Changing epidemiology of community-acquired methicillin-resistant *Staphylococcus aureus*

Increasing rates of methicillin-resistant *Staphylococcus aureus* (MRSA) globally have been accompanied by the increase in MRSA infections among healthy individuals in the community without apparent risk factors. This emergence of community-acquired MRSA (CA-MRSA) strains over the past decade represents a significant change in the epidemiology of MRSA infections.[1] Community-acquired MRSA infections are now regarded as a serious public health concern.[2] The Centers for Disease Control and Prevention (CDC) defines CA-MRSA as MRSA isolated in an out-patient setting, or isolated from patients within 48 hours of hospital admission. Furthermore, these patients must have no medical history of MRSA infection/colonisation or have been admitted to a healthcare institution in the past year.[3]

Sporadic cases of CA-MRSA infection have been appearing since the 1980s and its prevalence is increasing worldwide.[4] It has been described as an endemic pathogen in the USA, Europe and Australia.[5] Outbreaks of CA-MRSA have been reported in community settings (e.g., athletic team facilities, correctional facilities, military training camps) as those who encounter frequent skin-to-skin contact and share personal items, particularly where there is a higher incidence of MRSA carriage, show an increased risk of CA-MRSA acquisition.[6]

Early characterisations of CA-MRSA strains demonstrate several differences from conventional endemic hospital-acquired MRSA (HA-MRSA). First, CA-MRSA can cause infection in otherwise healthy individuals, especially children and adolescents. These strains have been shown to be more susceptible to antibiotic classes other than β-lactam antibiotics, their genotypes differ from those of HA-MRSA primarily by harbouring different methicillin resistance cassettes, and they are more likely to encode the putative virulence factor Panton-Valentine leukocidin (PVL). However, over recent years the once-clear distinction between HA-MRSA and CA-MRSA strains has begun to fade.[5]

A number of molecular techniques have been used to establish the prevalence and molecular evolution of MRSA. In general, 'band-based' and 'sequence-based' methods can be used to investigate the genetic background of MRSA; however, sequence-based methods have proved more popular because the data obtained are exchangeable between different laboratories worldwide. The typing methods most commonly used today are pulsed field gel electrophoresis (PFGE), multilocus sequence typing (MLST), spa typing and SCC*mec* typing. While PFGE, a band-based method, remains the gold standard, its lack of reproducibility, relatively high cost and long turnaround time has led to the emergence of MLST as the method of choice for many laboratories.[3]

Clinically, the vast majority (70–80%) of CA-MRSA manifest as skin and soft tissue infections (SSTIs) including pyogenic skin infections,[7] and these also have the potential to cause serious life-threatening illnesses, most notably pneumonia.[8] In recent years the types of infection caused by CA-MRSA have become more diverse and serious, which strengthens the suggestion that certain strains of CA-MRSA may be more virulent than HA-MRSA.[8] Examples of this have been reported in various studies which show CA-MRSA to be the primary cause in such diseases as severe necrotising pneumonia, fatal sepsis,[9] surgical site infection,[1] chronic wound infection, urinary tract infection (UTI), infections of the eye and orbit, meningitis, sinusitis[7] and rhabdomyolysis.[10]

The majority of CA-MRSA primary cases are resolved with appropriate treatment; however, a small number of these cases may develop severe life-threatening infections, denoted CA-MRSA-related secondary infections, which include pelvic abscess, lung abscess, osteomyelitis, arthritis, brain abscess, myositis and endocarditis.[7] Community-acquired MRSA has been reported as a causative agent of respiratory infection in cystic fibrosis patients,[11] and has been acknowledged to be a contributory factor in a number of pandemics such as human immunodeficiency virus (HIV) infection and, more recently, with swine influenza (H1N1).[12,13]

Several reports have described severe co-infection with seasonal influenza virus and CA-MRSA. A 2010 Australian study reported cases of swine influenza (H1N1)/CA-MRSA co-infection.[13] An important finding from this study highlighted that PVL was not necessary for the development of CA-MRSA pneumonia in the setting of pandemic A(H1N1) 2009 influenza virus co-infection.[13] This questions the previously held assumption that PVL is responsible for the increased virulence of certain CA-MRSA strains.

