



INVESTIGATION OF COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* SKIN INFECTIONS AMONG HIV-POSITIVE MEN WHO HAVE SEX WITH MEN

BACKGROUND

In November 2002, several physicians notified the Los Angeles County Department of Health Services (LACDHS) of approximately 30 cases of skin infections with methicillin-resistant *Staphylococcus aureus* (MRSA) among predominantly HIV-positive men who have sex with men (MSM) in their practices. The physicians noted that the infections were recurrent and difficult to treat, with several patients requiring hospitalization. Most did not have traditional risk factors for nosocomial MRSA—which include history of hospitalization, surgery, dialysis, stay in a skilled nursing home, or presence of an indwelling medical device in the past year. The Cedars-Sinai Medical Center (CSMC) laboratory tested a convenience sample of 10 isolates from the index clinic and found that eight (80%) isolates matched the same pulsed-field gel electrophoresis (PFGE) pattern and that one (10%) isolate differed by only one band, indicating a predominant clonal MRSA strain. The predominant PFGE strain did not match any nosocomial MRSA strains. The number of patients reported by this clinic, anecdotal reports from other local clinics, evidence for a clonal MRSA strain, and lack of nosocomial associations indicated a possible outbreak of community-associated MRSA (CAMRSA) skin infections among HIV-positive MSM. This was the first time this group had been reported with CAMRSA skin infections and it was important to determine if this group had specific outbreak risk factors that could be identified and addressed.

METHODS

Risk Factor Investigation: A matched case-control study was performed to determine risk factors for CAMRSA skin infection among HIV-positive MSM.

Questionnaire Design: The questionnaire included items regarding demographics, close contacts, visits to public places (e.g., fitness gyms), hygiene practices, history of skin lesions, health care and jail exposures, and past medical history including antibiotic use, substance abuse, sex behaviors, and visits to commercial sex venues and group sex (circuit) parties. The chart abstraction form included items regarding clinical presentation, diagnosis, and treatment of MRSA skin lesions, past medical history, immune status, and history of opportunistic infections. Also collected were CD4 and viral load counts dated closest to (either before or after) the initial clinic visit for the case-patient.

Case Definition: For purposes of the case-control study, a case was identified as a person with a community-onset (identified in the outpatient setting or within the first 72 hours of hospital admission) culture-positive MRSA skin infection during September 2002 to May 2003 in an HIV-positive MSM enrolled in continuity care at one of the three participating clinics in LAC.

Case and Control Selection: Healthcare providers from the clinics of three local organizations agreed to participate in the investigation. Recruitment into the study was restricted to HIV-infected patients because recruitment of adequate numbers of HIV-negative cases and controls from these clinics would delay the investigation—the continuity patients in these clinics were predominantly HIV-positive—and because HIV status might confound risk factors of CAMRSA infection. For each case identified, three HIV-positive MSM controls were selected from daily manifests, matched on the same physician, clinic, and day (or week) that the case patient presented with a skin infection subsequently diagnosed as CAMRSA.

Questionnaire Administration and Chart Abstraction: Experienced interviewers from LACDHS were trained to administer the survey. The investigators reviewed medical charts on interviewed patients for additional information. Investigators received consent from the cases and controls before reviewing medical charts.



Data Entry and Analysis: Bivariate analysis on matched cases and controls and logistic regression of multivariate models were employed. Analyses were performed with the SAS statistical software package (version 8.2, SAS Institute, NC). For multivariate analyses, the final model included history of hospitalization, race/ethnicity, and number of sex partners as a categorical variable.

Laboratory Investigation: One isolate taken from a patient included in the case-control analysis was selected to represent the predominant CAMRSA strain among isolates from the index clinic. The representative isolate was sent to the LACDHS Public Health Laboratory and the CDC laboratory and analyzed with PFGE by using *Smal* for comparison with collected outbreak CAMRSA strains.

