How Common is MRSA in Adult Septic Arthritis?

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Study objective: We determine the proportion of methicillin-resistant Staphylococcus aureus (MRSA) in adult septic arthritis patients presenting to the emergency department (ED).

Methods: This was a cross-sectional retrospective review in 2 urban academic EDs in northern California, one tertiary care and one public. Subjects included patients who underwent arthrocentesis in the ED from April 2006 through July 2007. We queried the microbiology laboratory databases for synovial fluid cultures sent from the ED. We reviewed synovial fluid culture results and corresponding synovial fluid analyses and then classified positive culture results as true septic arthritis or likely contaminant. For septic arthritis cases, we reviewed medical records and abstracted presenting features. We report our findings with descriptive statistics.

Results: One hundred nine synovial fluid cultures were sent from the EDs. Twenty-three results (21%; 95% confidence interval [CI] 14% to 30%) were positive, of which 9 were likely contaminants; 1 was from a soft tissue abscess and 1 was from bursitis. Of 12 septic arthritis cases, 6 cultures (50%; 95% CI 21% to 78%) grew MRSA, 4 (33%; 95% CI 7% to 60%) methicillin-susceptible S aureus, and 1 each (8%; 95% CI 0% to 24%) Streptococcus pneumoniae, Enterococcus faecalis, and Pseudomonas aeruginosa. Of the 6 MRSA cases, 4 were in male patients; median age of patients was 47.5 years, 3 patients had previously diseased joints, 2 patients injected drugs, 2 patients were febrile, 3 patients had previously diseased joints, median synovial fluid leukocyte count was 15,184 cells/μL (range 3,400 to 34,075 cells/μL), and 5 patients received appropriate ED antibiotics.

Conclusion: In this 2-ED population from a single geographic region, MRSA was the most common cause of community-onset adult septic arthritis. Synovial fluid cell counts were unexpectedly low in MRSA septic arthritis cases. [Ann Emerg Med. 2009;54:695-700.]

INTRODUCTION

Background

Acute monoarticular arthritis is a common problem in emergency medicine. Among the leading causes, septic arthritis is the most important emergency to identify because it leads to rapid cartilage destruction and is associated with significant inhospital mortality.1 Because the clinical examination is unreliable to rule out septic arthritis,2 emergency physicians must maintain a very low threshold for performing diagnostic arthrocentesis. The level of synovial fluid leukocytosis generally correlates with likelihood of bacterial infection; however, a low cell count does not rule out the diagnosis.2 Synovial fluid culture is considered the criterion standard test to establish the diagnosis. The decision whether to admit and begin empiric antibiotics while awaiting culture results often must be based on the overall clinical picture, including age, comorbidities, and presence of fever, as well as synovial fluid leukocyte count, crystals, and Gram’s stain. The choice of empiric antibiotics is dictated by the susceptibility patterns of the most likely pathogens.

Although Staphylococcus aureus is the predominant causal pathogen in septic arthritis,1,3 the current prevalence of methicillin-resistant S aureus (MRSA) in this infection type is not clear. Community-associated MRSA is now the predominant cause of skin and soft tissue infections in US emergency departments (EDs),4 and MRSA is an increasingly common cause of invasive infections of all types, both community and hospital acquired.5,6 At the public hospital in this study, 41% of all clinical S aureus isolates in 2007 were MRSA.

Importance

We sought to evaluate the current cause of septic arthritis in a predominantly adult ED population. We hypothesized that MRSA would account for a significant proportion of recent cases. If so, antibiotics with activity against MRSA should be included in the empirical treatment of septic arthritis.
Editor’s Capsule Summary
What is already known on this topic
*Staphylococcus aureus* is the predominant pathogen in septic arthritis. Methicillin-resistant *S aureus* (MRSA) has become common in many infections caused by *S aureus*.

What question this study addressed
Laboratory records of synovial fluid cultures with positive results from 2 hospitals in 2006 to 2007 were reviewed to determine the proportion of septic arthritis caused by MRSA.

What this study adds to our knowledge
Among 12 cases that appeared to be true septic arthritis by chart review, half were caused by MRSA, and most of these had synovial fluid WBC counts less than 20,000 cells/mm³.

How this might change clinical practice
Empiric antimicrobial therapy for septic arthritis should include activity against MRSA, pending culture results.

