

Challenge M112-4

August 2011

Blood: methicillin-resistant *Staphylococcus aureus* (MRSA)

HISTORY

A sample simulating blood obtained from a one year old male admitted with empyema (as a complication of previous surgery) was sent to category A labs.

Participants were expected to isolate, identify, and perform susceptibility on the isolate. Laboratories were also expected to report the isolation of MRSA to infection control (IC).

CMPT QA

CMPT quality control yielded a pure culture of methicillin resistant *Staphylococcus aureus* viable for at least 18 days.

SURVEY RESULTS

Reference Labs

15/15 labs reported MRSA and to IC. 14 labs reported oxacillin resistant (R), 1 lab did not report, but did report MRSA. 15/15 labs reported Vancomycin susceptible (S). As a result of the consensus amongst the reference labs, the identification, infection control notification, and susceptibility testing elements of the challenge were suitable for grading.

Participants

Identification (Table 1) 92% of the participants correctly identified the isolate as a MRSA and were graded 4. Two laboratories reported *S. aureus*, but not a MRSA, and were graded 0.

One participant reported the isolate as coagulase negative staphylococcus (CNS) and was graded 0. Those laboratories that do not normally process this kind of sample were ungraded.

Table 1. Identification results

Reported	Total	Grade
MRSA	75	4
<i>S. aureus</i> , refer	1	0
<i>S. aureus</i>	1	0
CNS	1	0
snp	4	ungraded
Total	83	

snp: sample not normally processed; CNS: coagulase negative *Staphylococcus*

Infection control notification (Table 2) All, but three, laboratories indicated they would report to the Infection Control department or to Public Health and were graded 4. Those labs that did not report to Infection Control or Public Health were graded 0, including one participant who explained that they would consider this isolate a critical result and thus, they would contact the physician (see comment A).

Table 2. Infection control notification

Reported	Total	Grade
yes	74	4
PH (Public Health)	2	4
comment A	1	0
Not done?	2	0
snp	4	ungraded
Total	83	

snp: sample not normally processed

Comment A. *Staphylococcus aureus* (MRSA) in 1 out of 1 bottle (aerobic bottle). Critical result, phoned gram stain result to Dr. ABC (RN or physician most responsible for patient) on 18/8/2011 at 1300 by XXXX.

Antimicrobial susceptibility (Table 3)

Amongst the laboratories that process blood cultures, all reported oxacillin resistant and/or reported MRSA and were graded 4.

83% of laboratories reported vancomycin susceptible and were grade 4. One participant did not report a vancomycin susceptibility result, but did comment that the isolate would be referred for susceptibility testing and was ungraded. The nine laboratories that did not report a vancomycin susceptibility result were graded 0.

COMMENTS ON RESULTS

In general, laboratories successfully isolated and correctly identified the MRSA from this simulated blood culture. Labelling the isolate as MRSA in the identification is important and laboratories which failed to do this were given a grade of 0.

As per previous CMPT critiques¹ pertaining to MRSA, the purpose of reporting is to ensure

Grading

Maximum grade: 16

The following components were graded:

Identification

Reporting MRSA was graded 4.

Reporting *S. aureus* only was considered unacceptable and was graded 0.

Reporting CNS was considered unacceptable and graded 0.

Notification to IC

Reporting to IC or PH was graded 4.

Not reporting or just calling the doctor was considered unacceptable and was graded 0.

Susceptibility to oxacillin and vancomycin

Reporting the organism resistant to oxacillin or reporting as MRSA was graded 4.

Reporting vancomycin susceptible or referring the sample for susceptibility testing was graded 4.

Not reporting vancomycin susceptibility was graded 0.

Table 3. Reported susceptibility results

Reported oxacillin	Total	Grade
R	74	4
no report (but reported MRSA)	5	4
snp	4	ungraded
Total	83	

Reported vancomycin	Total	Grade
S	69	4
no report	9	0
refer	1	ungraded
snp	4	ungraded
Total	83	

snp: sample not normally processed

that appropriate isolation precautions are put in place. In facilities that do not have specific infection control staff, the laboratory should notify the ward staff about the MRSA isolate and the report should indicate that isolation precautions are needed. Even contacting a physician by phone with the Gram stain result and later with the susceptibility result does not necessarily ensure that appropriate precautions are instituted. Therefore failure to specifically alert for isolation precautions is graded as 0.

All laboratories successfully determined the isolate to be oxacillin resistant. A large majority of participants (83%) successfully tested and reported vancomycin as susceptible. As vancomycin is typically chosen to treat MRSA bacteremia, laboratories are expected to test and report vancomycin susceptibility results or else refer to a reference laboratory for susceptibility testing.

