Clinical characteristics and outcomes of community-acquired methicillin-resistant *Staphylococcus aureus* septic arthritis

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ABSTRACT

Objective: *We investigated the clinical characteristics, treatment patterns and outcomes of community-acquired methicillin resistant* Staphylococcus aureus *(CA-MRSA) septic arthritis.*

Methods: *This was a retrospective chart review of CA-MRSA septic arthritis in a tertiary care hospital from 2000-2013. We compared CA-MRSA septic arthritis cases with HA-MRSA septic arthritis cases to identify important differences between the two groups.*

Results: *We identified 11 cases of CA-MRSA septic arthritis and 34 cases of hospital-acquired methicillin-resistant SA (HA-MRSA) septic arthritis. Community-acquired methicillin-resistant* Staphylococcus aureus *caused 25% of the MRSA septic arthritis cases. Community-acquired methicillin-resistant* Staphylococcus aureus *septic arthritis occurred in younger patients with fewer comorbidities or risk factors. There was no difference in initial presentation between CA-MRSA and HA-MRSA. Community-acquired methicillin-resistant* Staphylococcus aureus *patients were less likely to be treated with appropriate antibiotics initially. Community-acquired methicillin-resistant* Staphylococcus aureus *septic arthritis was associated with increased morbidity with a high percentage of patients developing poor joint outcomes or osteomyelitis complications. Community-acquired methicillin-resistant* Staphylococcus aureus *septic arthritis was also associated with increased utilization of health care resources due to long hospital stays, high readmissions rates, and increased requirements for rehabilitation facility placement and home health support. There was no difference in mortality, poor joint outcome, readmissions, and osteomyelitis complications between CA-MRSA septic arthritis and HA-MRSA septic arthritis.*

Conclusions: *Community-acquired methicillin-resistant* Staphylococcus aureus *septic arthritis is associated with increased morbidity and health care resource utilization. Increased awareness into CA-MRSA as a cause of septic arthritis in younger patients with no risk factors is important, especially when considering empiric treatment.*

Keywords: *Staphylococcus aureus*, methicillin resistance, septic arthritis, community–acquired, hospital-acquired

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Introduction

The incidence of community-acquired methicillin resistant *Staphylococcus aureus* (CA-MRSA) infections is increasing.[1] In infections, such as skin and soft tissue infections and pneumonia, CA-MRSA causes 12-44.9% of MRSA infections.[2,3] To our knowledge no previous studies have focused on CA-MRSA septic arthritis, and the prevalence of CA-MRSA in MRSA septic arthritis is unknown. The clinical characteristics, treatment patterns, and outcomes of CA-MRSA septic arthritis remain poorly characterized.

We undertook this study to better understand the clinical and laboratory features, treatment patterns, and outcomes of CA-MRSA native joint septic arthritis. This was a retrospective chart review of CA-MRSA native joint septic arthritis cases admitted to a single hospital from 2000-2013. We reviewed the clinical characteristics of CA-MRSA cases and compared CA-MRSA septic arthritis cases with hospital-acquired methicillin-resistant *Staphylococcus aureus* (HA-MRSA) septic arthritis cases to identify key differences between the two groups.

Methods

We screened patients admitted to University Medical Center (a 410-bed tertiary care hospital in Lubbock, Texas) from January 1, 2000, to December 31, 2013, for the ICD-9 discharge diagnosis of pyogenic arthritis. We reviewed patient charts and included cases that met the definition of septic arthritis, defined by: (1) positive synovial fluid cultures, or (2) a clinically infected joint with positive blood cultures and negative synovial fluid cultures, or (3) pus obtained from the joint but joint culture sterile due to prior administration of antibiotics, or (4) definite radiological or postmortem diagnosis of septic arthritis. We excluded septic joint infections involving prosthetic joints.

