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Original Article

Necrotizing fasciitis in a medical center in northern Taiwan: emergence of methicillin-resistant *Staphylococcus aureus* in the community

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Background and Purpose: Necrotizing fasciitis (NF) is a rapidly progressive life-threatening infection. It is located in the deep fascia, with secondary necrosis of the subcutaneous tissues requiring urgent surgical and medical therapy. *Staphylococcus aureus* is, historically, a very uncommon cause of NF, but we have recently noted an increasing number of these infections being caused by community-acquired methicillin-resistant *S. aureus* (CA-MRSA).

Methods: The medical records of 53 patients diagnosed with NF between January 2001 and December 2005 were reviewed. A standardized instrument was used to abstract information from the medical records of each patient.

Results: *S. aureus* monomicrobial infection accounted for 37.7% (20/53) of the causal organisms noted. Of the 20 strains of *S. aureus*, 8 were methicillin-sensitive *S. aureus* and 12 were MRSA. In the 12 patients with MRSA infection, 7 had CA-MRSA. All patients with NF caused by CA-MRSA had no serious coexisting conditions or risk factors. All CA-MRSA isolates were susceptible to ciprofloxacin, trimethoprim-sulfamethoxazole, and vancomycin in vitro. All were cured after surgical intervention and medical treatment.

Conclusions: For patients with severe invasive NF caused by CA-MRSA, glycopeptides may be prescribed as an empirical treatment until susceptibility results. The prognosis of NF caused by CA-MRSA was good after adequate surgical and antimicrobial treatment.

Key words: Community-acquired infections; Fasciitis, necrotizing; Methicillin resistance; *Staphylococcus aureus*

Introduction

Staphylococcus aureus is one of the most common causes of infections in both hospitals and communities, causing diseases ranging from skin and soft tissue infections to fulminant septicemia [1]. In the times before antibiotics became available, invasive staphylococcal disease was often fatal. The introduction of penicillin in the 1940s, and the other antibiotics subsequently, dramatically improved survival. However, mounting recognition of isolates circulating in the community that are resistant to methicillin has increased the level of concern about this important pathogen in recent times.

In the past decade, community-acquired methicillin-resistant *S. aureus* (CA-MRSA) infections among individuals without health care-associated (HCA) risk factors have surfaced in several areas [2]. In Taiwan, MRSA was first documented in the early 1980s. In the 1990s, the incidence of nosocomial MRSA infections increased in Taiwan, especially in teaching hospitals [3,4]. In 2000, methicillin resistance was identified in 53-83% of all *S. aureus* isolates from 12 major hospitals in Taiwan [5].

Predisposing factors for the acquisition of MRSA include recent hospitalization, admission to an intensive care unit, nursing home residence, exposure to a patient who is colonized or infected with MRSA, household contact with individuals harboring hospital-acquired

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MRSA, and prolonged antimicrobial therapy and surgery [6]. Although the majority of CA-MRSA infections are mild skin and soft tissue infections, severe life-threatening cases, such as necrotizing pneumonia, necrotizing fasciitis (NF), myonecrosis, and sepsis are emerging [7,8].

NF is a term that was first used to describe rapidly spreading gangrene of the skin and subcutaneous tissues above the fascial layer in the 1950s [7]. It is a rapidly progressive life-threatening infection located in the deep fascia, with secondary necrosis of the subcutaneous tissues. Two types are recognized — type I, in which one or more anaerobic bacteria are isolated with one or more facultative anaerobic and/or aerobic bacteria, and type II, in which the responsible organism is group A *Streptococcus*, either alone or in combination with other organisms (most commonly, *S. aureus*) [8].

Diagnosis of NF might be delayed because of the initial minimal skin cellulites, even as the subcutaneous tissue suffers extensive necrosis and pronounced systemic toxicity develops. The mainstay treatment of NF is a combination of surgical and medical therapies. Adequate and repetitive surgical debridements, empirical antibiotics with a broad coverage of aerobes and anaerobes, and aggressive supportive care should be provided [9]. Worryingly, *S. aureus* too has emerged as a monomicrobial cause of NF in recent times [10].

We analyzed the risk factors, clinical manifestations, antimicrobial susceptibilities, management, and prognostic determinants of NF caused by the monomicrobial infection of *S. aureus* in 53 cases of NF diagnosed surgically and pathologically during a 5-year period.

