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ORIGINAL ARTICLES

The Asssociation of Pre-Operative Hospital Stay with Surgical Site Infection Among Pediatric Patients After A Clean Neurosurgical Operation

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BRIEF REPORTS

INSTRUCTIVE CASE

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The authors declare that the data presented are original material and have not been previously published, accepted or considered for publication elsewhere; that the manuscript has been approved by all the authors, who have met the requirements for authorship. **BRIEF REPORT**

PROFILE OF COMMUNITY-ACQUIRED METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS SKIN AND SOFT-TISSUE INFECTIONS AMONG CHILDREN ADMITTED AT THE PHILIPPINE GENERAL HOSPITAL

ABSTRACT

Objective: CA-MRSA infection is a global concern. It is important to determine the local prevalence of CA-MRSA skin and soft-tissue infection as this information will provide a more accurate and rational basis for empiric treatment, improve management and outcomes in patients, and reduce the economic burden associated with failed treatment. This study was conducted to determine the clinical profile and prevalence of CA-MRSA skin and soft tissue infections among pediatric patients admitted at the Philippine General Hospital.

Methods: A prospective, observational study was performed involving all pediatric patients admitted at U-PGH for skin and soft-tissue infections from September to December 2012. Demographic profile, clinical characteristics of patients, results of laboratory examinations, the outcome of treatment were described and summarized. Risk factors for acquisition of MRSA were also determined. Period-prevalence was computed.

Results: There were 25 children admitted for SSTIs, 16 have positive cultures and 62.5% of these had CA-MRSA. The majority were male children younger than 5 years old without identifiable risk factors. Infections presented as solitary masses and cellulitis usually at the head and neck area. Isolates were taken from aspirates during incision and drainage. Invasive infections were seen in 3 patients. The length of hospital stay, type of antibiotics used and surgery performed was variable. All patients were discharge well and there were no mortalities. The period prevalence of CA-MRSA among children with SSTI was 0.36.

Conclusion: CA-MRSA as a cause of SSTIs in Filipino children is an emerging concern, especially in very young patients even without risk factors. Management of SSTIs should include incision and drainage of abscesses and prompt submission of aspirates for culture and antibiotic sensitivity testing. The period prevalence of pediatric patients with SSTI is high among hospitalized patients. Empiric antibiotics with MRSA coverage such as clindamycin and vancomycin should be considered in clinical situations wherein MRSA is deemed likely.

KEYWORDS:

MRSA, CA-MRSA, Methicillin resistant Staphylococcus aureus, skin and soft tissue infection



INTRODUCTION

Before the emergence of community acquired Methicillin-resistant Staphylococcus aureus (CA-MRSA), antibiotic treatment for Staphylococcus aureus infections acquired from the community was simple because practically all isolates were susceptible to penicillinase-resistant β -lactam antibiotics such as methicillin, oxacillin, and cephalosporins. But with the changing of epidemiology staphylococcal infections reported in different areas around the world, the approach to the treatment of these infections has become more complex and challenging as more antibiotic-resistant Staphylococcus aureus strains are encountered in the communitysetting.

Methicillin resistant Staphylococcus aureus (MRSA) are S. aureus isolates that are resistant to all available penicillins and other beta-lactam antibiotics. They were previously seen and confined mostly in the hospital setting, other health care facilities and from patients exposed to these medical care institutions. But the recognition of an explosive number of MRSA infections from populations lacking risk factors for exposure to health care facilities has lead to the identification of a new MRSA strain called community-associated or community-acquired MRSA (CA-MRSA). This strain is responsible for the recent increased disease burden and public health concern associated with this infection.¹

Although invasive and life threatening infections occur, the majority of CA-MRSA-associated diseases are skin and soft-tissue infections (SSTI). ^{1,3,5,6,7,8} The clinical spectrum of these SSTIs is wide, ranging from a simple impetigo to small abscesses, cellulitis or severe or extensive diseases involving multiple sites and deeper soft-tissue infections. Folliculitis and scalded-skin syndrome may also occur but to a lesser frequency.³