From cases of septic arthritis that met inclusion criteria, we identified the *Staphylococcus aureus* cases. We then identified MRSA cases and classified them into CA-MRSA or HA-MRSA. Community-acquired methicillin-resistant *Staphylococcus aureus* was defined using definitions of the Centers for Disease Control: Any MRSA infection diagnosed in an outpatient or within 48 hours of hospitalization if the patient lacks the following health care-associated MRSA risk factors: hemodialysis, surgery, residence in long-term care facility or hospitalization during the previous year, the presence of an indwelling catheter or a percutaneous device at the time of culture.[4] Cases of MRSA septic arthritis that did not meet criteria for CA-MRSA were grouped as HA-MRSA.

We extracted information on patient demographics, clinical characteristics, treatment patterns and outcomes. Poor joint outcome was defined by the following: (1) greater than 10% reduction in range of motion compared to premorbid state, (2) infections resulting in a chronically draining abscess, (3) arthrodesis, (4) amputation, (5) severe chronic articular pain or an unstable irritable joint, and/or (6) recurrent joint infection with the same organism. The data were summarized, and comparisons were made using Student's t-test, Fisher's exact test, and Pearson's chi-square test. We performed statistical analysis using Statistical Package for the Social Sciences (SPSS) software version 21. The Institutional Review Board at Texas Tech University Health Sciences Center approved this study.

Results

From January 1, 2000, to Dec 31, 2013, there were 492 cases of pyogenic arthritis. Two hundred and seventy-five cases met inclusion criteria; 122 cases were due to *Staphylococcus aureus.* Forty-five patients had MRSA native joint septic arthritis. We classified 11 cases as CA-MRSA and 34 cases as HA-MRSA. Table 1 summarizes the patient demographics and clinical profile for CA-MRSA septic arthritis cases. Community-acquired methicillin-resistant *Staphylococcus aureus* occurred in men and women almost equally. The mean age of CA-MRSA patients was 24.4 years. The CA-MRSA group included six children aged 18 or less and five adults. Excluding the children in the series, the mean age of the adults was 43.8 years. The CA-MRSA patients had fewer comorbidities, and 63.6% had no host risk factors. In comparison to CA-MRSA cases, HA-MRSA cases

Table 1. Patient demographics, clinical profile of CA-MRSA and HA-MRSA septic arthritis cases

Characteristic	CA-MRSA	HA-MRSA	P
Male	5/11 (45.5%)*	26/34 (76.5%)	0.070
Age	24.4±22.4	51.4±15.8	<0.001**
Host risk factors			
Number of comorbidities	1.2±1.9	3.9±2.4	0.003**
No risk factors	7/11 (63.6%)	7/34 (20.6%)	0.002**
Pre-existing joint disease	2/11 (18.2%)	3/34 (8.8%)	0.582
Diabetes mellitus	0/11 (0%)	7/34 (20.6%)	0.168
ESRD on hemodialysis***	0/11 (0%)	4/34 (11.8%)	0.558
Immunosuppressive medications, Glucocorticoids	0/11 (0%)	1/34 (2.9%)	0.999
Causative risk factors			
Contiguous spread from soft tissue infection	5/11 (45.5%)	8/34 (23.5%)	0.251
Direct inoculation (joint injections, trauma)	1/11 (14.3%)	2/34 (9.1%)	0.999
Hematogenous (IVDU, intravascular catheter)***	3/11 (27.3%)	6/34 (17.6%)	0.666

*Means±SD or N (%).
**P<.05, t test or Fisher's exact test, as appropriate.
***ESRD-End stage renal disease, IVDU-intravenous drug use.

were older (mean age CA-MRSA 24.4; HA-MRSA 51.4, p<0.001) and had more comorbidities (mean number of comorbidities CA-MRSA 1.2; HA-MRSA 3.9 p=0.003). Two patients had prior joint injections before the diagnosis of septic arthritis.