Molecular and Inducible Resistance Analysis: The CDC laboratory used polymerase chain reaction methods to determine the staphylococcal cassette chromosome methicillin resistance complex (SCC*mec*) and to test for the presence of genes for Panton-Valentine leukocidin (PVL), toxic shock toxin, and staphylococcal enterotoxins (SE) A–E and H. The isolate was evaluated for inducible clindamycin resistance by using the standard disk induction (“D-zone”) test.

RESULTS

Case-Control Study Demographic Characteristics: A total of 35 case-patients and 76 controls completed interviews. Case-patients and controls had similar demographic characteristics, except that case-patients were significantly more likely than controls to be white (cases n=24, 68.6% versus controls n=34, 44.7%, p=.01). Among case-patients compared with controls, median CD4 counts were lower (cases=338 copies/ml versus controls=410 copies/ml) and median viral loads were higher (cases =8,154/mm³ versus controls=594.5), but the differences were not statistically significant.

Clinical Characteristics and Treatment of Cases: Skin lesions were most often diagnosed as abscesses and most often involved the legs, buttocks, and arms. All case isolates with antibiotic sensitivity data available from chart review were resistant to the beta-lactam antibiotics evaluated. Most isolates were resistant to ciprofloxacin and erythromycin; one isolate was intermediately resistant to trimethoprim/sulfamethoxazole. No isolates were reported as resistant to vancomycin, rifampin, or gentamicin. Antibiotics to which the isolates were commonly resistant (i.e., amoxicillin, amoxicillin/clavulanate, cephalexin, ciprofloxacin, clarithromycin, and dicloxacillin) were used as initial treatment among 13 of the 31 patients (42%) for which we have initial treatment information.

Matched Case-Control Analysis: Exposures that remained significant in multivariate analysis included public hot tub or sauna use and methamphetamine use (Table 1). Exposures with significant negative associations to infection included always using a condom during sex and prophylaxis for opportunistic infections. Exposures that were significant in multivariate but not bivariate analysis included having a sex partner with a skin infection. When hospitalized patients were excluded in the multivariate analysis, similar results were found.

Table 1. Results of multivariate analysis in a case-control study of CAMRSA skin infections among HIV-positive MSM

Exposures During the Past 3 Months	Adjusted Matched		
	OR*	(95% CI)	χ^2 p-value
Sex partner with skin infection	9.2	(1.4–61.5)	.022
Methamphetamine use	8.5	(1.6–45.1)	.012
Routinely used a public hot tub or sauna	3.9	(1.2–12.6)	.023
History of antibiotic prophylaxis for opportunistic infection, self-reported or on medical record	0.3	(0.1–1.0)	.042
Always used a condom during sex (among sexually active)	0.1	(0.0–0.6)	.019

* Controlling for history of hospitalization during the past 12 months, race/ethnicity, and number of sex partners (as a categorical variable during the past 3 months).



Laboratory Investigation: The LACDHS Public Health Laboratory determined that an isolate representing the predominant strain from the index clinic matched the PFGE pattern of previously collected outbreak strains of CAMRSA in LAC. The PFGE pattern of the isolates also matched a predominant CAMRSA strain, USA300, which has been identified in several outbreaks nationwide. The CDC laboratory identified genes for PVL and SCC*mec* complex, type IVa. The isolate was clindamycin-susceptible and erythromycin-resistant and did not exhibit inducible clindamycin resistance.

DISCUSSION

We found that close contact, such as intimate sexual contact, with a person infected with an MRSA skin infection might be a risk factor for MRSA skin infection. Drainage from MRSA skin lesions can be very infectious. MSM with high-risk sex and drug use behaviors might be more likely to have unprotected skin-to-skin contact with persons with MRSA skin lesions. Our identification of an association between MRSA skin infection and use of steam baths or saunas further supports the possibility of contact transmission of MRSA, either by direct skin-to-skin contact or via an environmental source, further facilitated by skin macerated during prolonged exposure to moisture and heat. Other researchers have found that a wood sauna bench was a likely source of *S. aureus* transmission in an outbreak of boils in an Alaskan village (*West J Med*, 2000; 172(4):2359).