The Philippine General Hospital is a tertiary training and referral medical center that caters to various kinds of patients coming from different areas in the country. Although majority of patients come from Metro Manila and nearby provinces by virtue of proximity, the composition of patients coming for medical treatment is variable. As one of the leading referral centers in the country, it is important to determine the local prevalence of MRSA infection particularly among skin and soft-tissue infections as these represent the bulk of community-acquired MRSA. This study was intended to determine presence or absence of risk factors for acquisition of MRSA among pediatric patients with CA-MRSA skin and soft-tissue infections and determine antibiotic susceptibility of clinically significant MRSA isolates in order to provide accurate recommendations for empiric antibiotic Information obtained treatment. from prospective studies will provide a more accurate and rational basis for local guidelines and recommendations specifically on the empiric antibiotic treatment of SSTIs. This will further improve the outcome of pediatric patients with such infections as well as reduce the economic burden associated with these infections.

MATERIALS AND METHODS:

This was a prospective observational study involving all pediatric patients 0 to 18 years of age admitted at UP-PGH for skin and soft-tissue infections from September to December 2012. Demographic profile and clinical characteristics of patients were described and tabulated. Results of appropriate laboratory examinations as determined by the patients' attending physicians were also summarized. Staphylococcal isolates were classified as MSSA, CA-MRSA, HA-MRSA based on the CDC definition⁴ described below. Risk factors for acquisition of MRSA were also identified.



Clinically significant isolates of CA-MRSA were obtained from patients and their antibiotic susceptibility patterns were determined. Management based on the discretion of the attending physician including medical and/or surgical procedures were analyzed. Antibiotic treatment, the length of hospital stay and clinical outcome of patients were likewise determined. Period prevalence of CA-MRSA among patients with skin and soft-tissue infections was computed based on the number of CA-MRSA infections identified during the study period.

Based on the CDC definition⁴, the following definitions of terms were used in the study.

- Methicillin-sensitive Staphylococcus aureus (MSSA) – S. aureus isolates susceptible to oxacillin and cefoxitin.
- 2. Community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) infection with MRSA diagnosed by a culture positive for MRSA within 48 hours of admission to the hospital without medical history of MRSA infection or colonization, medical history of hospitalization, no dialysis, surgery or admission to a nursing home, skilled nursing facility or hospice in the past year and absence of permanent percutaneous catheters indwelling or medical devices that pass through the skin into the body.
- Hospital-associated methicillin-resistant Staphylococcus aureus (HA-MRSA) – MRSA organism isolated >72 hours after admission to the hospital and with any one of the risk factors listed above.

For the purpose of this study, MRSA colonization as evidenced by positive nasal swab culture for MRSA was not routinely done for each patient hence this was not considered as part of the criteria to differentiate CA-MRSA from HA-MRSA. Also, if MRSA was isolated from a patient after 48 hours from admission but clinical evidence suggested that it was community acquired, then the isolate was classified as CA-MRSA. For example, if MRSA was isolated from an exudate taken from an incision and drainage procedure performed after 48 hours from admission but the lesion was already present on admission, then the isolate was classified as community-acquired. In addition to the risk factors for MRSA acquisition stated above, the presence of underlying chronic disease and recent antibiotic use were also included in the inclusion criteria for HA-MRSA.

This study was approved by the UP-PGH Ethics and Review Board. A written informed consent and assent were obtained from the participant and/or from the parent or legal guardian of the patient. The study was self-funded.

RESULTS

A total of 25 pediatric patients were admitted for skin and soft-tissue infections at UP-Philippine General Hospital from September to October 2012 (Table 1). Of these patients, nine patients or 36% did not grow any isolate from blood, aspirate and/or tissue cultures. All the 9 patients were eventually discharged improved.

Two of the 3 patients with growth of MSSA in wound cultures presented as abscess and cellulitis, and underwent drainage and debridement, respectively. Both patients were treated with Oxacillin. The third patient who grew MSSA in blood culture had cellulitis and was treated with antibiotics alone. All 3 patients were sent home clinically well.

A two-year old leukemia patient who was admitted due to periorbital cellulitis had wound discharge culture of Methicillin resistant *Staphylococcus epidermidis* (MRSE). This patient was sent home improved after 28 days of intravenous Vancomycin for cavernous sinus thrombosis. On the other hand, a 10-year-old patient underwent incision and drainage of a left



lateral neck abscess which grew Enterococcus spp. This patient was given Clindamycin and was discharged well.

