USA300 Genotype Community-Associated Methicillin-Resistant *Staphylococcus aureus* as a Cause of Surgical Site Infections[▽]

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Received 30 April 2007/Returned for modification 11 June 2007/Accepted 24 July 2007

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) strains are increasingly recovered from nosocomial settings. We conducted a retrospective study of surgical site infections (SSI) during 2004 and 2005 to determine the prevalence of CA-MRSA; 57% of MRSA strains tested belonged to the USA300 genotype. CA-MRSA has become a prominent cause of SSI at our institution.

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) strains have become endemic in many communities in North America. Characteristics of most CA-MRSA strains include the presence of a type IV staphylococcal chromosome cassette *mecA* (SCC*mecA*) and Panton-Valentine leukocidin (PVL) genes. Initial reports focused on infections in patients without traditional health care exposures. Increasing reports now indicate that CA-MRSA, particularly the USA300 genotype, is being recovered from the nosocomial setting (3, 7, 10–13). The proportion of surgical site infections (SSI) due to MRSA at our institution increased from 17% to 24.5% between 2001 and 2005. We hypothesized that the rise may have been due to infections caused by CA-MRSA and conducted a retrospective study to describe the prevalence of CA-MRSA as a cause of SSI.

(This work was presented in part at the 46th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, CA, 27 to 30 September 2006 [7a].)

Active surveillance for SSI at University Hospital, a tertiary-care hospital with approximately 1,000 beds, is conducted by the University of Alabama at Birmingham (UAB) Infection Control Service (ICS) using definitions established by the Centers for Disease Control and Prevention (5). We reviewed UAB ICS data from 2004 to 2005 for all SSI due to MRSA and retrieved the corresponding bacterial isolates, when available, that had been frozen and stored at minus 80°C. Bacteria were identified and antibiotic susceptibilities were determined by broth microdilution using MicroScan Walkaway (Dade MicroScan, West Sacramento, CA) and LabPro software, version 1.6 or 1.61 in 2004 and version 2.0 in 2005, and interpreted in accordance with Clinical and Laboratory Standards Institute guidelines (1).

Medical records for patients for whom a bacterial isolate was available were reviewed for demographic information, surgical

antibiotic chemoprophylaxis, and hospitalization. Prior health care exposure was defined as hospitalization, residence in a long-term health care facility, or dialysis in the previous year.

Among MRSA isolates, the SCC*mec* type was determined using PCR (9). Detection of the PVL gene was performed by real-time PCR with Lightcycler 2.0 and Lightcycler software (Roche Diagnostics, Indianapolis, IN) (6). We used *S. aureus* ATCC 49775 as a PVL-positive *S. aureus* control strain and a PVL-deficient *S. aureus* strain donated by F. Perdreau-Remington as a negative control. Molecular typing of isolates was performed by pulsed-field gel electrophoresis (PFGE) using SmaI restriction endonuclease (8). Ethidium bromide-stained gels were digitized using a GelDoc2000 (Bio-Rad, Hercules, CA) and analyzed using Bionumerics, version 4.05 (Applied Maths, Austin, TX). Dendrograms were produced using the Dice similarity coefficient and the unweighted pair group method with arithmetic average. Genotypes were assigned by comparison to USA100 to -800 reference strains (8). Strains not matching any of the USA genotypes (<80% similarity) were designated unclassified.

Statistical analyses were performed using software available at www.openepi.com. Bivariate analyses were conducted using the chi-square test or Fisher's exact test, and continuous variables were analyzed using a two-sample independent *t* test. All *P* values presented are two-tailed. This study was approved by the UAB Institutional Review Board.

During the study period 391 SSI were identified; 188 occurred in 2004 and 203 in 2005. Methicillin-susceptible *S. aureus* (MSSA) was responsible for 46 (24.5%) and 37 (18.2%) of SSI in 2004 and 2005, respectively. MRSA was responsible for 55 (22.6%) and 66 (24.5%) of SSI in 2004 and 2005, respectively. Among the 121 MRSA SSI, 46 (35%) nonduplicate bacterial isolates were available for further testing and hereafter represent the population studied. Ten isolates were available from 2004 and 36 from 2005. Type IV SCC*mec* was identified in 29 (63%) isolates, type IVa SCC*mec* in 3 (7%), and type II SCC*mec* in 8 (17%), and 6 (13%) isolates had an undetermined SCC*mec* type. The PVL gene was detected in 27 (93%) of 29 type IV SCC*mec* isolates, 1 (33%) of 3 type IVa SCC*mec* isolates, and 0 of 14 type II or undetermined SCC*mec* isolates. All type II and IVa SCC*mec* MRSA SSI occurred

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[▽] Published ahead of print on 1 August 2007.

FIG. 1. Number of MRSA isolates tested with known SCCmec types per month, 2004 to 2005.

during 2005; type IV SCCmec MRSA SSI occurred throughout the study period (Fig. 1). PFGE genotypes present among the 46 isolates were USA300 in 26 (57%) and USA100 in 11 (24%), and unique patterns were present in 9 (19%).

No significant differences were noted between patients with USA300 and non-USA300 MRSA with regard to age, gender, race, or type of surgery (Table 1). Orthopedic surgery and neurosurgery were the most common types of surgery associated with infection. Patients with USA300 SSI had a shorter initial hospitalization (10.8 days versus 16.2 days; $P = 0.047$). The numbers of patients with same-day surgery or prior health care exposures were not significantly different between the two groups.

