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Short Communication

Role of nasal swab culture in guiding antimicrobial therapy for acute cellulitis in the era of community-acquired methicillin-resistant *Staphylococcus aureus*: A prospective study of 89 patients

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Abstract In this prospective study of 89 patients with acute cellulitis, we showed nasal swab culture of methicillin-resistant *Staphylococcus aureus* (MRSA), taken at enrollment, has a high specificity of 95% in predicting MRSA cellulitis among the 24 patients whose cellulitis became purulent. However, the sensitivity is only 20%.

Introduction

Cellulitis is the most common soft tissue infection. Cellulitis is usually caused by bacterial flora colonizing skin, such as *Staphylococcus aureus* or streptococci. Staphylococcal cellulitis and streptococcal cellulitis have similar initial manifestations, although *S. aureus* cellulitis is more likely to subsequently develop abscesses.[1] Oxacillin had been the

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preferred empirical therapy because of its good activity against both *S. aureus* and streptococci.

Since 2005, community-acquired methicillin-resistant *S. aureus* (MRSA) emerged as an important pathogen for cellulitis.[1] The emergence of community-acquired MRSA, which was resistant to oxacillin, posed a challenge to empirical therapy for acute cellulitis. The issue is further complicated by the difficulty in establishing etiology in the majority of cellulitis cases since most cases have neither abscess formation nor bacteremia.

In contrast to difficulties in obtaining pus culture in acute cellulitis at the presentation, nasal swab culture is easy to perform. Nasal *S. aureus* colonization is a known risk factor for subsequent *S. aureus* infections.[2–4] The 2014 Infectious Diseases Society of America (IDSA) guidelines for skin and soft tissue infections recommended that, for people with nasal MRSA colonization, empirical therapy for acute cellulitis should be active against MRSA.[1] Two retrospective studies (of cutaneous abscesses) reported that nasal carriage of MRSA had a sensitivity of 55%–62% and a specificity of 93%–100% for MRSA soft tissue infections.[2,3] However, no prospective study data are available for the diagnostic value of nasal swab cultures in guiding antimicrobial therapy for acute cellulitis.

This prospective observational study aimed to assess whether nasal MRSA colonization predicts acute MRSA cellulitis and a delayed response to antimicrobial therapy.

Method

This prospective observational study was conducted in Far Eastern Memorial Hospital (FEMH). FEMH is a 1000-bed medical center in Taipei metropolitan area. The research ethic committee reviewed and approved the study procedure (IRB #101087-F). All participants gave informed consent.

Adult (>20 years old) patients were eligible if they visited the FEMH emergency service and received a diagnosis of acute cellulitis which required hospitalization. At enrollment, all participants received a nasal swab culture (BBL CultureSwab EZ, Becton Dickinson, Sparks, MD, USA) to detect *S. aureus* carriage. The nasal swab was performed by a trained nurse or physician. Nasal swab was performed by inserting the swab tube 1 cm into the nostril, and then placing it on trypticase soy agar supplemented with 5% sheep blood (BBL, Microbiology Systems, Cockeysville, USA) which were incubated overnight at 37 °C. We selected one colony from each single culture. Identification and susceptibility testing of *S. aureus* was based on standard methods.[5]

We obtained the baselines clinical characteristics, including age, sex, underlying diseases, prior hospitalizations, prior antibiotics use, or other medical treatment in the recent three months. Primary care physicians decided the empirical and definite antibiotic therapies. We monitored clinical response to therapy, including duration of fever, local inflammation, and whether abscess occurred.

The primary outcome was a delayed response to therapy, as defined by (1) fever that persisted for more than 3 days under empirical antibiotics, or (2) erythema that persisted or enlarged under treatment for more than 3 days. The secondary outcomes included (1) the total duration of antibiotic use; (2) the length of hospitalization; (3) computed tomography (CT) or magnetic resonance imaging (MRI); and (4) surgical interventions: incision, drainage, or debridement.

Sensitivity and specificity of nasal swabs culture in predicting etiology of acute cellulitis, as defined by pus culture results, were calculated for patients who developed suppurative cellulitis with pus formation.

A P value less than 0.05 was considered significant. All P values were two tailed. Statistical Package for Social Sciences (SPSS) ver 17.0 (IBM, Armonk, New York, USA) was used for all statistical analyses.

