-associated methicillin-resistant *Staphylococcus aureus* in northwest Ontario: a five-year report of incidence and antibiotic resistance. *Can J Infect Dis Med Microbiol* 2013;24:e42-4.
2. Simor AE, Gilbert NL, Gravel D, et al. Methicillin-resistant *Staphylococcus aureus* colonization or infection in Canada: national surveillance and changing epidemiology, 1995–2007. *Infect Control Hosp Epidemiol* 2010;31:348-56.
3. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infection Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections adults and children. *Clin Infect Dis* 2011;52:e18-55.
4. McConeghy KW, Mikolich DJ, LaPlante KL. Agents for the decolonization of methicillin-resistant *Staphylococcus aureus*. *Pharmacotherapy* 2009;29:263-80.
5. Walker R, St. Pierre-Hansen N, Cromarty H, et al. Measuring cross-cultural patient safety: identifying barriers and developing performance indicators. *Healthc Q* 2010;13:64-71.

6. Nichol KA, Adam HJ, Hussain Z. Comparison of community-associated and health care-associated methicillin-resistant *Staphylococcus aureus* in Canada: results of the CANWARD 2007–2009 study. *Diagn Microbiol Infect Dis* 2011;69:320-5.
7. Nichol KA, Adam HJ, Roscoe DL, et al. Changing epidemiology of methicillin-resistant *Staphylococcus aureus* in Canada. *J Antimicrob Chemother* 2013;68:i47-55.
8. Laupland KB, Ross T, Gregson DB. *Staphylococcus aureus* bloodstream infections: risk factors, outcomes, and the influence of methicillin resistance in Calgary, Canada, 2000–2006. *J Infect Dis* 2008;198:336-43.
9. Golding GR, Levett PN, McDonald RR, et al. High rates of *Staphylococcus aureus* USA400 infection, northern Canada. *Emerg Infect Dis* 2011;17:722-5.
10. Lo W, Wang C. Panton-Valentine leukocidin in the pathogenesis of community-associated methicillin-resistant *Staphylococcus aureus* infection. *Pediatr Neonatol* 2011;52:59-65.
11. Thomas R, Ferguson J, Coombs G, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* pneumonia: a clinical audit. *Respirology* 2011;16:926-31.
12. Moellering RC. Why has methicillin-resistant *Staphylococcus aureus* become such a successful pathogen in adults? *Infect Dis Clin Pract* 2010;18:286-91.
13. Cooke FJ, Brown NM. Community-associated methicillin-resistant *Staphylococcus aureus* infections. *Br Med Bull* 2010;94:215-27.
14. Skov RL, Jensen KS. Community-associated methicillin-resistant *Staphylococcus aureus* as a cause of hospital-acquired infections. *J Hosp Infect* 2009;73:364-70.
15. Tenover FC, Goering RV. Methicillin-resistant *Staphylococcus aureus* strain USA300: origin and epidemiology. *J Antimicrob Chemother* 2009;64:441-6.
16. Tong SYC, Bishop EJ, Lilliebridge RA, et al. Community-associated strains of methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *S. aureus* in Indigenous northern Australia: epidemiology and outcomes. *J Infect Dis* 2009;199:1461-70.
17. Porter J. First Nations housing shortage getting worse. *CBC News*. 2012 June 14. Available: www.cbc.ca/news/canada/thunder-bay/first-nations-housing-shortage-getting-worse-report-says-1.1129945 (accessed 2013 Dec. 10).
18. Neskantaga issues call to action over living conditions. *Wawatay News* 2014 May 15. Available: www.wawataynews.ca/archive/all/2014/5/16/neskantaga-issues-call-action-over-living-conditions_25586 (accessed 2014 June 3).
19. Freek K. State of emergency. One reserve's battle with unsafe water. *Water Canada*. 2011 May 6. Available: http://watercanada.net/2011/state-of-emergency (accessed 2014 June 3).

Country Cardiograms

Have you encountered a challenging ECG lately?

In most issues of *CJRM* an ECG is presented and questions are asked.

On another page, the case is discussed and the answer is provided.

Please submit cases, including a copy of the ECG, to Suzanne Kingsmill, Managing Editor, *CJRM*, 45 Overlea Blvd., P.O. Box 22015, Toronto ON M4H 1N9; cjrm@cjrm.net

Cardiogrammes ruraux

Avez-vous eu à décrypter un ECG particulièrement difficile récemment?

Dans la plupart des numéros du *JCMR*, nous présentons un ECG assorti de questions. Les réponses et une discussion du cas sont affichées sur une autre page.

Veuillez présenter les cas, accompagnés d'une copy de l'ECG, à Suzanne Kingsmill, rédactrice administrative, *JCMR*, 45, boul. Overlea, C. P. 22015, Toronto (Ontario) M4H 1N9 ; cjrm@cjrm.net