Goals of This Investigation
The primary goal of this study was to determine the proportion of ED patients with septic arthritis caused by MRSA. The secondary goal was to describe clinical features of adult MRSA septic arthritis case patients.

MATERIALS AND METHODS

Study Design
This is a cross-sectional retrospective chart review study.

Setting
The study was conducted at 2 academic EDs in northern California, one a tertiary care hospital with an annual census of 39,000, and the other a public hospital with an annual census of 75,000.

Selection of Participants
We queried the microbiology laboratory databases from both study institutions for synovial fluid specimens obtained in the EDs and submitted for culture from April 2006 through July 2007.

Data Collection and Processing
Microbiology staff performed an electronic search of their databases and provided a list of all synovial fluid specimens submitted for culture from the EDs during the study period. We reviewed the synovial fluid culture results, and for cultures that grew any bacteria, we used a structured data collection form to abstract the following information from the electronic laboratory record: synovial fluid indices, including leukocyte count, crystals, and Gram’s stain (where reported); bacterial species; microbiology report comments, including number of colonies and medium that produced growth; and results of antibiotic susceptibility testing on *S aureus* isolates. In selected cases, to identify likely contaminants, we reviewed the electronic medical record for clinical course and subsequent discharge diagnoses. For all cases categorized as true septic arthritis, we reviewed the ED electronic medical record and abstracted the following information: patient age; sex; presenting chief complaint; comorbidities, including presence of previous joint disease; history of injection drug use; presenting ED temperature; peripheral WBC count; joint involved, if blood cultures were obtained (if so, the result); whether antibiotics were administered in the ED (if so, what antibiotics); ED diagnosis; and disposition. Missing data were documented as missing or not obtained. One investigator from each institution (B.W.F. and C.F.), who was not blinded to the study hypothesis, performed all data abstraction on cases from his institution. These data were entered into a Microsoft Word table (Microsoft Word 2004 for Mac, version 11.3; Microsoft, Redmond, WA).

Outcomes Measures
The main outcome was whether MRSA was isolated on synovial fluid culture. Secondary outcomes were results of synovial fluid analyses and antibiotic susceptibility of MRSA isolates.

Primary Data Analysis
We calculated the percentage of positive synovial fluid cultures in which MRSA was isolated. For continuous variables, we calculated and report medians and ranges. We report 95% confidence intervals (CIs) where appropriate.

This study was approved by the institutional review boards of both participating sites.

RESULTS

Characteristics of Study Subjects and Main Results
Results of the microbiology records search are presented in the Figure. Of 109 synovial fluid cultures submitted from the EDs during the study period, 23 (21%; 95% CI 13% to 29%) grew bacteria and 86 (79%; 95% CI 70% to 86%) were sterile. Nine cultures that grew bacteria were classified as likely contaminants, including 1 MRSA isolate, leaving 14 true infections. Chart review revealed that, although labeled synovial fluid, 1 culture that grew MRSA actually came from a superficial abscess, and 1 that grew methicillin susceptible *S aureus* (MSSA) came from prepatellar bursitis, leaving 12 cases of true septic arthritis.

*S aureus* isolates were identified in 10 of 12 septic arthritis cases, of which 6 were MRSA and 4 were MSSA (Table 1). The proportion of cases caused by MRSA was 50% (95% CI 21% to
Figure. Summary of main study results.
MRSA comprised 7 of 22 (31%) of all bacterial isolates and 6 of 12 (50%) putative septic arthritis cases. *Based on microbiology characteristics and fluid analysis. UCSF, University of California San Francisco Medical Center; ACMC, Alameda County Medical Center.

Table 1. Pathogens isolated from synovial fluid cultures in the 12 true septic arthritis cases.

<table>
<thead>
<tr>
<th>Number* (%; 95% CI)</th>
<th>Pathogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (50; 21-78)</td>
<td>MRSA</td>
</tr>
<tr>
<td>4 (33; 7-60)</td>
<td>MSSA</td>
</tr>
<tr>
<td>1 (8; 0-24)</td>
<td>Streptococcus pneumoniae</td>
</tr>
<tr>
<td>1 (8; 0-24)</td>
<td>Enterococcus faecalis</td>
</tr>
<tr>
<td>1 (8; 0-24)</td>
<td>Pseudomonas aeruginosa</td>
</tr>
</tbody>
</table>

MSSA, Methicillin-susceptible S aureus.
*One culture grew both MSSA and E faecalis.