Surgical antibiotic prophylaxis records were available for 42 patients. Cefazolin was used alone in 22 patients or in combination with piperacillin-tazobactam (2 patients), ticarcillin-clavulanic acid (1 patient), azithromycin (1 patient), and metronidazole (1 patient). Four patients received vancomycin in combination with cefazolin (one patient), gentamicin (one patient), or ceftazidime (two patients). Other regimens included piperacillin-tazobactam (four patients), piperacillin-tazobactam and cephalexin (one patient), clindamycin (one patient), cefotaxime (one patient), cefotaxime and metronidazole (one patient), and ciprofloxacin and metronidazole (one patient). No chemoprophylaxis was used in two cases.

The emergence of CA-MRSA as a nosocomial pathogen has been noted in a variety of clinical settings, including a single report of postsurgical infection (7). The proportion of SSI due to CA-MRSA in this study was unexpectedly high. Though this study is small and only a subset of isolates from SSI were available for testing, the data suggest that USA300 CA-MRSA is an important cause of SSI at our institution. CA-MRSA strains were previously uncommon, with fewer than 2% of MRSA isolates found to be USA300 in a survey from 2000 (unpublished data). To our knowledge, this is the largest study describing the role of USA300 genotype CA-MRSA in SSI. Given its propensity for causing soft-tissue infections, CA-MRSA seems well suited to causing SSI. While the pathogenicity has not been fully elucidated, it is clear that CA-MRSA strains are associated with the development of both soft-tissue and disseminated infections. The role of PVL as a virulence factor remains unclear, and it may not be the single factor responsible for the pathogenicity of CA-MRSA (15).

Surgical chemoprophylaxis active against MRSA was noted in only four patients in this study. These data do not provide evidence that current antibiotic prophylaxis protocols are in-

effective but rather that the epidemiology of MRSA in our medical center is dynamic and active reevaluation of the optimum antibiotic prophylaxis should be considered if further studies indicate a growing risk for SSI due to CA-MRSA.

There are several limitations in this study. First, this is a small retrospective study. Not all MRSA isolates were available from patients with SSI. Moreover, some of the isolates retrieved from early 2004 were part of other MRSA studies that stored only erythromycin-resistant, clindamycin-susceptible isolates, a phenotype that is biased toward CA-MRSA strains. However, all MRSA isolates, regardless of phenotype, were collected after August 2004, thus limiting the subsequent bias. Also, the timing and duration of surgical antibiotic prophylaxis could impact development of SSI. We did not study this aspect of the patients' care and the differences between CA-MRSA- and non-CA-MRSA-infected patients that may be present. The source of the CA-MRSA was not investigated specifically in this study. Nosocomial sources should also be considered, though in this study, MRSA SSI were not restricted to a single type of surgery, surgeon, or hospital ward (data not shown), reducing the likelihood of single-source nosocomial acquisition. Many patients with CA-MRSA SSI underwent same-day surgery, suggesting that these patients were colonized with CA-MRSA prior to their surgery.

Previous studies indicate that asymptomatic colonization with *S. aureus* is a risk factor for subsequent infection with the colonizing strain, though no similar data exist for CA-MRSA (2, 14). One study suggested that colonization with CA-MRSA may represent a greater risk for infection than colonization with MSSA (4). Whether CA-MRSA colonization presents a greater risk for postoperative infection than colonization with traditional nosocomial strains of MRSA or MSSA remains unanswered.

In summary, we found that CA-MRSA strains were responsible for a significant proportion of the SSI at our institution. Further studies should be performed to determine the role of colonization with CA-MRSA as a risk factor for subsequent

TABLE 1. Patient characteristics based on PFGE genotype

Parameter	Value for:			<i>P</i>
	All cases (<i>n</i> = 46)	USA300 (<i>n</i> = 26)	Non-USA300 (<i>n</i> = 20)	
Mean age (yr) (range)	47.7	42.6 (18–76)	54.3 (23–85)	0.61
No. Caucasian (%)	34 (74)	19 (73)	15 (75)	0.88
% Male	54.3	53.8	55.5	0.94
Type of surgery				
Orthopedic	25	15	10	0.60
Neurosurgery	6	4	2	0.94
CABG ^a	3	0	3	0.15
Vascular	5	3	2	0.99
Abdominal	3	1	2	0.80
OB/GYN ^b	2	1	1	0.99
Other	2	2	0	0.63
No. with same-day surgery (%)	26 (57)	17 (65)	9 (45)	0.17
No. with prior health care exposure (%)	21 (46)	15 (58)	6 (30)	0.06
Mean duration of hospitalization ^c (days)	13.2	10.8	16.2	0.047

^a CABG, coronary artery bypass grafting.

^b OB/GYN, obstetrics/gynecology.

^c Duration of the initial hospitalization at time of the surgery.

infection and the role of decolonization strategies in preventing infections in surgical patients.

We are grateful to Hermínia de Lencastre for the kind gift of SCCmecA control strains and Francoise Perdreau-Remington for the kind gift of a PVL-negative control strain. We also thank Jennifer Whiddon for technical assistance.

This work was supported by grants from the University of Alabama at Birmingham Health Services Foundation General Endowment Fund and bacterial pathogenesis postdoctoral fellowship T32AI07041 (for M.P.). The PFGE reference strain isolates were obtained through the Network on Antimicrobial Resistance in *Staphylococcus aureus* program, supported under NIAID, NIH contract no. N01-A1-95359.

There are no conflicts of interest for any of the authors.

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