Table 1. Distribution of Patients According to			
Isolates from Culture Studies			
No Isolate	9		
With Isolate	16		
MRSA			
CA-MRSA	10		
HA-MRSA	1		
MSSA	3		
MRSE	1		
Enterococcus spp.	1		

Eleven (42.3%) of the patients admitted for skin and soft-tissue infections had growth of MRSA in cultures. Among these, one had HA-MRSA (Table 1). This patient was admitted to another hospital for pneumonia and developed right periorbital swelling 3 days after admission. With the development of seizure and progression of eye swelling, the patient was transferred to PGH. Eye discharge culture showed MRSA but since the lesion from where the culture was taken developed 72 hours after admission from the previous hospital, this was classified as hospital-acquired MRSA based on the CDC criteria. The patient expired after two weeks of admission due to progressing pneumonia.

The demographic and clinical characteristics of patients with CA-MRSA skin and/or soft-tissue infections are shown in Table 2. The majority of the patients admitted with CA-MRSA infections were male children below 5 years old, with a mean age of 38.5 months and the median age of 13.5 months. The bulk of these patients were from Metro Manila and the rest from neighboring provinces of Cavite, Laguna, and Bulacan. No risk factors for MRSA

infection were identified in all these patients. Previous antibiotic use as a risk factor for MRSA was not considered in five patients who were given oral antibiotics for the SSTI by another physician few days prior to admission to the hospital as the infection and lesions were already present before initiation of the treatment.

History of MRSA colonization as a risk factor, however, was not included in the criteria since not all the patients had nasal swab cultures done. Of the two patients with nasal swab cultures, no MRSA was isolated. Seven of the 10 patients with CA-MRSA had normal nutritional status for age. Two patients had mild wasting and one had moderate wasting.

A large proportion of the patients had solitary lesions, located mostly in the head and neck area, and the rest were seen either at the trunk or the lower extremities. Patients with CA-MRSA infection presented with lesions either as an abscess or a cellulitis.

All the initial complete blood count of the patients had elevated white blood cell count with neutrophilic predominance. The WBC count ranges from 16.8 to 39.5, with a mean of 23.03. Fever was present in all the patients at the time of admission. Of the 5 patients with cellulitis, four were treated with antibiotics alone and one underwent tissue and bone debridement in conjunction with antibiotic administration. All the five patients with abscess were subjected to incision and drainage of the abscess together with antibiotic administration.

MRSA was isolated in cultures of exudates obtained from eight patients. Three of the 10 patients had both blood and abscess cultures done but only one patient grew the organism in both blood and aspirate cultures. Aside from abscess aspirate, other sources of cultures include ear and eye discharges as well as wound swab in a patient with leg cellulitis with a



draining sinus. The patient who presented with leg cellulitis and				
Table 2. Demographic and clinica	al profile of p	ediatric patients with CA-MRSA skin a	and soft-tissue	
infections.				
Age (months)		Type of Infection		
Range	0.5 – 216	Abscess	5	
Mean	38.5	Cellulitis	4	
Median	13.5	Abscess and cellulitis	1	
Sex		WBC count in CBC		
Male	8	Range	16.8 – 39.5	
Female	2	Mean	23.03	
		Median	22.1	
Place of Origin	_	Management		
Metro Manila	6	Antibiotic treatment alone	4	
Cavite	2	Antibiotics + incision and drainage	5	
Laguna	1	Antibiotics + debridement	1	
Bulacan Diak fastara far MDCA	1	Antibiotico		
RISK TACTORS FOR MIRSA	0	Antibiotics		
Chronia disease	0	Oxacillin	2	
Admission to long term care	0	Clindamycin	2	
facility	0	Oindaniyen	2	
Dialysis	0	Oxacillin → Clindamycin	4	
Surgery	Õ	Clindamycin → Cotrimoxazole	1	
Permanent indwelling	0			
catheters or devices	-	Vancomycin	1	
History of MRSA infection	0			
Previous antibiotic use	0			
Nutritional status		Length of Hospital Stay (Days)		
Normal	7	Range	1-43	
Mild wasting	2	Mean	16.2	
Moderate wasting	1	Median	13	
Location of Infection Outcome				
Solitary	9	Discharged	8	
Head/scalp	5	Transferred to another hospital	1	
Trunk	2	Went home against medical advice	1	
Lower extremity	2	Mortality	0	
Multiple Sites	1			

underwent tissue and bone debridement showed MRSA in the culture of bone debris (Table 3).