78%). Demographic and presenting features of the MRSA septic arthritis cases and non-MRSA cases are presented in Tables 2 and 3, respectively. Among all 12 cases, median age was 46 years, there were no prosthetic joint infections, and 6 occurred in injection drug users. Only 2 patients, both with MRSA, were febrile at triage. The median synovial fluid leukocyte count in MRSA cases was 15,184 cells/μL (range 3,400 to 34,075 cells/μL) compared with 84,700 cells/μL (range 37,750 to 193,000 cells/μL) in non-MRSA cases.

Of the 6 MRSA cases, 5 were administered appropriate antibiotics in the ED and were admitted for further management. One patient did not receive antibiotics and was discharged to home but was later called to return and admitted when the synovial fluid culture grew MRSA. All 6 MRSA isolates from septic arthritis were susceptible to vancomycin, trimethoprim-sulfamethoxazole, and doxycycline; 5 were susceptible to clindamycin; and 4 were susceptible to to levofloxacin.

LIMITATIONS
This study has significant limitations. The results may not be generalizable because the study involved a relatively young patient population with a high prevalence of injection drug use and without prosthetic joint infections. The main outcome, proportion of MRSA, might also be skewed by the fact that the study was conducted at just 2 EDs from a single geographic region. However, we believe our community prevalence of MRSA is typical of that in other urban areas, according to the prevalence of community-associated MRSA in skin and soft tissue infections at our public hospital ED compared with that at 11 EDs distributed across the United States.4,7

We identified what we believed to be 9 cases of joint fluid contamination (43% of positive synovial fluid culture results). The authors determined this according to the bacterial species isolated, number of colonies, medium that produced growth (broth versus plate), and synovial fluid indices. Four of 5 specimens that grew a nonpathogenic species but had an increased cell count also contained monosodium urate crystals. A limited review of the medical records of these 9 patients revealed no discharge diagnosis of septic arthritis after the index ED visit, although hospitalization elsewhere is possible. There is a paucity of literature discussing the issue of bacterial joint fluid contamination1,8 and no published diagnostic criteria. Our unique study methodology, which began with and reported all microbiologic results, may explain the seemingly high contamination rate. In addition, our methodology would have missed any cases of culture-negative septic arthritis, a fairly common entity.4

Finally, we did not attempt a formal comparison of MRSA to non-MRSA infections because the number of cases was too small.

DISCUSSION
S aureus is the most common causal organism in adult septic arthritis, accounting for approximately 50% of cases in large case series.1,3,9 Gonococcal arthritis has become uncommon since the 1980s.10 Most cases of septic arthritis are caused by hematogenous spread, although the source of S aureus bacteremia is often occult.1 Although the occurrence of MRSA septic arthritis has been recognized for decades,11 it is still considered rare, particularly in patients without risk factors.1,12 In recent series from the United Kingdom of predominantly community-onset septic arthritis, MRSA was isolated in 6% to 8% of infections.3,9

Evidence is mounting, however, that MRSA should be considered a likely pathogen in any patient presenting to the ED with septic arthritis. Community-onset invasive MRSA infections, including bacteremia and osteomyelitis, are now common and widespread in the United States.6 Septic arthritis accounted for 1% of all community-associated MRSA isolates in a large 2002 surveillance study involving 3 geographic regions of the United States.13 Studies specifically showing a high prevalence of MRSA in community-onset septic arthritis are limited to recent pediatric case series, in which MRSA accounted for 47% to 70% of S aureus infections.5,14 Evidence on MRSA septic arthritis in adults is limited to case reports15 and case series of predominantly nosocomial infections.16,17 Ross and Davidson18 reported that 15 of 59 (25%) adult septic
arthritis cases at a single Massachusetts hospital between 2000 and 2005 were due to MRSA. Mean patient age was 69 years, 80% had been hospitalized within 6 months, and the mean number of comorbidities was 6. It is unclear how many cases were community onset or how many patients were admitted from the ED.