Table 2 summarizes the clinical presentation and laboratory features of CA-MRSA septic arthritis. There were no differences in the initial presentation between CA-MRSA and HA-MRSA. There was no difference in the rates of development of bacteremia or polyarticular involvement between the two groups. The most common joint affected in both groups was the knee, followed by the shoulders and hips. Compared to HA-MRSA, CA-MRSA was more likely to involve the knee. Community-acquired methicillin-resistant *Staphylococcus aureus* isolates were more likely to be sensitive to ciprofloxacin and clindamycin. There were high rates of resistance to erythromycin in both groups. Among the CA-MRSA patients, all children (under age 18) had CA-MRSA strains that were sensitive to clindamycin. In adults, this was much lower at 25% only (p=0.024). Children with CA-MRSA had higher rates of ciprofloxacin sensitivity than adults, but the difference was not statistically significant (ciprofloxacin sensitive strains 60% versus 40%, p=0.999). We did not identify any cases of vancomycin-intermediate *Staphylococcus aureus*.

Table 3 summarizes the treatment patterns and outcomes of CA-MRSA and HA-MRSA septic arthritis. Community-acquired methicillin-resistant *Staphylococcus aureus* and HA-MRSA patients were treated with antibiotics for an average of 5.4 weeks. More than 90% of patients in both CA-MRSA and HA-MRSA groups had surgical drainage. Only 55.6% of CA-MRSA patients received empiric coverage for MRSA on initial admission compared to 93.3% of HA-MRSA patients. The average hospital length of stay for CA-MRSA patients was 10.1 days, 27.3% had

Table 2. Clinical characteristics and laboratory features of CA-MRSA and HA-MRSA septic arthritis cases

Characteristic	CA-MRSA	HA-MRSA	P
Clinical features on initial presentation			
Fever (More than 100 Fahrenheit)	4/11 (36.4%)*	12/34 (35.3%)	0.999
WBC count (/μL)**	14490.9±5989.2	13035±7328.3	0.555
ESR (mm/hr)**	72.7±34.0	90.1±37.3	0.189
CRP (mg/dL)**	4.3±1.5	4.4±1.2	0.695
Joint WBC (/mm^3)	81458.1±50421.5	122064.8±88712.1	0.158
Polyarticular involvement	1/11 (9.1%)	3/34 (8.8%)	0.999
Joint involved			
Knee	7/11 (63.6%)	9/34 (26.5%)	0.035***
Hip	2/11 (18.2%)	7/34 (20.6%)	0.999
Shoulder	1/11 (9.1%)	7/34 (20.6%)	0.657
Ankle	1/11 (9.1%)	3/34 (8.8%)	0.999
Wrist	0/11 (0%)	1/34 (2.9%)	0.999
Other laboratory features			
Positive blood cultures	2/11(18.2%)	11/34 (32.4%)	0.467
Ciprofloxacin sensitive	10/11 (90.9%)	8/33 (24.2%)	<0.001***
Clindamycin sensitive	8/11 (72.7%)	3/16 (18.8%)	<0.001***
Erythromycin sensitive	1/11 (9.1%)	1/33 (3%)	0.442

*Means± SD or N (%).
**WBC-white blood cell, ESR-erythrocyte sedimentation rate, CRP-C - reactive protein.
***P<.05, t test or Fisher's exact test, as appropriate.

a readmission due to recurrence of septic arthritis, and 18.2% had a poor joint outcome or osteomyelitis complications. There were no differences in mortality rates, osteomyelitis complication rates, readmissions, and poor joint outcomes between CA-MRSA and HA-MRSA. About 20% of patients in both groups required skilled nursing facility or rehabilitation facility placement. For those who did not require placement at a facility, 58.8% of the HA-MRSA patients and 45.5% of the CA-MRSA patients required home health services for administration of intravenous antibiotics.