IDENTIFICATION

Routine identification of *S. aureus* usually involves tube coagulase tests or latex agglutination test. Other tests such as DNase tests and negative results in slide coagulase tests should be confirmed with tube coagulase or latex agglutination tests.²

ANTIMICROBIAL SUSCEPTIBILITY

Standard routine susceptibility testing methods are generally sufficient to determine susceptibility of *S. aureus* to the different antimicrobial agents. Detection of penicillin binding protein 2a (PBP 2a) by latex agglutination methods or using polymerase

chain reaction (PCR) methods to detect the *mecA* gene are usually reserved for the confirmation of equivocal results.²

Oxacillin disk diffusion or the 30 µg cefoxitin disk tests are used to determine methicillin resistance. The cefoxitin disk test has shown to be more efficient in predicting methicillin resistance and thus, cefoxitin is preferred over oxacillin for the recognition of MRSA.³

Warning: MRSA strains that show susceptibility in vitro to oxacillin and cefoxitin have been described.⁴

Laboratories may hasten the presumptive reporting of MRSA isolates by culturing samples from positive blood culture vials that demonstrate Gram positive cocci in clusters directly onto MRSA chromogenic media.

CLSI states that disk testing is not reliable for testing vancomycin and that MIC tests should be performed to determine the susceptibility of all isolates of staphylococci to vancomycin.³ In 2006, the vancomycin MIC breakpoints for *Staphylococcus aureus* were lowered (from ≤4 mg/L to ≤2 mg/L for “susceptible”) to increase detection of heterogeneously resistant isolates.⁵

Recent studies have questioned the treatment of serious MRSA infections with vancomycin because of treatment failures, despite vancomycin MICs in the “susceptible” category (i.e. MICs of = 2 mg/L).⁶⁻⁹ Additionally, there have been some discordant MIC results between different susceptibility test methods.⁹⁻¹² Until more reliable tests are available to determine the vancomycin susceptibility of MRSA strains that is predictive of treatment outcome, an interim testing solution is needed. Hsu et al. have proposed that E-test be used simultaneously with automated systems and broth microdilution methods for MRSA strains isolated from sterile body sites which are associated with invasive infections, patients with high APACHE II score, or cases associated with prolonged therapy or therapy relapse.¹²

CLINICAL RELEVANCE

Staphylococcus aureus bacteremia is often associated with a local focus of infection that has gained access to the bloodstream and it carries increased morbidity and mortality.¹³

Pneumonic sources are frequently involved in *S. aureus* bacteremia as this organism shows a propensity to invade the bloodstream from

Infection Control

Hand hygiene is an essential element of infection control. Although the benefits of hand hygiene were first documented by Semmelweis in 1846 and many studies have demonstrated impressive reductions in the incidence of MRSA transmission with improvement in hand hygiene adherence,²¹ adherence rates of less than 70% after the deployment of an intervention by health care workers have been reported.²²

Isolation of infectious individuals has been used as a method of infection control for thousands of years. Jerningan and colleagues showed a 15 fold increase in the transmission rate of MRSA to uncolonized patients when patients were not placed in isolation precautions.²³

The usefulness of active surveillance in the reduction of MRSA transmission has been more variable and relies heavily on the timely availability of the results of microbiological sampling and the use of PCR or other rapid testing methods.²²

The main limitation of these strategies is adherence to basic measures by the health care workers, as Hebert explains:

*“The entire effectiveness of this approach absolutely depends on the adherence of providers to more basic practices such as hand hygiene and the use of personal protective equipment. Shortcomings in adherence to these standards will ultimately limit the overall effectiveness of even the most sophisticated control strategy.”*²²

them. In a review, nosocomial *S. aureus* pneumonia accounted for 8% of all bacteremias, 30% of all nosocomial bacteremias, and 68% of bacteremias in patients in the ICU. ¹⁴

Staphylococcus aureus is the leading cause of nosocomial and health care-associated bacteremias which in turn are more likely to be caused by methicillin-resistant *S. aureus* (MRSA). ¹⁵

The reservoir of MRSA is infected and colonized patients, and the major mode of transmission from patient to patient is on the contaminated hands of healthcare workers.

Methicillin-resistant *Staphylococcus aureus* is a major cause of hospital-acquired infections (HAI). In Europe, the extra in-hospital costs attributed to MRSA infections are estimated to reach approximately 380 million euros annually. ^{16,17}

Vancomycin has been the cornerstone of therapy for serious MRSA infections for many years but, as noted above, concerns about its efficacy have been increasing.⁸ The failure of treatment with vancomycin has been attributed to its slow bactericidal activity, reduced susceptibility of organisms, and the presence of sub-therapeutic concentrations.^{5,7,8,18}

Pharmacodynamic studies have shown that the area under the vancomycin concentration curve-to-MIC ratio (AUC/MIC) is the optimal method for predicting vancomycin efficacy against *S. aureus* infections.¹⁹ The probability of achieving an optimal AUC/MIC ratio is much lower when the vancomycin MIC is 2 mg/L than when it is 1 mg/L. For highly susceptible MRSA strains (MIC ≤ 1 mg/L) vancomycin remains effective but for isolates with higher MICs the treatment of choice remains.

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