EDITORIAL

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Microbiological and genotypic factors affecting mortality in methicillin-resistant *Staphylococcus aureus* bacteremia

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Staphylococcus aureus causes a wide range of skin, soft tissue, bone, and joint infections and invasive infections associated with indwelling catheters or prosthetic devices, bacteremia, endocarditis, and pneumonia. Methicillin-resistant *S. aureus* (MRSA) is a leading cause of nosocomial bacteremia and is associated with increased morbidity and mortality compared to susceptible isolates in *S. aureus* bacteremia (SAB) [1]. MRSA features associated with poor clinical outcomes include the vancomycin minimum inhibitory concentration (MIC), vancomycin heteroresistant phenotype, expression of virulence toxins, and accessor gene regulator (*agr*) functionality. In a prospective cohort of Korean patients with MRSA bacteremia, Kim et al. [2] found that the severity of illness was significantly associated with early mortality. Interestingly, a higher vancomycin MIC was inversely associated with severe sepsis or septic shock [2].

It is controversial whether SAB caused by an isolate with reduced vancomycin susceptibility is associated with poorer outcomes than that caused by isolates highly susceptible to vancomycin [3-5]. Paradoxically, a higher risk of mortality has been seen with an E-test for an MIC < 1 μg/mL than for an MIC > 1.5 μg/mL [6]. In a study of the fitness of MRSA and glycopeptide-intermediate *S. aureus* strains, a reduction in the growth rate was observed in the two strain types [7]. *S. aureus* strains with high vancomycin MICs might be less virulent than strains with low vancomycin MICs. Therefore, an increase in vancomycin MIC within the susceptible range might be a surrogate marker for intrinsic microbiological traits and not associated with worse clinical outcomes [8].

Another important issue is whether the virulence factor of MRSA strains increases mortality in MRSA infections, especially by community-genotype strains. The USA300 clone is most often associated with community-acquired (CA) skin and soft tissue infections and belongs to multilocus sequence type (ST) 8. This isolate characteristically contains the SCC*mec* type IV element and a phage carrying the genes encoding Panton-Valentine leucocidin (PVL), which involves in interactions between the pathogen and neutrophils and contributes to the establishment of *S. aureus* infection and determines the increased virulence of CA-MRSA compared to hospital-acquired MRSA. In South Korea, a PVL-negative CA-MRSA clone, ST72-SCC*mec* type IV, is widespread in both the community and hospitals [9,10]. Despite heightened

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concerns that ST72 MRSA may cause more severe disease and have poorer clinical outcomes than the hospital-genotype strain ST5-SCC*mec* type II, the clinical impact of ST72 MRSA on mortality in patients with MRSA bacteremia indicates that it has relatively lower virulence [11]. Although it is still not clear what virulence factor has facilitated the successful settlement of ST72 MRSA in healthcare settings, the introduction of ST72 MRSA into Korean hospitals seems to have fewer adverse effects with regard to disease distribution and all-cause mortality in patients with nosocomial MRSA infections [9].

In a prospective study of the risk factors for persistent MRSA bacteremia in the Korean population [12], no significant differences in the vancomycin MIC distribution or genotypic distribution of putative virulence genes and *agr* dysfunction were found in MRSA isolates between groups with persistent and resolving bacteremia. Clinical features such as the severity of illness, site of infection, and control of infection sources may have a greater effect on persistent MRSA bacteremia and risk for death from MRSA bacteremia, rather than the microbiological and genotypic features of the MRSA strain. Given the limitations of available treatments, especially with regard to vancomycin, which has a relatively slow onset of bactericidal activity and poor penetration of infected tissues, an early imaging approach that identifies hidden sources of infection and removes them by drainage and debridement should be implemented as a treatment strategy in MRSA bacteremia. Timely and appropriate vancomycin dosing may play a significant role in clinical and microbiological success.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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