The mean length of stay for the HA-MRSA group was 7.1 days longer than the CA-MRSA group. After adjusting for comorbidities (age, number of comorbidities, diabetes, malignancy, end-stage renal disease, oral glucocorticoid use, osteoarthritis, rheumatoid arthritis, liver disease) and septic arthritis complications (polyarticular involvement, bacteremia) using multivariate regression, we found that MRSA status (CA-MRSA or HA-MRSA) did not affect the mean length of stay.

Discussion

We found that CA-MRSA septic arthritis occurs in younger patients with few comorbid conditions or risk factors. These findings are consistent with other epidemiologic studies comparing CA-MRSA and HA-MRSA in bacteremia, skin and soft tissue infections, and pneumonia.[3] There was a high prevalence of MRSA in our study, with CA-MRSA causing 25% of

Table 3. Treatment patterns and outcomes of CA-MRSA and HA-MRSA septic arthritis cases

Characteristic	CA-MRSA	HA-MRSA	P
Treatment patterns			
Appropriate empiric coverage for MRSA	5/9(53.6%)*	28/30 (93.3%)	0.018**
Number of weeks of antibiotics treatment	5.4±2.4	5.4±1.6	0.963
Number of joint surgeries	2.9±1.2	2.5±1.8	0.571
Outcomes			
Number of admission days	10.8±8.9	17.9±7.6	0.021**
Patients with readmissions	3/11 (27.3%)	15/34 (44.1%)	0.482
Number of readmissions	0.6±1.2	0.7±1.1	0.619
Mortality	0/11 (0%)	4/34 (11.8%)	0.558
Patients with poor joint outcome	2/11 (18.2%)	13/34 (38.2%)	0.288
Patients developing osteomyelitis in adjacent joint	2/11 (18.2%)	11/34 (32.4%)	0.373
Patients requiring placement at Nursing home/Rehabilitation facility	2/11 (18.2%)	6/30 (20%)	0.999

*Means± SD or N (%).
**P<.05, t test or Fisher's exact test, as appropriate.

the MRSA septic arthritis cases. Methicillin-resistant *Staphylococcus aureus* caused 16.5% of all septic arthritis cases. This is consistent with other studies that showed MRSA caused 25-50% of all septic arthritis cases.[5,6] In areas with high rates of MRSA infections, clinicians should be aware that CA-MRSA causes septic arthritis even in patients without risk factors. In these areas, beta-lactam antibiotics alone are not adequate for empirical treatment. Choosing empiric therapy based on patient risk factors alone may not be helpful either. Empiric coverage with an agent active against MRSA should be considered based on knowledge of the local prevalence of drug-resistant pathogens.[7]

We found that CA-MRSA septic arthritis patients were less likely to be covered empirically for MRSA infection on initial presentation. Therefore, CA-MRSA patients are at increased risk for the delayed administration of effective antibiotics. Delayed initiation of appropriate treatment in MRSA infections increases the risk of irreversible damage to cartilage, the risk of seeding other joints, the number of poor joint outcomes, and mortality; it is also associated with increased length of hospital stay and cost.[8,9] The deficiency in empiric antibiotic coverage noted in our study reflects a lack of awareness among providers about the increasing prevalence of CA-MRSA in the community.[10] To our knowledge there have not been any previous studies on the adequacy of empiric antibiotic coverage for CA-MRSA septic arthritis patients. Our research suggests that adequate administration of empiric treatment may represent a priority to improve outcomes in MRSA septic joint arthritis.

Community-acquired methicillin-resistant *Staphylococcus aureus* septic arthritis was associated with increased morbidity with a high percentage of patients developing poor joint outcomes and osteomyelitis complications. Community-acquired methicillin-resistant *Staphylococcus aureus* septic arthritis is also associated with increased health care resource utilization due to long hospital stays, higher readmission rates, and increased need for facility placement and home health care. There were no differences in mortality from sepsis, poor joint outcomes, readmission,

and osteomyelitis complication rates between CA-MRSA septic arthritis and HA-MRSA septic arthritis despite CA-MRSA septic arthritis's affecting younger patients with no significant comorbidities. Therefore, CA-MRSA septic arthritis should be regarded as a severe infection, with similar adverse outcomes as HA-MRSA septic arthritis, warranting attention and consideration from clinicians involved in the evaluation of a possibly septic joint. Our data support the fact that CA-MRSA infections are associated with significant economic burden and morbidity.[11] Therefore, focusing our efforts on prevention and control is worthwhile and well justified.