Four of the 10 patients were initially treated with intravenous Oxacillin but eventually shifted to Clindamycin once culture results were known. Three patients received intravenous Clindamycin empirically and were shifted to oral Clindamycin in two patients and Cotrimoxazole in one patient upon discharge. The patient who was given Cotrimoxazole had persistent MRSA growth in blood cultures despite 21 days of intravenous Clindamycin, to which the organism was sensitive to. Although the growth in blood remained, the patient was clinically improving hence he was discharged.

A single patient was treated with Vancomycin due to the extension of the periorbital cellulitis to the cavernous sinus area.



One of the two patients given Oxacillin was a case of multiple carbuncles and small abscesses in a neonate. The family opted to transfer the patient to another hospital even prior to the release of the results of wound culture studies. The other patient was a 5-month-old patient with scalp abscess at the temporal area who underwent incision and drainage, given intravenous Oxacillin for three days at the emergency room and sent home on oral Cloxacillin. The culture results showing MRSA came out after the patient was discharged.

Eighty percent of the patients with MRSA were discharged with a mean hospital stay of 16.1 days and with no mortality seen. The patient on Vancomycin went home against advice due to financial constraints and another patient was transferred to another hospital for completion of antibiotics. The patients with the longest hospital stay were those with osteomyelitis, bacteremia and cavernous sinus thrombosis with 43, 27 and 26 days, respectively.

All the MRSA isolates showed good sensitivity to Clindamycin, Erythromycin, and Tetracycline. Other antibiotics commonly used to treat MRSA such as Vancomycin and Linezolid were not tested. Cotrimoxazole was only tested in one specimen.

The period prevalence of CA-MRSA skin and soft-tissue infection among children in Philippine General Hospital from September to December 2012 is 0.36.

Table 3. Distribution of CA-MRSA isolates according to specimen type

Type of Culture Specimen	No. of Patients
Wound/ abscess aspirate (exudates)	9
Bone	1
Blood	1

Table 4.	Percentage	Resistance	of	CA-MRSA
isolates fo	or Antibiotics	Tested		

Antibiotics*	Total number of isolates tested	CA-MRSA % (n)
Chloramphenicol	5	20% (1)
Ciprofloxacin	4	25% (1)
Clindamycin	8	0%(8)
Cotrimoxazole	1	0% (1)
Erythromycin	8	0% (8)
Oxacillin	8	100% (8)
Penicillin G	8	100% (8)
Tetracycline	5	0% (5)

*Vancomycin and Linezolid were not tested

DISCUSSION:

Among pediatric patients admitted for skin and soft-tissue infections, 64% had isolates from culture studies with majority of them showing community-acquired MRSA. The mechanism of resistance of MRSA is conferred by the presence of mecA gene in the S. aureus chromosome. The gene encodes for the production of unique penicillin-binding protein (PBP) with markedly reduced binding affinity to beta-lactam antibiotics compared to an intrinsic set of PBPs. However, there are some cases of MRSA infections which demonstrate the absence of this mecA gene. The mechanism of resistance in these particular cases is hypothesized to be from hyperproduction of beta-lactamase.²

This study, although with a limited number of patients, further supports the findings of previous studies that CA-MRSA are typically associated with skin and soft-tissue infections ^{1,3,5,6,7,8, 12} presenting mostly as simple solitary abscesses or cellulitis in our cohort of patients. These infections were mostly seen among very



young healthy male children with no known risk factors for MRSA. In contrast to a study done in Texas where they concluded that there is no difference in age and sex among pediatric patients with CA-MRSA and CA-MSSA¹², the findings in this present study are consistent with other reports of SSTIs due to CA-MRSA being more frequent among males³. All previous studies^{3,11,12,13} have consistently shown that many patients with CA-MRSA infections are healthy children who do not have identified risk factors for acquisition of MRSA as demonstrated also in this study. This observation does not only corroborate the results of previous studies but also emphasizes that community-acquired MRSA infections are becoming more frequent in our pediatric patients despite the absence of risk factors for MRSA.

