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Community-acquired MRSA infection: An emerging trend

The use of culture as backup to empiric treatment of staphylococcal infection can help deal with widespread antibiotic resistance.

ABSTRACT: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are becoming increasingly prevalent in North America among community populations. A case series of prospectively identified MRSA infections in one practice in the Fraser Valley suggests that aggressive infections among patients without risk factors, including pediatric patients, are becoming more common. The prevalence of MRSA infections in the community has made the empiric treatment of skin and soft tissue infections more complicated, and also suggests that culture should be used more often as a backup to treatment.

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Methicillin-resistant *Staphylococcus aureus* (MRSA) has long been recognized and was cited soon after the development of beta-lactam-resistant anti-staphylococcal antibiotics. In Canada, most MRSA infection and colonization has occurred among patients in hospital. However, patients in the community with chronic antibiotic exposure have also been a source of MRSA.

Recent reports from international sources indicate that community-acquired MRSA infections are becoming more prevalent,[1] in keeping with the high frequency of MRSA in health care institutions. Recent reports also suggest the occurrence of more virulent MRSA pathogens in the community, again a reflection of changes in nosocomial MRSA. Severe infections among children and other historically low-risk populations are being documented increasingly.

Case data

The 15 cases of MRSA infection described here occurred in a general practice setting in the Fraser Valley between September 2002 and November 2005. The demographic and clinical details are provided in the **Table**.

The majority of the infections (9) were identified in 2005. All but three of the infections occurred in adults. Infections were generally initiated in the skin and progressed aggressively to ulceration, cellulitis, boils, and deep abscesses. The only exception was one infection that began after a traumatic ear perforation. Seven patients had infections associated with drug abuse; two of these patients had direct knowledge of MRSA infections by name, and one had been instructed on the percutaneous drainage of abscesses by a drug user who apparently encountered many such infections among peers. Another patient developed MRSA infection shortly after being physically traumatized by drug users. Two patients had recent exposure to family or friends who had been either residing in a chronic care facili-

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Table. Demographic and clinical data for prospectively identified MRSA infections in a general practice setting, Sept. 2002 to Nov. 2005.

Patient	Date	Age (years)	Gender	Infection site	Risk factor	Treatment	Susceptibility	Resistance
1	Sept. 02	51	M	Folliculitis, cellulitis, axillary abscess	Previous MRSA infection after visiting relative in a nursing home	cipro	cipro, SXT, clinda, fuc, mup, lin	erythro
	Apr. 03			Hand cellulitis		SXT		
	May 03			Nasal		chlorhexidine wash and nasal mup (no further MRSA detected)		
2	Oct. 03	26	M	Forearm cellulitis and abscess		ceph changed to SXT	SXT, fuc, mup, lin	erythro, clinda, cipro
3	Mar. 04	8	F	Buttock abscess and boils		erythro changed to ceph	SXT, clinda, fuc, mup, lin	erythro, cipro
4	July 04	39	M	Forearm abscess	Suspected drug use	cefaz in hospital changed to ceph; mup and fuc ointments	SXT, clinda, fuc, mup, lin	erythro, cipro
5	July 04	45	M	Forearm cellulitis		ceph	SXT, clinda, fuc, mup, lin	erythro, cipro
6	Nov. 04	49	F	Multiple torso abscesses	Drug use	ceph changed to SXT	SXT, clinda, fuc, mup, lin	erythro, cipro
7	Dec. 04	22	M	Hand lesions and forearm cellulitis		telithro changed to cefaz IV then clinda (sulfa allergy)	SXT, clinda, fuc, mup, lin	erythro, cipro
8	Feb. 05	46	M	Otitis externa	Traumatic exposure to drug addicts 3 weeks prior	chloro	SXT, fuc, mup, lin	erythro, clinda, cipro
	Feb. 05			Perianal abscess			SXT, clinda, fuc, mup, lin	erythro, cipro
9	Apr. 05	6	M	Boils on thigh and buttocks		ceph	SXT, clinda, fuc, mup, lin	erythro, cipro
10	Apr. 05	31	M	Perianal abscess	Suspected drug use	ceph	SXT, clinda, fuc, mup, lin	erythro, cipro
11	July 05	62	F	Abdominal skin	Visited two friends who had recent surgery in hospital	erythro changed to SXT; topical Polysporin	SXT, clinda, fuc, mup, lin	erythro, cipro
12	July 05	6	F	Forearm boil	Drug use in a parent and family history of boils	SXT	SXT, clinda, fuc, mup, lin	erythro, cipro
13	Aug. 05	26	F	Breast ulcers	Had previous MRSA	SXT	SXT, clinda, fuc, mup, lin	erythro, cipro
14	Nov. 05	36	M	Buttock abscess	Past drug use	SXT	SXT, clinda, fuc, mup, lin	erythro, cipro
15	Nov. 05	31	M	Forearm cellulitis	Past drug use	SXT	SXT, clinda, fuc, mup, lin	erythro, cipro

Antibiotics listed under Treatment, Susceptibility, and Resistance: cefaz=cefazolin, ceph=cephalexin, chloro=chloramphenicol, cipro=ciprofloxacin, clinda=clindamycin, erythro=erythromycin, fuc=fusidic acid, lin=linezolid, mup=mupirocin, sulfa=sulfonamides, SXT=cotrimoxazole, telithro=telithromycin

ty or who had undergone an inpatient surgery in a large hospital. Five patients, however, did not have any apparent risk factors, including two of the three infected children. Apart from the localized infection site manifestations, several of these patients were clinically septic and considerably unwell; no episodes of toxic shock were evident.