Our study demonstrates that MRSA strains in CA-MRSA septic arthritis are more susceptible to other antibiotics than HA-MRSA stains (usually multidrug resistant). Community-acquired methicillin-resistant *Staphylococcus aureus* cases were more likely to be sensitive to ciprofloxacin and clindamycin. As compared to adult CA-MRSA patients, all children with CA-MRSA had strains that were sensitive to clindamycin. This is consistent with a study previously published by David et al.[12] The current practice of using clindamycin as empiric therapy for MRSA in the pediatric population seems to be a reasonable choice, but not in adults since 75% of adult CA-MRSA septic patients had clindamycin resistance. In adults, vancomycin, daptomycin, linezolid are good options for empiric therapy. Notably, although many cases of CA-MRSA had *in-vitro* susceptibilities to fluoroquinolones, anecdotally there is a significant history of clinical failure with fluoroquinolone use in treating MRSA. Therefore, fluoroquinolones are not usually used in the treatment of MRSA. Fluoroquinolones should not be used in children due to the concern about possible tendon rupture. Despite reports of vancomycin-intermediate *Staphylococcus* stains causing septic arthritis, we did not identify any of these cases in our study.[15] This may be explained by the fact that many of our patients came from rural areas.

One of the strengths of our study is our focus on septic arthritis caused by CA-MRSA. To our knowledge, despite several previous studies comparing HA-MRSA and CA-MRSA in other infections, such as bloodstream infections and pneumonia, there have not been any previous studies providing information about the differences between HA-MRSA and CA-MRSA septic arthritis. Because of the high prevalence of MRSA, we were able to identify a sufficient number of CA-MRSA cases to make meaningful comparisons between HA-MRSA septic arthritis and CA-MRSA septic arthritis. We do acknowledge that this study does have several limitations. First, our study was a retrospective chart review. Our findings may be affected by the fact that information was not recorded in the electronic medical records. This could lead to misclassification of HA-MRSA and CA-MRSA and underreporting of certain risk factors for MRSA septic arthritis. Second, we do not have information about molecular typing of MRSA strains because this information is not routinely reported. Third, this was a study performed at a single medical center with a high prevalence of MRSA; therefore, our results may not be generalizable to hospitals in other regions. Last, the lack of difference in outcomes of mortality, readmissions, poor joint outcome, and osteomyelitis complications may be due to a relatively small number of patients leading to insufficient power to detect small differences in these outcomes.

CA-MRSA septic arthritis will likely become more common and will be more frequently encountered by clinicians managing joint infections. Recognizing and treating CA-MRSA septic arthritis are important to improve outcomes in these patients. We have demonstrated that CA-MRSA septic arthritis does differ from HA-MRSA septic arthritis in several important epidemiological and microbiologic aspects. Community-acquired methicillin-resistant *Staphylococcus aureus* septic arthritis affects younger patients who have no risk factors. Consideration of appropriate empiric therapy is important and should be based on the local prevalence of antibiotic resistance and not solely on patient risk factors. Although CA-MRSA septic arthritis patients had shorter lengths of stay, there were no differences in mortality, poor joint outcome, readmissions, and osteomyelitis complications between CA-MRSA septic arthritis and HA-MRSA septic arthritis. Community-acquired methicillin-resistant *Staphylococcus aureus* septic arthritis is a serious infection associated with significant morbidity and health care resource utilization, and clinicians should be aware of its emergence as a cause septic arthritis.

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