Noteworthy from this study are the findings of very young children with median age of 13.5 months who have CA-MRSA SSTI infections located most commonly in the head and neck region. Findings in the study of Athar et al.¹⁴ also showed that the head and neck was the most frequent site of soft tissue abscesses in children. However, there was a high frequency of malnourishment among their subjects which is in contrast to the majority of the patients seen in our study who had normal weight for age. This observation may be attributable to a selection bias in terms of the quality of patients admitted to our institution, where patients who are very young, sick-looking and with more complicated lesions located at critical areas are likely to be brought to the hospital for a consult and are eventually admitted. This is supported by the presence of signs and symptoms of systemic involvement such as fever upon admission in all our patients with CA-MRSA and the findings of relatively high initial peripheral WBC count with mean and median values of 23.03 and 22.1, respectively. On the other hand, Stryjewski and Chambers³ report that abscess and cellulitis caused by CA-MRSA are usually solitary lesions located at the extremities, with fever and leukocytosis often absent in patients with an abscess.

Similar to the findings of Uy-Aragon et al.¹¹, the most common source of isolates for CA-MRSA infections in this study were from exudates which include abscess aspirate, wound swab, ear and eye discharges. Although CA-MRSA infections predominantly present as skin and soft-tissue infections and only one of the three patients with blood cultures yielded positive results in this study, the ability of this organism to cause invasive disease must also be emphasized ^{5,7,12,15}. Included among the clinical syndromes associated with CA-MRSA infections which were seen in our patients were bacteremia, osteomyelitis and cavernous sinus thrombosis which presented initially as preauricular, thigh, periorbital swelling, and respectively.

CA-MRSA can be differentiated from health care-associated MRSA (HA-MRSA) by molecular characteristics. HA-MRSA is associated with large staphylococcal chromosomal cassette mec (SCCmec) elements belonging to types I, II and III whereas CA-MRSA carries smaller SCCmec of types IV or V. The former is often resistant to many classes of non-beta lactam antibiotics but CA-MRSA is usually resistant to fewer classes of non-beta lactams and they also frequently carry the virulence factor Panton-Valentine leukocidin (PVL) which is related to abscess formation and tissue necrosis.^{1, 2, 3}

An international surveillance study from September 2004 to August 2006 involving 17 medical institutions from eight Asian countries including the Philippines, demonstrated an increasing prevalence of MRSA infections. MRSA accounted for 25.5% of all community acquired *Staphylococcus aureus* infections and 67.4% of



hospital associated infections. Among CA-MRSA infections, the most common type was skin and soft-tissue infection comprising 66.7%. Also noteworthy is the finding from the above study that MRSA isolates of SCCmec type IV, representing a major genotype of CA-MRSA in Asian countries, were found among hospitalassociated (HA-MRSA) infections in Taiwan, Korea, and the Philippines. The presence of some HA-MRSA isolates with the same genotypic characteristics as that of CA-MRSA suggests the spread of MRSA between the community and hospitals in these countries.⁹ However, since only one institution from the Philippines participated in this study, it is unknown if the same findings hold true for the whole nation.

Similarly, several studies have been conducted in major teaching and training hospitals documenting this increasing trend of MRSA infections from the community. In a prospective observational study done in a tertiary renal center from November 2008 to October 2009, MRSA comprised 30% of all Staphylococcus aureus isolates. Among these MRSA isolates, 43% were community acquired (CA-MRSA) and a significantly high proportion of 69% of these CA-MRSA presented as skin and soft-tissue infections.¹⁰ Likewise, a review of *S. aureus* infections from 1991 to 2001 in Philippine Children's Medical Center, a tertiary government hospital, showed an increasing trend of *S. aureus* and MRSA infections. A more recent study from 2004-2006 conducted in the same institution also showed that MRSA consisted 57% of community acquired *S. aureus* infections.¹¹

Management of pediatric patients with CA-MRSA SSTIs is not absolute and very well defined. In this study, management of patients is variable. Administration of antibiotics and/or performance of surgical procedures depend mostly on the clinical presentation of the patients and the evaluation of their admitting physician. In the cohort of subjects included in this study, all patients with abscess underwent incision and drainage procedure in conjunction with antibiotic administration. This conforms to expert recommendations that surgical drainage is essential for the cure of soft-tissue abscesses hence it must be the primary treatment for these infections ^{3,15}. The role of surgical drainage alone in the clinical cure of patients is still controversial. However, experts recommend antibiotic therapy in addition to surgery in patients with abscesses >5cm in diameter³, with systemic or extensive disease, in those with comorbidities, immunosuppression or extreme age, those with lesions at areas difficult to drain and in patients who did not respond to incision and drainage¹⁵.