The findings of our investigation indicate that CAMRSA is an important causative organism of soft tissue infections among HIV-positive MSM, sometimes resulting in hospitalizations and surgical interventions. In addition, a large proportion of the case-patients in this study were initially treated with antibiotics that CAMRSA has been predominantly resistant to, highlighting the need for a high index of suspicion among high-risk patients in order to facilitate early and appropriate diagnosis. Furthermore, the laboratory investigation identified a predominant clonal strain of CA-MRSA, USA300, which is common to outbreaks in LAC and elsewhere in the US.

Our risk factor investigation is subject to following limitations. First, our case-control study did not have the power to implicate specific behaviors or a point source of infection. However, surveillance from both County and national sources suggest an increase in MRSA infections in the overall population that is not likely to be explained by a point source. Second, the analysis relied on recall of exposures from patients and medical charts. Case-patients might be more likely to recall certain exposures, especially in the setting of media reports and increased community awareness of MRSA skin infections. Third, we did not collect specific data on income or education from persons interviewed. Cases and controls were similar in the proportion of age, racial/ethnic group, and health insurance status. However, persons with high-risk sex behaviors or drug use might represent a more marginalized population at higher risk of MRSA skin infections due to exposures not accounted for in this study.

Control Measures: In parallel with our investigation, we instituted measures to help prevent and control CAMRSA skin infections, as well as to inform healthcare providers and the public. The following are some of the measures taken. First, we developed patient and healthcare provider guidelines on CAMRSA skin infections, links to relevant internet sites and posted them on a dedicated web page on the LACDHS website (www.lapublichealth.org/acd/MRSA.htm) and made them available on the LACDHS website. Healthcare provider fact sheets were faxed to healthcare providers, HIV community-based organizations, clinics, and hospitals throughout LAC.

We also notified the local and national medical community about CAMRSA in MSM by posting articles in *The Public's Health* (an LAC Department of Health Services publication), Epi-X (a national public health web site), the National Association of County and City Health Officers, and the Infectious Diseases Association of California Listserv. We made local presentations about CAMRSA to healthcare provider groups, especially those concerned with HIV/AIDS, and made regional and national presentations on risk factors for CAMRSA in MSM. We provided an oral presentation and health education materials to managers of commercial sex venues regarding hygiene measures to control MRSA in the environment. With assistance from CDC, we have developed guidelines for preventing the spread of MRSA in public venues—these can be found on the LACDHS website at: www.lapublichealth.org/acd/MRSA.htm.



Final Recommendations: MRSA in the community is an emerging disease in both the MSM and general population, and at both the local and national levels; control and improved understanding of this disease will require continued local participation in the national response. The findings of this investigation support the initial recommendations and advice outlined in our original patient and healthcare provider fact sheets. These recommendations are summarized below.

First, clinicians must recognize CAMRSA as a cause of skin and soft tissue infections. Incision, drainage, and local care remain first-line treatments for soft tissue infections, when appropriate. Wound culture can guide the selection of appropriate antibiotics when necessary. Patients should be encouraged to complete prescribed courses of antibiotics, or return to the healthcare provider if the infection does not resolve as expected. Patients with MRSA should be educated in proper hygiene and wound care to prevent transmission to close contacts. Additionally, healthcare providers can take measures to prevent the spread of MRSA in the healthcare setting.

Managers and owners of public venues such as fitness gyms, sex clubs, and bathhouses should be aware of measures to prevent the spread of MRSA among patrons by direct and indirect contact. For example, steam bath users should be directed not to share towels and to place a clean towel between their skin and steam bath surfaces. Patrons should be directed to carefully cover any skin lesions and dispose of used dressings properly.

Individuals can help protect themselves by maintaining personal hygiene and handwashing with soap, especially before and after going to places where bare skin can contact public surfaces or other people. Use of a barrier, such as a towel, over public surfaces might be useful. Also, we encourage individuals to be aware of other people that they have close contact with. Persons should seek the advice of a healthcare provider immediately for any suspicious lesions.