Methods

A retrospective review of the medical records of patients with NF admitted to the Tri-Service General Hospital, one of the major teaching hospitals located in northern Taiwan, from 1 January 2001 to 31 December 2005 was done. The diagnosis of NF in 53 patients was based on either the clinical and/or surgical finding of extensive necrosis of the fascia and subcutaneous tissues, or histological findings. All surgical reports were reviewed to determine preoperative diagnosis, intraoperative findings, and postoperative diagnosis, and the patient was included in the study if both the intraoperative and postoperative diagnoses were NF. A standardized instrument was used to abstract information from the medical records of each patient. Information was obtained from several broad categories — demographics, associated conditions, duration of symptoms prior to admission, microbiological data, antibiotic treatment, clinical features, surgical intervention, and outcome. An investigator reviewed the cultures of the 53 patients and isolated 95 unique pathogens (Table 1). Twenty five strains of *S. aureus* were isolated, and 20 were monomicrobial infections. *S. aureus* as a concomitant pathogen was noted in 25% of the polymicrobial infections. All in vitro susceptibilities were performed with the disk diffusion test according to the protocols of the National Committee for the Clinical Laboratory Standards (NCCLS) [11].

CA-MRSA infection was defined as the identification of MRSA in a patient with signs and symptoms of the infection, either in the outpatient setting or within 48 h of hospital admission, with no prior histories of MRSA infection or colonization and admission to a hospital or nursing home in the previous year, and the absence of dialysis, surgery, permanent indwelling catheters, or medical devices that pass through the skin to the body [12].

Table 1. Etiology of necrotizing fasciitis

Organism	No. of organisms (%)
Gram-positive	
Staphylococcus aureus	25 (26.3)
Enterococcus	7 (7.4)
Streptococcus, non-A, -B, -D	6 (6.3)
Viridans Streptococci	5 (5.3)
Coagulase-negative *Staphylococcus*	4 (4.2)
Group B *Streptococcus*	1 (1.1)
Group D *Streptococcus*	1 (1.1)
Gram-negative	
Klebsiella pneumoniae	10 (10.5)
Escherichia coli	5 (5.3)
Enterobacter cloacae	4 (4.2)
Acinetobacter baumannii	3 (3.2)
Pseudomonas aeruginosa	3 (3.2)
Citrobacter spp.	3 (3.2)
Serratia marcescens	2 (2.1)
Proteus spp.	2 (2.1)
Vibrio spp.	2 (2.1)
Aeromonas spp.	2 (2.1)
Morganella spp.	2 (2.1)
Fungi	
Candida albicans	2 (2.1)
Anaerobic	
Peptostreptococcus spp.	4 (4.2)
Bacteroides fragilis	1 (1.1)
Fusobacterium spp.	1 (1.1)

Results

Demographics

Fifty three patients (38 males and 15 females; mean age, 62 years; range, 22 to 103 years) with NF were identified. Forty two patients (79%) were over 50 years old. The median length of hospitalization was 27.1 days. Twenty patients had monomicrobial infections caused by *S. aureus* (Table 2). In the eight patients with methicillin-sensitive *S. aureus* (MSSA), seven were male (85.7%), the mean age was 48.9 years, and the mean length of hospitalization was 31.8 days. Of the 7 patients with CA-MRSA, 4 were male (57%), the mean age was 56.7 years, and the mean length of hospitalization was 12.6 days. For the 5 patients with HCA-MRSA, 4 were male (80%), the mean age was 60.8 years, and the mean length of hospitalization was 49.4 days.

Predisposing factors and associated disease

Twenty eight patients (56%) had events leading to the development of NF. Prior trauma and skin lesions were the most common predisposing factors. Most patients had documented coexisting conditions or risk factors, the most common of which were diabetes mellitus (30 patients) and hypertension (16 patients). Eleven patients had no serious coexisting conditions. None of the patients with CA-MRSA had any serious coexisting conditions, and all patients with HCA-MRSA had underlying chronic disease. Of the 8 patients with MSSA, 6 had underlying chronic diseases.

Site of infection

Sites of NF involvement included a lower extremity in 34 patients (64%), an upper extremity in 7, trunk in 7, head and neck in 2, and Fournier-like gangrene in 2. One patient had involvement of four extremities.

Bacteriology

Among the 53 patients, 95 pathogens were isolated. The number of microbial species isolated in each patient varied from 0 to 8, with a mean of 1.76. Twenty patients (37.7%) were polymicrobial, 26 patients (49.1%) monomicrobial, and 7 patients (13.2%) showed negative results in the culture specimens. Mixed aerobic and anaerobic infections were recovered in 6 patients (11.3%).

