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Abstract

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Title: Antimicrobial resistance profile and genetic characteristics of Methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from otolaryngology and pediatric outpatients

Purpose: To elucidate the antimicrobial resistance profile and genetic characteristics of MRSA isolates recovered from patients seen in otolaryngology and pediatric outpatients with ear discharge and upper respiratory tract infections. In addition, as there is an increasing trend in the prevalence of community-acquired MRSA (CA-MRSA) in Japan, our goal was to better understand the distribution and genetic characteristics of these isolate.

Method: *S. aureus* isolated recovered from ear discharge and nasopharynx specimens along with the associated case history were obtained from 6 healthcare sites participating in the study.

Minimum inhibitory concentration (MIC) testing of isolates was performed according to the Clinical and Laboratory Standards Institute (CLSI) agar dilution method. A S. aureus isolate with a cefoxitin MIC ≧8μg/mL was classified as MRSA. PCR was used for detection of the *mecA* gene as well as SCC*mec* typing. The MRSA isolates classified as SCC*mec* type Ⅳ and Ⅴ were examined for carriage of the PVL gene.

The clinical background associated with the sample was used to determine whether the isolate met the definition of a CA-MRSA case which was a patient with MRSA with no history of the following: hospitalization, residence in a long-term care facility a medical procedure such as surgery, dialysis or implanted medical devices at the time of MRSA isolation within a past year or previous MRSA infection or colonization. An isolate was determined to be CA-MRSA on the basis of carriage of SCC*mec* type IV or V and if the clinical background met the case definition of a CA-MRSA case. All other isolates were considered to be hospital-acquired MRSA (HA-MRSA).

Results: Of the 663 *S. aureus* isolates, 126 (19.0%) were MRSA. MRSA isolation rates from the 6 study sites were variable: facility A, 35/214 (16.4%), facility B, 2/27 (7.4%), facility C, 24/89 (27.0%), facility D, 55/144 (38.2%), facility E, 4/33 (12.1%), and facility F, 6/156 (3.8%).

MRSA isolates were recovered from all participating facilities, and testing confirmed that all isolates carried the *mecA* gene.

None of the 126MRSA isolates tested were resistant to vancomycin. Resistance rates in the MRSA isolates were as follows: Imipenem, 21/126 (16.7%), minocycline, 55/126 (43.7%), clindamycin, 56/126 (44.4%), gentamicin, 64/126 (50.8%), erythromycin, 89/126 (70.6%), amoxicillin, 104/126 (82.5%), and levofloxacin, 105/126 (83.3%).

The distribution of SCC*mec* types of the MRSA isolates were SCC*mec*II, 48/126 (38.1%), SCC*mec*III, 1/126 (0.8%), SCC*mec*IV, 61/126 (48.4%), SCC*mec*V, 3/126 (2.4%). And 13/126 (10.3%) isolates were non-typeable (NT). SCC*mec* type IV was detected in all six outpatient facilities with the highest detection rates at facilities A and C (50.0% and 76.0%, respectively), followed by SCC*mec* type II (32.4% and 20.0%, respectively). Overall, SCC*mec* type II was the most frequently detected at 58.2%, followed by SCC*mec* type IV which was detected at frequency of 29.1%.

Of the MRSA isolates studied, 56.6% were CA-MRSA (SCC*mec* type IV and V) while 43.4% were HA-MRSA (SCC*mec* type II and III). Only one isolate carrying the PVL gene was detected (facilities C and E).

Among the 113 MRSA isolates, 29 (45.3%) isolates from outpatient sites were CA-MRSA compared to 35 (54.7%) from hospital sites, while 11 (22.4%) HA-MRSA isolates were observed from outpatient sites compared to 38 (77.6%) isolates from the hospital sites.

Not all of the MRSA isolates classified as CA-MRSA and HA-MRSA according to SCC*mec* type met the clinical definitions used to characterize isolates as CA-MRSA and HA-MRSA.

Conclusion: The overall isolation rate of MRSA from outpatients seen in otolaryngology and pediatrics was 19.0% of the total number of MRSA isolates studied which is consistent with the severity of disease and antimicrobial usage in the hospital setting.

While genetic analysis showed that over half of the MRSA isolates recovered from outpatients were CA-MRSA, HA-MRSA compromised about 40% of the MRSA isolates, a relatively high percentage, reflecting extensive HA-MRSA emergence outside of the hospital-setting. As HA-MRSA exists in both the hospital and outpatient settings, the findings show that HA-MRSA has already expanded outside the hospital setting resulting into the contraction of MRSA in the community and detection in the outpatient setting. This trend is consistent with changes in the healthcare environment where repeat courses of antimicrobial treatment are administered and more invasive medical procedures are performed in the outpatient setting. As a result, it is necessary to select the most appropriate antimicrobial agents, as well as, provide medication guidance and continued treatment until clinical cure is achieved.

In the classification of CA-MRSA and HA-MRSA, differentiation based only on the clinical background is difficult, however, as genetic analysis is not practical in the administration of routine medical care, antimicrobial susceptibility profiles may be useful in classifying MRSA isolates as CA-MRSA or HA-MRSA.

In the outpatient setting, many patients have relatively mild illnesses, but in recent years, due to the use of highly invasive medical procedures, attention must be paid to the possibility of severe illness caused by CA-MRSA. While infections seen in the outpatient setting are usually relatively minor, as more invasive procedures are performed in the outpatient setting, there is a need to be alert to the potential of invasive infections caused by PVL gene positive CA-MRSA.