In our study, among 12 cases of culture-positive septic arthritis in patients presenting to the ED, all adults, the prevalence of MRSA was 50% and MRSA accounted for 6 of 10 S aureus isolates. We used a novel, explicitly described method of case ascertainment to find all cases of culture-positive septic arthritis evaluated in the ED. Taken together with other studies involving children and older adults elsewhere in the United States, our results strongly suggest that antibiotics with activity against MRSA should be included in the empirical treatment of suspected septic arthritis encountered in the ED. Recent authoritative sources continue to recommend that empirical anti-MRSA therapy be reserved for patients with risk factors for this organism.\textsuperscript{1,12,18} However, the current Sanford Guide to Antimicrobial Therapy\textsuperscript{19} does recommend vancomycin, in addition to a third-generation cephalosporin, as first-line

### Table 2. Demographic and presenting features of the 6 MRSA septic arthritis cases.

<table>
<thead>
<tr>
<th>Demographic and Presenting Features</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>25</td>
<td>41</td>
<td>44</td>
<td>57</td>
<td>51</td>
<td>61</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>Female</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>ED chief complaint</td>
<td>Ankle pain</td>
<td>Knee pain</td>
<td>Knee and hand pain</td>
<td>Elbow and knee pain</td>
<td>Shoulder pain</td>
<td>Weakness</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>None</td>
<td>None</td>
<td>Diabetes</td>
<td>Polymyositis of unclear cause (6 mo)</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>History of joint disease</td>
<td>Previous open reduction and internal fixation of ankle, history of hardware infection</td>
<td>Previous open reduction and internal fixation of tibial plateau fracture and removal of hardware</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Injection drug use</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Presence of traditional hospital-acquired MRSA risk factors*</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Temperature, C (F°)</td>
<td>38.4 (101.1)</td>
<td>36.0 (96.8)</td>
<td>37.0 (98.6)</td>
<td>38.4 (101.1)</td>
<td>37.9 (100.2)</td>
<td>36.7 (98.1)</td>
</tr>
<tr>
<td>Peripheral WBC count, cells/mm(^3)</td>
<td>11.5</td>
<td>13.1</td>
<td>8.5</td>
<td>15.9</td>
<td>14.6</td>
<td>17.6</td>
</tr>
<tr>
<td>Site</td>
<td>Ankle</td>
<td>Knee</td>
<td>Knee</td>
<td>Knee</td>
<td>Shoulder</td>
<td>Knee</td>
</tr>
<tr>
<td>Synovial fluid leukocyte count, cells/(\mu L)</td>
<td>No analysis</td>
<td>15,195</td>
<td>34,075</td>
<td>16,500</td>
<td>3,400</td>
<td>6,750</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>None</td>
<td>Negative</td>
<td>None</td>
<td>Negative</td>
<td>Positive (MRSA)</td>
<td>Positive (MRSA)</td>
</tr>
<tr>
<td>ED diagnosis</td>
<td>Hardware infection, septic joint</td>
<td>Septic arthritis</td>
<td>Polymyositis</td>
<td>Elbow cellulitis, knee arthritis, r/o endocarditis</td>
<td>Septic arthritis</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Disposition</td>
<td>Admit Vancomycin</td>
<td>Admit Vancomycin, clindamycin</td>
<td>Discharge None</td>
<td>Admit Vancomycin, clindamycin, levofloxacin</td>
<td>Admit Vancomycin</td>
<td>Admit Vancomycin, clindamycin, piperacillin/tazobactam</td>
</tr>
</tbody>
</table>

*Hospitalization within 1 year, hemodialysis, resident of a skilled nursing facility, indwelling intravenous catheter.
therapy for septic arthritis in adults not at risk for sexually transmitted disease and children older than 3 months.

The antibiotic susceptibility patterns of our 6 septic arthritis MRSA isolates are typical of genetically defined community-associated MRSA, particularly the USA 300 clonal group. However, 3 of 6 patients with MRSA septic arthritis had significant recent contact with the health care system in the form of hospitalization within the previous 12 months. These cases are therefore considered health care–associated MRSA infections by widely accepted clinical criteria. Two of the remaining 3 patients injected drugs, which is a recognized risk factor for MRSA infection. (However, injection drug use was actually more common in non-MRSA cases.) One patient had no discernable risk for MRSA infection.