S. aureus

Twelve patients had infections of MRSA and 8 had MSSA. The annual incidence of MRSA NF was one of 4 in 2001, one of 6 in 2002, two of 11 in 2003, four of 8 in 2004, and four of 24 in 2005. Wound cultures were monomicrobial for CA-MRSA in 7 patients. All CA-MRSA isolates were susceptible to ciprofloxacin, trimethoprim-sulfamethoxazole, and vancomycin (Table 3).

Management and outcomes

All patients were treated with initial surgical debridement, parenteral antibiotics, and repeated debridement as necessary. The most commonly used antibiotic regimen was a combination of oxacillin, clindamycin, and gentamicin. The median number of surgeries was 2.76 per patient (range, 1-9). Multiple surgical debridements were required in 40 patients (78%). Five patients required amputation. Two patients had an above knee amputation and 3 patients had a below knee amputation. Eight patients (16%) died of causes directly attributable to NF.

Of the 7 patients with CA-MRSA NF, the mean number of surgeries performed was 1.86 per patient (range, 1-3). Four patients initially received in vitro active therapy — 1 patient received gentamicin for 4 days, then was shifted to oral ciprofloxacin; and 3 patients were prescribed vancomycin for 5 days, and then shifted to oral ciprofloxacin after discharge. Three patients received initial inactive therapy with oxacillin for 3-4 days. Two patients were shifted to vancomycin after obtaining wound culture results while 1 patient was shifted to teicoplanin. Blood cultures were all negative and all 7 patients survived.

Of the five patients with HCA-MRSA NF, the mean number of surgeries was 10.2 per patient (range, 1-41). Of the 8 patients with MSSA NF, the mean number of surgeries was 3.38 per patient (range, 1-8). The clinical characteristics, treatment, and outcome of patients with CA-MRSA, HCA-MRSA, and MSSA NF are summarized in Table 2.

Discussion

CA-MRSA has become increasingly endemic in many parts of the world, including Taiwan. What is more, the rapid increase in reports of CA-MRSA outbreaks in young, healthy populations with no apparent risk factors for infection is alarming. Two main types of MRSA now circulate in the community: 1) hospital strains that have spread to the community and are infecting patients with risk factors, referred to as HCA-MRSA; and 2) strains arising de novo in the community and infecting patients with no established risk factors; these are the true CA-MRSA [13,14].

Table 2. Characteristics of patients with community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), health care-

Patient	Gender/age (years)	Duration of hospitalization (days)	Duration of symptoms before (days)	Site of infection	Antibiotic use within past 12 months	Hospitalization within past 24 months
CA-MRSA						
1	F/55	13	7	Back	–	–
2	F/66	11	7	Right buttock	–	–
3	F/70	26	20	Anterior chest wall	–	–
4	M/35	8	7	Left foot	–	–
5	M/52	10	5	Right knee	–	–
6	M/57	6	5	Right hand 3rd web space	–	–
7	M/62	14	7	Left foot	–	–
HCA-MRSA						
8	F/53	10	7	Left hand	+	–
9	M/42	86	7	Right hip	+	+
10	M/67	25	7	Right thigh	+	+
11	M/71	74	7	Left lower leg	–	–
12	M/72	52	3	Left foot	+	+
MSSA						
13	F/59	37	2	Back	–	–
14	M/34	21	5	Left gluteal region	+	+
15	M/42	57	3	Right foot	+	+
16	M/46	29	10	Right lower leg	+	+
17	M/50	7	5	Back	–	–
18	M/51	19	5	Left upper limb	+	+
19	M/53	27	7	Right thigh	+	+
20	M/56	57	14	Four limbs	–	–

Abbreviations: F = female; M = male; – = no; + = yes; DM = diabetes mellitus; CAD = coronary artery disease; AK = above knee

CA-MRSA has been recognized as a novel pathogen genetically different from nosocomial MRSA [15]. Community-acquired strains are characterized by limited antibiotic resistance, and with cellulitis and abscess as the major clinical manifestations. Most infections are located on the extremities, but may involve other sites as well [16-18]. They have a common pulsed-field gel electrophoresis pattern, which is distinct from the major pandemic clones of hospital-acquired isolates [19]. MRSA isolates carry the methicillin resistance gene (*mecA*) on a horizontally transferred genetic element called the staphylococcal chromosome cassette *mec* (SCC*mec*). CA-MRSA isolates usually carry SCC*mec* type IV. SCC*mec* VT is a novel SCC*mec* variant that is found in multiply resistant CA-MRSA strains with the sequence type 59 in Taipei in association with the Panton-Valentine leukocidin genes [20]. Panton-Valentine leukocidin, a synergohymenotropic cytotoxin, is associated with furunculosis, severe necrotizing hemorrhagic pneumonia, NF, and other lesions involving