MRSA are considered to be resistant to all beta-lactam antibiotics. Other resistance profiles are variable. For example, the isolate from Patient 1 (see **Table**) manifested erythromycin resistance but was susceptible to cotrimoxazole, clindamycin, and ciprofloxacin. Most other isolates in the 15 cases described here showed resistance to erythromycin and ciprofloxacin but susceptibility to cotrimoxazole and clindamycin, with two exceptions in which clindamycin resistance was found. For one patient, two isolates were obtained from different infection sites over 1 week, and these were discrepant for clindamycin susceptibility. All bacterial isolates were susceptible to fusidic acid, mupirocin, and linezolid.

Not all patients were available for follow-up. For most patients, initial empiric treatment included either cephalexin or a macrolide antibiotic. For three patients, foreknowledge of MRSA in the given context led to the use of an antibiotic to which the bacterium was susceptible.

The increasing resistance of *S. aureus* should prompt physicians to use culture as a backup to empiric treatment more often.

Discussion

S. aureus continues to be a major infectious agent,[2] and there has been little real progress in vaccination. MRSA are now complicating the treatment of both inpatient and community-acquired infections. Initially, the evolution of these bacteria meant only limitations to the use of beta-lactam antibiotics. Unfortunately, these bacteria have now developed resistance to a variable number of other antibiotics. Indeed, some strains have acquired resistance to most antibiotics.

Most of the isolates from the patients described here demonstrated erythromycin and ciprofloxacin resistance. Both of these antibiotics are commonly used for outpatient therapy. Erythromycin is commonly used as a practical alternative to beta-lactam agents for community-acquired skin and soft tissue infections, especially when *S. aureus* and beta-hemolytic streptococci are likely to be involved. Quinolones have also become popular agents for outpatient skin and soft tissue infections. Thus, the resistance profile of the majority of isolates has come to complicate the empiric therapy. Our patient data indicated that the antibiotic chosen for first-line treatment often did not match the antibiotic for which the bacterium was susceptible. While sulfa and clindamycin remain options for most infections, the increasing resistance of *S. aureus* should prompt physicians to use culture as a backup to empiric treatment more often.

The prevalence of community-acquired MRSA infections in the Lower Mainland is perhaps best reflected by antibiogram reports from predominantly community-based laboratories. In this light, a profile published by BC Biomedical Laboratories[3] itemized *S. aureus* as having an 8% frequency of methicillin resistance among isolates from 2002. Of these general isolates (n=4259), 23% were deemed to be resistant to erythromycin, 8% to clindamycin, and 9% to cotrimoxazole. For MRSA in particular (n=328), 94% were resistant to erythromycin, 83% to clindamycin, 79% to cotrimoxazole, and 94% to ciprofloxacin.

When MRSA first emerged, most infections were occurring among high-risk patients (e.g., chronic antibiotic users, individuals exposed to nosocomial infection, intravenous drug users) and modification of first-line treatment for these patient groups could be anticipated. The emerging trend, however, is toward infections in patients without traditional risk factors, including pediatric patients.[1] Recent reports in the United States cite epidemic proportions of infection among the pediatric population.[4-6] Other reports cite MRSA as an emerging problem in athletics.[7] Although sulfa drugs remain low cost, the same cannot be said of other oral antibiotics, including clindamycin.

The mere presence of antibiotic resistance does not equate with increased virulence.[8] That is, MRSA are not necessarily more likely to cause disease because of modifications in antibiotic susceptibility genes. It is possible, however, that the continued presence of MRSA in an environment where more virulent strains are circulating could lead to the emergence of *S. aureus* that is both antibiotic resistant and more virulent. This already appears to have occurred elsewhere.

In both the United States and United Kingdom, MRSA are emerging as common community pathogens.[9,10] Simultaneously, the nasal carrier rate of MRSA is rapidly increasing.[11] Mulvey and colleagues recently found evidence of more virulent and resistant *S. aureus* among community infections in Saskatchewan.[12] The latter report also presents evidence that a large proportion of the bacterial isolates are similar to those with greater virulence that are currently affecting community patients in the United States. The Panton-Valentine leukocidin gene appears to be a major virulence marker, and an increasing number of epidemic and community-acquired strains carry the trait.

As community-acquired MRSA infections become more prevalent, infection will inevitably occur among individuals who apparently lack risk factors. Such widespread infection is documented in the recent medical literature, and the cases described here are part of this emerging trend.