A remarkable finding in our study was the relatively low synovial fluid leukocyte count in the MRSA cases. It was less than 25,000 cells/μL in 4 of 5 cases in which it was measured and generally much lower than in the non-MRSA cases. In large studies before 1998, only between 12% and 37% of all septic arthritis patients had a synovial fluid leukocyte count less than 25,000 cells/μL.² In recent studies of MRSA septic arthritis, synovial fluid leukocyte count was not reported. None of the MRSA patients in our study reported receiving antibiotics at admission, nor were they known to be immunosuppressed. The low synovial fluid leukocyte count may be related to toxins produced by community-associated MRSA, such as Panton Valentine leukocidin. Although the reason for the finding is not clear, it underscores the need to maintain a low threshold for

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**Table 3.** Demographic and presenting features of the 6 non-MRSA cases.

<table>
<thead>
<tr>
<th>Demographic and Presenting Features</th>
<th>Case Number</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Age, y</td>
<td>51</td>
</tr>
<tr>
<td>Sex</td>
<td>51</td>
</tr>
<tr>
<td>ED chief complaint</td>
<td>Knee pain, GI bleed</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>Alcoholic cirrhosis</td>
</tr>
<tr>
<td>History of joint disease</td>
<td>Osteoarthritis</td>
</tr>
<tr>
<td>Injection drug use</td>
<td>No</td>
</tr>
<tr>
<td>Presence of traditional hospital-acquired MRSA risk factors*</td>
<td>No</td>
</tr>
<tr>
<td>Temperature, C (F)° (triage)</td>
<td>36.5 (97.7)</td>
</tr>
<tr>
<td>Peripheral WBC count, cells/mm³</td>
<td>5.7</td>
</tr>
<tr>
<td>Site</td>
<td>Knee</td>
</tr>
<tr>
<td>Synovial fluid culture</td>
<td>MSSA</td>
</tr>
<tr>
<td>Synovial fluid leukocyte count, cells/μL</td>
<td>193,000</td>
</tr>
<tr>
<td>Blood cultures</td>
<td>MSSA</td>
</tr>
<tr>
<td>ED diagnosis</td>
<td>Admit (ICU)</td>
</tr>
<tr>
<td>Disposition</td>
<td>Levofloxacin, piperacillin/tazobactam Metronidazole Vancomycin</td>
</tr>
<tr>
<td>ED antibiotics</td>
<td>Ceftriaxone, vancomycin</td>
</tr>
</tbody>
</table>

GI, Gastrointestinal; HCV, hepatitis C virus; OR, operating room.

*Hospitalized within 1 year, hemodialysis, resident of a skilled nursing facility, indwelling intravenous catheter.
admission and empirical anti-MRSA treatment in possible septic arthritis cases, even in the face of a low synovial fluid cell count.

IN RETROSPECT

We hope that future larger studies seek to confirm our finding of low synovial fluid leukocyte counts in MRSA septic arthritis, formally compare MRSA with non-MRSA cases, and examine the issue of contaminants in unselected synovial fluid cultures.

Our data suggest that antibiotics with activity against MRSA should be used in the empiric treatment of suspected septic arthritis in the ED and that treatment be strongly considered even when the synovial fluid leukocyte count is less than 25,000 cells/μL.

Supervising editor: Gregory J. Moran, MD

Author contributions: BWF and CF conceived and designed the study. BWF, CF, and LL collected and analyzed the data. CF performed the statistical analysis. BWF and CF drafted the article, and all authors contributed substantially to its revision. BWF takes responsibility for the paper as a whole.

Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article that might create any potential conflict of interest. The authors have stated that no such relationships exist. See the Manuscript Submission Agreement in this issue for examples of specific conflicts covered by this statement.

Publication dates: Received for publication March 25, 2009. Revision received June 13, 2009. Accepted for publication June 24, 2009. Available online August 8, 2009.

Presented as an abstract at the Western Regional Society of Academic Emergency Medicine meeting, January 2009, Park City, UT; and the National Society of Academic Medicine meeting, May 2009, New Orleans, LA.

Reprints not available from the authors.

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REFERENCES


CORRECTION

In the September 2009 Research Forum supplement, in abstract 6 by Green, (“Effect of Hyperlactatemia on the Likelihood of In-patient Mortality for Patients with a Normal and Abnormal Anion Gap”; page S3), the following authors’ names and affiliations are missing: Tony Berger, MD, Jacobi Medical Center; Nidhi Garg, MD, New York Hospital Queens; Krista Gitkind, RN, New York Hospital Queens.