Table 3. Susceptibility rates of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA), health care-associated MRSA (HCA-MRSA), and methicillin-sensitive *S. aureus* (MSSA) isolates to antimicrobial agents, 2001-2005

Antimicrobial susceptibility	No. of susceptible isolates/total no. (%)		
	CA-MRSA (n = 7)	HCA-MRSA (n = 5)	MSSA (n = 8)
Penicillin G	0 (0.0)	0 (0.0)	0 (0.0)
Erythromycin	1 (14.3)	0 (0.0)	5 (62.5)
Oxacillin	0 (0.0)	0 (0.0)	8 (100.0)
Clindamycin	1 (14.3)	0 (0.0)	8 (100.0)
Gentamicin	6 (86.0)	0 (0.0)	8 (100.0)
Vancomycin	7 (100.0)	5 (100.0)	8 (100.0)
Ciprofloxacin	7 (100.0)	1 (20.0)	8 (100.0)
Trimethoprim-sulfamethoxazole	7 (100.0)	2 (40.0)	8 (100.0)

associated MRSA (HCA-MRSA), and methicillin-sensitive *S. aureus* (MSSA) necrotizing fasciitis

Coexisting conditions	Bacteremia	Initial antimicrobial therapy	Definitive antimicrobial therapy	No. of surgical procedures	Outcome
–	–	Oxacillin	Vancomycin	1	Survived
–	–	Vancomycin	Ciprofloxacin	2	Survived
–	–	Oxacillin	Vancomycin	3	Survived
–	–	Gentamicin	Ciprofloxacin	1	Survived
–	–	Vancomycin	Ciprofloxacin	2	Survived
–	–	Vancomycin	Ciprofloxacin	1	Survived
–	–	Oxacillin	Teicoplanin	3	Survived
DM	–	Vancomycin	Vancomycin	4	Survived
DM	–	Oxacillin	Teicoplanin	41	Survived
Malignancy	–	Vancomycin	Vancomycin	3	Survived
DM	–	Oxacillin	Teicoplanin	1 (AK amputation)	Survived
DM, CAD	–	Oxacillin	Vancomycin	2	Survived
DM	+	Ceftriaxone	Oxacillin	1	Survived
DM	–	Cefazolin	Ciprofloxacin	2	Survived
DM	–	Oxacillin	Oxacillin	6	Survived
–	+	Vancomycin/cefpirome	Oxacillin/gentamicin	2	Survived
DM	–	Penicillin G	Oxacillin	3	Expired
DM	+	Flomoxef	Oxacillin	2	Expired
DM	–	Oxacillin	Oxacillin	3	Survived
–	+	Ceftriaxone/penicillin G	Oxacillin	8	Survived

the skin or mucosa in both CA-MRSA and CA-MSSA strains [21,22].

In this study, 58% of the MRSA isolates collected as part of the retrospective population-based surveillance were not associated with traditional risk factors and were classified as CA-MRSA. Most of these isolates were associated with clinically relevant infections that required treatment. There were substantial common factors among our CA-MRSA cases. Firstly, it was surprising that all patients survived, since the typical mortality rate of NF has been reported to be about 33% in Los Angeles [10]. The absence of death in our series suggested that NF caused by CA-MRSA may be less virulent than that caused by other organisms.

S. aureus has also been isolated from patients with NF, usually as part of a mixed flora. Because NF caused by CA-MRSA is an emerging clinical syndrome, clinicians should now consider MRSA as a potential pathogen in patients with suspected *S. aureus* infections in the community setting [23-25]. The retrospective design of this study, using chart reviews, is also a limitation that might have resulted in an inability to confirm whether cases had no previous medical events associated with health care facilities in the year before the *S. aureus* infection. However, the antibiograms for our CA-MRSA isolates from patients without identifiable risk factors are clearly different from those for the analogous HCA-MRSA isolates. Clinicians should obtain appropriate material for bacterial culture; follow-up on the results of susceptibility testing of all *S. aureus* isolates, since by definition MRSA organisms are not susceptible to beta-lactam antibiotics; and recommend surgical drainage of infections when feasible [26]. The selection of appropriate antimicrobial agents for any suspected *S. aureus* infections of skin and soft tissue in patients in the community must now take into account the emergence of CA-MRSA and their varied antibiotic susceptibilities in different countries or areas.