The empiric treatment of skin and soft tissue infections has accordingly become more complicated than is generally appreciated. Treatment approaches for community-acquired MRSA infections have been detailed elsewhere,[13] and there are several new developments in the area. Such developments are necessary, given the alarming increase in community-acquired MRSA now recognized worldwide. Treatment guidelines for the management of skin and soft tissue infections have been published widely, but it is apparent that such guidelines have their limitations as the frequency of MRSA continues to increase.[14-15] Most such infections seen in general practice would fit into Eron's class 1 or 2.[16] Such categorization would lead to treating empirically with beta-lactam-resistant semisynthetic penicillins or first-generation cephalosporins. It is relevant, therefore, for general practitioners to make greater use of wound microbiology from bacterial culture specimens to ensure a precise "drug-bug" match.

Hospitals have historically been major foci for MRSA epidemics. Such hotbeds of infection have thereafter served as reservoirs for community-acquired infection.

Patients with risk factors for MRSA infection have then acted as vectors to reintroduce infection back into health care centres. Strategies to reduce MRSA in both hospitals and the community are critical. This is especially so when strains combining increased virulence and multiple antibiotic resistance become endemic. The economic impact of nosocomial MRSA in Canada is substantial.[17] The potential economic impact of community-acquired MRSA could parallel this, if not exceed it.

MRSA infection became reportable in British Columbia during the 1990s. Unfortunately, there is no longer a mandate to report these infections. Some major health centres in this province have now become sites with endemic MRSA. Some have experienced crises to the point of closing beds and nearly closing units. This trend will only continue unless more attention is directed to this very important infectious disease. The morbidity associated with MRSA in British Columbia is considerable, albeit largely unmeasured, and it is time to direct more resources to public health intervention.

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ment Guidelines" in the References.

Competing interests

None declared.

References

1. Weber JT. Community-associated methicillin-resistant Staphylococcus aureus. Clin Infect Dis 2005;41(suppl 4):S269-S272.
2. Cimolai N. Staphylococcus aureus outbreaks among newborns: New frontiers in an old dilemma. Amer J Perinatol 2003; 20:125-136.
3. BC Biomedical Laboratories, Surrey, BC. Empiric therapy antibiogram. www.bcbio.com/hcpros/references/treatment_guidelines.htm (accessed 15 December 2005).
4. Purcell K, Fergie J. Epidemic of community-acquired methicillin-resistant Staphylococcus aureus infections: A 14-year study at Driscoll Children's Hospital. Arch Pediatr Adolesc Med 2005; 159:980-985.
5. Stevenson KB, Searle K, Stoddard GJ, et al. Methicillin-resistant Staphylococcus aureus and vancomycin-resistant enterococci in rural communities, western United States. Emerg Infect Dis 2005;11:895-903.
6. Moran GJ, Amii RN, Abrahamian FM, et al. Methicillin-resistant Staphylococcus aureus in community-acquired skin infections. Emerg Infect Dis 2005;11:928-930.
7. Rihn JA, Michaels MG, Harner CD. Community-acquired methicillin-resistant Staphylococcus aureus: An emerging problem in the athletic population. Am J Sports Med 2005;33:1924-1929.
8. Cimolai N. Are all MRSA made equal? Can J Microbiol 2002;48:560-566.
9. Fridkin SK, Hageman JC, Morrison M, et al. Methicillin-resistant Staphylococcus aureus disease in three communities. N Engl J Med 2005;352:1436-1444.
10. Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant Staphylococcus aureus in Los Angeles. N Engl J Med 2005;352:1445-1453.
11. Creech CB, Kernodle DS, Alsentzer A, et al. Increasing rates of nasal carriage of methicillin-resistant Staphylococcus aureus in healthy children. Pediatr Infect Dis J 2005;24:617-621.
12. Mulvey MR, MacDougall L, Cholin B, et al. Community-associated methicillin-resistant Staphylococcus aureus, Canada. Emerg Infect Dis 2005;11:844-850.
13. Ellis MW, Lewis JS. Treatment approaches for community-acquired methicillin-resistant Staphylococcus aureus infections. Curr Opin Infect Dis 2005;18:496-501.
14. Eron LJ, Lipsky BA, Low DE, et al. Managing skin and soft tissue infections: Expert panel recommendations on key decision points. J Antimicrob Chemother 2003;52(suppl 1):i3-i17.
15. Fung HB, Chang JY, Kuczynski S. A practical guide to the treatment of complicated skin and soft tissue infections. Drugs 2003;63:1459-1480.
16. Eron J. Infections of skin and soft tissue: Outcomes of a classification scheme. Clin Infect Dis 2000;31:287(A432).
17. Kim T, Oh PI, Simor AE. The economic impact of methicillin-resistant Staphylococcus aureus in Canadian hospitals. Infect Control Hosp Epidemiol 2001; 22:99-104. BCMJ