Results

We enrolled 89 patients (mean age: 52 years, 60 were men) during 2013–2015 (Table 1). Fifteen (17%) of them carried *S. aureus*, of which 11 (12.4%) and four (4.5%) were methicillin-susceptible *S. aureus* (MSSA) and MRSA, respectively. Nearly all (88/89, 99%) participants received empirical antibiotics with activity against MSSA (oxacillin, cefazolin, dicloxacillin, or cephalexin). Sixteen (16/89, 18%) participants (none of them were MRSA carriers) received empirical antibiotics with activity against MRSA (vancomycin, teicoplanin, linezolid, fusidic acid, moxifloxacin, doxycycline, or trimethoprim-sulfamethoxazole). MRSA nasal carriers had a higher risk of delayed clinical response to empirical therapy (1/4 [25%] vs. 15/82 [18%]), or risk of abscess formation (2/4 [50%] vs. 22/82 [27%]), but the difference did not reach statistical significance (Ps = 0.93 and 0.17, respectively) (Table 1). Culture-confirmed MRSA cellulitis did have a significantly higher risk for delayed clinical response to therapy (4/5 [80%] vs. 12/81 [15%], P = 0.004, by Fisher's exact test).

Of the 24 patients developed purulent cellulitis (Table 1), five and two patients have nasal colonization of MSSA and MRSA, respectively. MRSA growth from nasal swab culture had a sensitivity of 20% (1/5) and specificity of 95% (18/19) in predicting MRSA growth from pus culture among the 24 purulent cellulitis cases.

Discussion

Our prospective study, designed to be as close to ordinary practice scenarios as possible, found that nasal MRSA carriage has a high specificity (95%) in predicting MRSA cellulitis. This high specificity may allow a recommendation of antimicrobial therapy against MRSA in acute cellulitis patients with nasal MRSA carriage as well as other risk factors for MRSA infections, such as recent stay in healthcare facilities.[6] However, the sensitivity (20%) was less impressive than the 55%–62% reported in two previous retrospective studies.[2,3] The low sensitivity of nasal swab culture in detecting MRSA cellulitis may explain the observation that nasal MRSA carriage was not a good predictor for delayed response to empirical antibiotic therapy in the present study (25% [MRSA carriers] vs. 18% [non-MRSA carriers]).

Our study may have a good generalizability, because participants of our study had a clinical spectrum of acute cellulitis and an MRSA carriage rate very similar to that

Table 1 Eighty-nine participants with acute cellulitis, by nasal *S. aureus* colonization status.

	No *S. aureus* colonization (n = 74)	Colonized with MSSA (n = 11)	Colonized with MRSA (n = 4)	P value[a]
Age (year), mean ± SD (range)	52 ± 16.5 (22–89)	44 ± 15.8 (21–62)	62 ± 10.4 (50–75)	0.14
Male	51 (69%)	7 (64%)	2 (50%)	0.71
Underlying conditions				
Diabetes mellitus	20 (27%)	1 (9%)	0	0.22
Gout	8 (11%)	2 (18%)	0	0.59
Hemodialysis	1 (1%)	0	0	0.90
Prosthetic devices	2 (3%)	1 (9%)	0	0.51
Recent[b] anti-MRSA agent[c]	3 (4%)	1 (9%)	1 (25%)	0.18
Recent[b] anti-MSSA agent[d]	4 (5%)	1 (9%)	1 (25%)	0.30
Recent[b] hospitalization	3 (4%)	0	0	0.40
Previous MRSA colonization or infection (within 1 year)[e]	2 (3%)	0	0	0.81
Sites of acute cellulitis				
Extremities	70 (95%)	11 (100%)	4 (100%)	0.65
Head or neck	1 (1%)	0	0	0.90
Trunk	3 (4%)	0	0	0.73
Body temperature (°C)	37.4 ± 1.1	38 ± 1.5	39 ± 1.1	0.07
Initial temperature >37.5 °C	29 (39%)	7 (64%)	2 (50%)	0.17
Blood culture				
S. aureus	0	0	0	—
Streptococcus	1	0	1	0.007
Other	2	0	0	0.81
Empiric antibiotics				
Anti-MSSA[d]	70 (95%)	11 (100%)	4 (100%)	0.65
Anti-MRSA[c]	13 (18%)	3 (27%)	0	0.47
Delayed response to antibiotic therapy [f]	13/71[g] (18%)	2/11 (18%)	1/4 (25%)	0.93
Pus formation	17/71[g] (23%)	5/11 (46%)	2/4 (50%)	0.17
S. aureus				
MSSA	3 (4%)	3[h] (27%)	0	0.014
MRSA	4 (5%)	0	1 (25%)	0.17
Streptococcus	2 (3%)	1[h] (9%)	0	0.51
Other	3 (4%)	2[i] (18%)	0	0.15
No growth	7 (9%)	0	1 (25%)	0.31
Total duration of antibiotics[g] (days)	17 ± 11 (1–66)	19 ± 11 (10–35)	16 ± 6.7 (12–26)	0.79
Surgical intervention[j]	8/71[g] (11%)	0/11	1/4 (25%)	0.32
Duration of hospitalization[g] (days)	7.6 ± 8 (0–56)	8.1 ± 6.4 (3–26)	6.5 ± 3.3[2–10]	0.87