The major difference in the antibiotic susceptibility patterns found by this study and others is that erythromycin and clindamycin resistance were extraordinarily high in our CA-MRSA isolates [15,27-29]. Although most CA-MRSA isolates were susceptible to several antimicrobial agents, selection of alternative agents must remain dependent on local susceptibility patterns. Clinicians should remain aware that

beta-lactam antimicrobials can no longer be relied on as empirical therapies for invasive CA-MRSA infections, and the treatment of non-invasive CA-MRSA infections should not routinely require the use of glycopeptides [23,30,31].

In conclusion, in *S. aureus* NF patients with risk factors (diabetes mellitus, hypertension, and chronic pulmonary disease) for harboring resistant strains, glycopeptides should be used empirically [32]. For Taiwanese patients with suspected mild MRSA infections, such as soft tissue infection, who lack these risk factors, antibiotics other than beta-lactams (e.g., clindamycin, gentamicin, ciprofloxacin or timethoprim-sulfamethoxazole) may be used empirically while awaiting the culture report. Identifying potential risk factors for CA-MRSA acquisition and fully characterizing the epidemiologic, clinical, and molecular properties of these strains are necessary for providing effective therapeutic guidelines. In the meantime, other interventions and the promotion of appropriate use of antimicrobial agents in communities need to be pursued.

References

1. Dryla A, Prustomersky S, Gelbmann D, Hanner M, Bettinger E, Kocsis B, et al. Comparison of antibody repertoires against *Staphylococcus aureus* in healthy individuals and in acutely infected patients. Clin Diagn Lab Immunol. 2005;12: 387-98.
2. Campbell KM, Vaughn AF, Russell KL, Smith B, Jimenez DL, Barrozo CP, et al. Risk factors for community-associated methicillin-resistant *Staphylococcus aureus* infections in an outbreak of disease among military trainees in San Diego, California, in 2002. J Clin Microbiol. 2004;42:4050-3.
3. Chen ML, Chang SC, Pan HJ, Hsueh PR, Yang LS, Ho SW, et al. Longitudinal analysis of methicillin-resistant *Staphylococcus aureus* isolates at a teaching hospital in Taiwan. J Formos Med Assoc. 1999;98:426-32.
4. Wang JT, Chen YC, Yang TL, Chang SC. Molecular epidemiology and antimicrobial susceptibility of methicillin-resistant *Staphylococcus aureus* in Taiwan. Diagn Microbiol Infect Dis. 2002;42:199-203.
5. Hsueh PR, Liu CY, Luh KT. Current status of antimicrobial resistance in Taiwan. Emerg Infect Dis. 2002;8:132-7.
6. Lin JC, Yeh KM, Peng MY, Chang FY. Community-acquired methicillin-resistant *Staphylococcus aureus* bacteremia in Taiwan: risk factors for acquisition, clinical features and outcome. J Microbiol Immunol Infect. 2004;37:24-8.
7. Wilson B. Necrotizing fasciitis. Am Surg. 1952;18:416-31.
8. Swartz MN, Pasternack MS. Cellulitis section of cellulitis and subcutaneous tissue infections. In: Mandell GL, Bennett JE, Dolin R, eds. Principles and practice of infectious diseases. 6th ed. Philadelphia: Elsevier Churchill Livingstone; 2005: 1172-94.
9. Moran GJ, Amii RN, Abrahamian FM, Talan DA. Methicillin-resistant *Staphylococcus aureus* in community-acquired skin infections. Emerg Infect Dis. 2005;11:928-30.
10. Miller LG, Perdreau-Remington F, Rieg G, Mehdi S, Perlroth J, Bayer AS, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. N Engl J Med. 2005;352:1445-53.
11. Kiehlbauch JA, Hannett GE, Salfinger M, Archinal W, Monserrat C, Carlyn C. Use of the National Committee for Clinical Laboratory Standards guidelines for disk diffusion susceptibility testing in New York state laboratories. J Clin Microbiol. 2000;38:3341-8.
12. Maltezou HC, Giamarellou H. Community-associated methicillin-resistant *Staphylococcus aureus* infections. Int J Antimicrob Agents. 2006;27:87-96.
13. Chambers HF. Community-associated MRSA-resistance and virulence converge. N Engl J Med. 2005;352;1485-7.
14. Del Giudice P, Blanc V, Durupt F, Bes M, Martinez JP, Counillon E, et al. Emergence of two populations of methicillin-resistant *Staphylococcus aureus* with distinct epidemiological, clinical and biological features, isolated from patients with community-acquired skin infections. Br J Dermatol. 2006;154: 118-24.
15. Herold BC, Immergluck LC, Maranan MC, Lauderdale DS, Gaskin RE, Boyle-Vavra S, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. JAMA. 1998;279:593-8.
16. Zinderman CE, Conner B, Malakooti MA, LaMar JE, Armstrong A, Bohnker BK. Community-acquired methicillin-resistant *Staphylococcus aureus* among military recruits. Emerg Infect Dis. 2004;10:941-4.
17. Nguyen DM, Mascola L, Brancoft E. Recurring methicillin-resistant *Staphylococcus aureus* infections in a football team. Emerg Infect Dis. 2005;11:526-32.
18. Lindenmayer JM, Schoenfeld S, O'Grady R, Carney JK. Methicillin-resistant *Staphylococcus aureus* in a high school wrestling team and the surrounding community. Arch Intern Med. 1998;158:895-9.
19. Chen CJ, Huang YC. Community-acquired methicillin-resistant *Staphylococcus aureus* in Taiwan. J Microbiol Immunol Infect. 2005;38:376-82.
20. Boyle-Vavra S, Ereshefsky B, Wang CC, Daum RS. Successful multiresistant community-associated methicillin-resistant Staphylococcus aureus lineage from Taipei, Taiwan, that carries either the novel staphylococcal chromosome cassette *mec* (SCC*mec*) type VT or SCC*mec* type IV. J Clin Microbiol. 2005; 43:4719-30.