The variability in the management of SSTIs in children is also evident in the choice of antibiotics administered to patients. The majority of patients were initially given Oxacillin but were eventually shifted to Clindamycin once culture The results were known. general recommendations regarding the choice of empiric antibiotics for outpatients with SSTI is to give beta-lactams for nonpurulent cellulitis^{15,16} and empiric coverage for CA-MRSA pending culture results for purulent cellulitis¹⁶. For hospitalized patients with complicated SSTIs, i.e. those with deep-seated infections, surgical or traumatic wounds, major abscesses, cellulitis and infected burns and ulcers should receive coverage for MRSA¹⁶. Some authors consider the prevalence of CA-MRSA isolates in a community at 10-15% or more should warrant empiric treatment for MRSA⁶. In our study, the fourmonth period prevalence for CA-MRSA among children with SSTI is 0.36 which is relatively high. However, the study was only done over a short duration of time hence it may not accurately represent the actual prevalence of CA-MRSA in the community. Nonetheless, it should not



discount the findings of this study that CA-MRSA SSTI is an emerging concern among Filipino children.

All CA-MRSA isolates showed susceptibility to clindamycin, tetracycline, and cotrimoxazole. Tetracycline is not recommended for patients <8 whereas cotrimoxazole is not years old recommended by some experts due to its association with treatment failure for nonpurulent SSTIs caused by group А streptococcus^{6,16}, limited data on its efficacy as a and treatment for MRSA issues of hypersensitivity and bone marrow suppression⁶. For hospitalized patients with complicated SSTIs, vancomycin is recommended ¹⁵. But due to the high cost of this drug, Clindamycin is a good alternative as empiric therapy especially if the patient is stable¹⁵. However, the existence of inducible resistance to clindamycin should caution medical practitioners to request for Dtest for all erythromycin-resistant clindamycinsusceptible MRSA isolates¹⁶. If the test is not done routinely in the laboratory and clinicians should monitor patients closely for signs of clinical failure. In such cases where treatment failure with clindamycin is likely and treatment of certain clinical conditions such as CNS infections where clindamycin is not suited, vancomycin is the recommended therapy.¹⁵

It is reasonable that those patients presenting initially with SSTIs but with deep-seated and infections will require invasive prolonged hospital stay. Despite these complicated diseases, no mortality was seen among the patients and majority of them were discharged well. However, follow-up post-discharge was not included in the scope of this study hence, the total duration of antibiotics therapy, clinical cure, recurrence of infections or relapse, or complications, if any, were not determined.

Limitations of this study include the short duration of observation and the inclusion of

patients presenting initially with SSTIs only, both of which may not accurately capture the actual local prevalence and demographics of CA-MRSA infections among our pediatric patients. In addition, no follow-up was done after discharge hence duration of antibiotics, response to treatment or occurrence of complications were unknown.

CONCLUSIONS:

CA-MRSA as a cause of skin and soft-tissue infections in Filipino children is common, presenting as simple solitary abscesses or cellulitis at the head and neck areas in the majority of cases and as deep-seated infections in some. SSTIs were mostly seen among very young healthy male children with no known risk factors for MRSA.

Management of SSTIs should include incision and drainage of abscesses and prompt submission of the aspirate specimen for culture and sensitivity testing as this will likely yield the etiologic agent. In this study, the period prevalence of CA-MRSA among pediatric patients with SSTIs is high but this maybe an over or underestimation of the true prevalence of CA-MRSA infection in the local setting. Hence, the choice of empiric antibiotics for SSTIs among pediatric patients admitted in our institution should be individualized and must be based on sound clinical evaluation and judgment. Empiric antibiotics with MRSA coverage such as clindamycin or vancomycin should be considered in appropriate clinical situations where MRSA is likely.

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