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Differing epidemiology of two major healthcare-associated meticillin-resistant *Staphylococcus aureus* clones

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SUMMARY

Background: Two meticillin-resistant *Staphylococcus aureus* (MRSA) clones, sequence type (ST) 22 and ST239, have successfully spread globally. Across Australia, ST22 has supplanted ST239 as the main healthcare-associated MRSA. To understand the reasons underlying this shift, the epidemiology and clinical features of infections due to ST22 and ST239 MRSA isolates from a tertiary hospital in Melbourne, Australia were compared.

Methods: Over six months, consecutive MRSA isolates with clinical data were collected from specimens referred to Alfred Health Pathology (AHP). Isolates were genotyped by a multi-locus-sequence-typing-based high-resolution melting method.

Findings: Three hundred and twenty-eight of 1079 (30%) *S. aureus* isolated by AHP were MRSA. Of these, 313 were genotyped; 78 (25%) were clonal complex (CC) 22 (representing ST22) and 142 (45%) were CC239 (representing ST239). Common clinical syndromes included skin or soft tissue, respiratory tract and osteo-articular infections. On multivariate logistic regression, compared with CC239, CC22 was associated with older patients [adjusted odds ratio (aOR) 1.04 for each year increase, 95% confidence interval (CI) 1.02–1.07)], and patients from subacute hospitals (aOR 2.7, 95% CI 1.2–5.8) or long-term care facilities (LTCFs; aOR 5.5, 95% CI 2.0–14.5). Median time from patient admission to MRSA isolation was nine days for CC239 and one day for CC22 ($P < 0.01$). MRSA strain epidemiology varied according to hospital unit.

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Conclusions: CC22 and CC239 MRSA have differing ecological niches. CC22 is associated with elderly patients in LTCFs, and CC239 is associated with nosocomial acquisition. Infection control strategies involving LTCFs and their residents will likely be required to achieve continued MRSA control.

Introduction

Meticillin-resistant *Staphylococcus aureus* (MRSA) first emerged in healthcare settings in the 1960s, and has subsequently spread through hospitals worldwide.[1] The acquisition of antimicrobial resistance provides a selective advantage in the nosocomial environment, and has complicated treatment regimens significantly. Today, MRSA is a major cause of morbidity and mortality in hospitals and the community.[2–7]

Circulating MRSA clones vary between hospital and community settings. A small number of MRSA clones have dominated globally in hospital settings, and progressive waves of different clones have occurred over time.[8,9] Currently, sequence type (ST) 22 (EMRSA-15) has been growing in importance in the UK, Europe, South-East Asia (i.e. Singapore) and Australia, and is replacing other MRSA clones (ST36 or EMRSA-16 in the UK, ST239 in Singapore and Australia).[10–13]

This study was performed to determine the relative prevalence of the healthcare-associated MRSA (HA-MRSA) clones ST22 and ST239 in a tertiary referral centre and affiliated hospitals in Melbourne, Australia. Clinical features were compared and differences were identified between these two clones to further our epidemiological understanding of why ST22 is increasingly prevalent.

Methods

Setting

Alfred Health Pathology (AHP) services the three hospitals of Alfred Health (The Alfred Hospital, Caulfield Hospital and Sandringham Hospital), all located in the inner south-east of Melbourne, with a total of approximately 580 acute inpatient beds and 220 subacute beds. The Alfred Hospital is a tertiary referral centre, while Caulfield and Sandringham Hospitals are smaller healthcare facilities with a large number of rehabilitation and long-term care facility (LTCF) beds (including aged care facility beds). Consecutive MRSA isolates were collected from clinical specimens referred to AHP between 1 July and 31 December 2010. Repeat isolates from a patient with the same antibiogram within 30 days were excluded. Samples collected for screening purposes were not included in the study.

Microbiology and typing

Isolates resembling Gram-positive cocci that were latex agglutination positive (Pastorex Staph-Plus, Bio-Rad, Hercules, CA, USA) were confirmed as *S. aureus* by the Vitek 2 Gram-positive identification card (bioMérieux, Marcy-l'Étoile, France). A DNAse plate was used to confirm isolate identification as *S. aureus* if latex agglutination and Vitek 2 gave discordant results. Meticillin resistance was identified by cefoxitin disc diffusion (using the breakpoints of the Clinical and Laboratory Standards Institute) and the Vitek 2 AST-P612 Gram-positive susceptibility card. Evaluation for penicillin-binding protein (PBP2′) by the Thermo Scientific Oxoid PBP2′ Latex Agglutination Test (Thermo Fisher Scientific Inc., Waltham, MA, USA) was used to delineate discordant Vitek 2 and cefoxitin susceptibility results. Susceptibility to other antimicrobials was performed by the Vitek 2 AST-P612 Gram-positive susceptibility card (see Table A, online supplementary material). MRSA isolates resistant to at least three non-beta-lactam antibiotics in different antibiotic classes were defined as multi-resistant MRSA (lincosamides and macrolides were considered a single antibiotic class); all other isolates were non-multi-resistant MRSA.[14]

Isolates were typed using a multi-locus sequence typing (MLST)-based high-resolution melting scheme that provides inferred MLST clonal complexes (CC), as described previously.[15] Isolates typed as CC22 and CC239 have previously been determined to represent ST22 and ST239 accurately in this context.[15] It was confirmed that the antibiograms of those typed as CC22 or CC239 were consistent with the typical antibiograms of known ST22 and ST239.[13]

Clinical details and definitions

Demographic and clinical data were collected on all patients by chart review. For the purposes of this study, patients occupying LTCF beds at Alfred Health were considered as community LTCF residents rather than Alfred Health inpatients. MRSA infections were defined as healthcare associated if any of the following criteria were met:[16] (a) discharge from a healthcare facility within the previous 30 days; (b) resident of a LTCF; (c) current haemodialysis, day oncology, home nursing or hospital in the home patient; or (d) if MRSA was isolated from a specimen collected >48 h after hospital admission. All other infections were considered to be community associated. Healthcare-associated infections were further divided into nosocomial and non-nosocomial. Nosocomial healthcare-associated infections represented MRSA acquired in the hospital setting (i.e. history of acute hospital admission within the last 30 days, or MRSA isolation >48 h after current hospital admission) and non-nosocomial healthcare-associated infections represented all other healthcare-associated infections. An implant-related infection was assumed if the isolate was recovered from a site directly involving a foreign body (e.g. intravascular catheter, indwelling urethral catheter, orthopaedic fixation device). For the purposes of this study, isolates for which a clinical syndrome was documented and specific treatment was provided were deemed to be clinically significant. Isolates that were not treated were deemed to be clinically non-significant.