[a] By 3 × 2 Chi-square test (categorial variables) or one-way ANOVA (continuous variables).
[b] Within 3 months.
[c] Anti-MRSA antibiotics: antibiotics with activity against MRSA (including vancomycin, teicoplanin, fusidic acid, trimethoprim-sulfamethoxazole, doxycycline, moxifloxacin, and linezolid); of these moxifloxacin (7/16, 44%) was the most commonly prescribed.
[d] Anti-MSSA antibiotics: the antibiotics with activity against methicillin-susceptible *S. aureus* (MSSA) (including oxacillin, cefazolin, dicloxacillin, and cephalexin); of these, oxacillin (54/89, 61%) was the most commonly prescribed.
[e] Including one patient who had MRSA isolated from urine and another one who had MRSA isolated from wound culture.
[f] Delayed response to therapy was defined by (1) fever that persisted for more than 3 days under empirical antibiotics, or (2) erythema that persisted or enlarged under treatment for more than 3 days.
[g] Three patients (all were nasal swab culture-negative) lost to follow-up. Only 86 patients were available for analyses regarding outcomes.
[h] One patient had both MSSA and group A streptococcus isolated from pus culture.
[i] One was methicillin-susceptible *S. epidermidis*; the other was *Pseudomonas aeruginosa*.
[j] Incision, drainage, or debridement.
Data are number (%) or mean ± standard deviation (SD) (range).
MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*.

reported in previous large sample size survey in Taiwan. A study of 465 cellulitis patients in Southern Taiwan showed that 96 of them (21%) had suppurative cellulitis, and 24 of the 96 (25%) had MRSA cellulitis.[7] Similarly, among our 89 participants, 24 (27%) had suppurative cellulitis, and 5 of the 24 (21%) had MRSA cellulitis. Meanwhile, we found 4.5% of our cases had nasal MRSA carriage. In a large surveillance study for *S. aureus* nasal carriage among healthy adults in

Taiwan, Wang et al. reported a 3.8% nasal MRSA carriage rate among 3098 participants.[8] Another study by Lu et al. reported a nasal MRSA carriage rate of 3.5% among 1838 subjects from the community.[9] Studies from the United States also reported a similar level (4.7%) of nasal MRSA carriage rate among their subjects.[10]

Our study has several important limitations. First, due to the small numbers of MRSA carriers (n = 4) and culture-confirmed MRSA cellulitis (n = 5), our estimates for sensitivity and specificity of using nasal MRSA carriage in predicating culture-confirmed MRSA cellulitis could be imprecise. Second, the present study was neither designed nor powered to examine the effectiveness of empirical anti-MRSA antimicrobial therapy. Likewise, this study was not designed nor powered to identify the risk factors of colonization by MRSA, and therefore, should not be compared with large epidemiological studies aimed to identify risk factors of *S. aureus* or MRSA carriage such as diabetes mellitus, age, and recent hospitalization.[8,9] Third, clinical isolates from pus/abscess were not available for pulsed-field gel electrophoresis to assess the clonality of the paired isolates from clinical and nasal swabs in our patients.

In conclusion, nasal MRSA carriage is highly specific in predicting community-acquired MRSA cellulitis for patients with purulent cellulitis. The high specificity of 95% may allow a recommendation of antimicrobial therapy against MRSA for acute cellulitis patients with nasal MRSA carriage as well as other risk factors of MRSA infections. Empirical anti-MRSA agents are not needed in patients without nasal MRSA colonization.

Conflict of interest

None declared.

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