21. Gillet Y, Issartel B, Vanhems P, Fournet JC, Lina G, Bes M, et al. Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. Lancet. 2002;359:753-9.
22. Lina G, Piémont Y, Godail-Gamot F, Bes M, Peter MO, Gauduchon V, et al. Involvement of Panton-Valentine leukocidin producing *Staphylococcus aureus* in primary skin infections and pneumonia. Clin Infect Dis. 1999;29:1128-32.
23. Naimi TS, LeDell KH, Como-Sabetti K, Borchardt SM, Boxrud DJ, Etienne J, et al. Comparison of community- and health care-associated methicillin-resistant *Staphylococcus aureus* infection. JAMA. 2003;290:2976-84.
24. Buck JM, Como-Sabetti K, Harriman KH, Danila RN, Boxrud DJ, Glennen A, et al. Community-associated methicillin-resistant *Staphylococcus aureus*, Minnesota, 2000-2003. Emerg Infect Dis. 2005;11:1532-8.
25. Morrison MA, Hageman JC, Klevens RM. Case definition for community-associated methicillin-resistant *Staphylococcus aureus*. J Hosp Infect. 2006;62:241.
26. Fridkin SK, Hageman JC, Morrison M, Sanza LT, Como-Sabetti K, Jernigan JA, et al. Methicillin-resistant *Staphylococcus aureus* disease in three communities. N Engl J Med. 2005;352:1436-44. Erratum in: N Engl J Med. 2005; 352:2362.
27. Wang CC, Lo WT, Chu ML, Siu LK. Epidemiological typing of community-acquired methicillin-resistant *Staphylococcus aureus* isolates from children in Taiwan. Clin Infect Dis. 2004; 39:481-7.
28. Gorak EJ, Yamada SM, Brown JD. Community-acquired methicillin-resistant *Staphylococcus aureus* in hospitalized adults and children without known risk factors. Clin Infect Dis. 1999;29:797-800.
29. Charles PG, Ward PB, Johnson PD, Howden BP, Grayson ML. Clinical features associated with bacteremia due to heterogeneous vancomycin-intermediate *Staphylococcus aureus*. Clin Infect Dis. 2004;38:448-51.
30. Diederen BM, Kluytmans JA. The emergence of infections with community-associated methicillin resistant *Staphylococcus aureus*. J Infect. 2006;52:157-68.
31. Chi CY, Wong WW, Fung CP, Yu KW, Liu CY. Epidemiology of community-acquired *Staphylococcus aureus* bacteremia. J Microbiol Immunol Infect. 2004;37:16-23.
32. Rybak MJ, LaPlante KL. Community-associated methicillin-resistant *Staphylococcus aureus*: a review. Pharmacotherapy. 2005;25:74-85.