One study by Brown *et al*. indicated the importance of PVL in CA-MRSA-induced muscle lesions and necrotising pneumonia in the murine model, along with the protective effects of PVL immunisation.[14] However, studies by Voyich *et al.* and Bubeck Wardenburg *et al*. contradicted this by providing data showing no significant difference in the virulence between PVL-positive and PVL-negative CA-MRSA.[15] Furthermore, necrotising pneumonia caused by PVL-negative MRSA has also been reported clinically.[7] While the exact role that PVL plays in pathogenesis remains unclear, its presence remains advantageous to CA-MRSA especially for bacterial survival in the early stage of infection.[7]

The pandemic spread of CA-MRSA and its capacity to cause serious and rapidly progressive fatal disease has alarmed healthcare professionals and the media alike.[16] An added dimension to the global problem of CA-MRSA is its recent diffusion into the hospital setting,[5] and as a result CA-MRSA is increasingly associated with hospital-acquired infections (HAIs) such as surgical site infection, ventilator-associated pneumonia and bacteraemia.[1]

Mathematical modelling suggests that transmission of MRSA in the community significantly influences the

occurrence of MRSA and in turn the number of HAIs in hospitals.[1] *Staphylococcus aureus* is a commensal organism in 30% of healthy individuals and, among these colonising strains, skin carriage of CA-MRSA has been shown to be a risk factor for subsequent MRSA infections especially in a hospital setting.[17] The nares remain the most common site of carriage, followed by the skin, for HA-MRSA, while skin has been shown to be the more common carrier site for CA-MRSA. This is important because asymptomatic carriers of CA-MRSA frequently develop an acute skin or soft tissue infection, while a carrier of HA-MRSA in the nares seldom becomes infected with the organism.[18]

It is possible that CA-MRSA will displace the traditional HA-MRSA in the future, as one study has reported the incidence density rate of infections caused by strains classified as community genotypes to have increased 20-fold (from 0.05 to 0.1) between 2003 and 2006.[1] In Greece, 40% of HAI MRSA infections were caused by CA-MRSA strains ST30-IVb and ST80-IV, while Denmark reported 72% of HAI MRSA cases were caused by strains carrying SCC*mec* IV.[1] In the USA, the CA-MRSA clone USA300 (ST8-IV) has been identified as a frequent cause of HAIs. A study by Liu *et al*. reported a prevalence of 43.4% of all hospital-onset MRSA infections in San Francisco, California, to be attributable to USA300, thereby replacing the dominant HA-MRSA strain ST5 (USA100) as the leading cause of MRSA HAIs.[19]

In Ireland, 80% of hospital MRSA isolates are non-multiantibiotic-resistant genotype ST22-IV,[8] and these strains have also been documented in the Irish community in the absence of HA-MRSA risk factors.[20] In the UK, the characterisation of the pandemic clone EMRSA-15 (ST22-IV) has proved to be clinically important as its emergence in UK hospitals coincided with a substantial increase in the incidence of MRSA infections between 1997 and 2002, from 1–2% to 40% of all *S. aureus* infections.[21]

An added dimension to this problem is co-colonisation of CA-MRSA and HA-MRSA. Previous studies assumed that individuals can only be colonised or infected with either HA-MRSA or CA-MRSA; however, conflicting data suggest that co-colonisation does occur.[22] Co-colonisation with CA-MRSA and HA-MRSA may have important clinical implications if exchange of genetic material were to occur among strains which typically have different antimicrobial susceptibilities. This may, in turn, lead to the emergence of MRSA strains with new biological properties.[22]

This recent and rapid emergence of CA-MRSA has changed the biology and epidemiology of MRSA.[1] From its origin in 1961 to the late 1990s, MRSA was almost exclusively a hospital-acquired infection.[1] The emergence of CA-MRSA in the early 1980s signified a new dimension to the threat posed by MRSA, with transmission and infection now no longer confined to healthcare institutions but increasingly seen in the community.[1] Within a relatively short space of time, CA-MRSA has evolved to become the most frequent cause of SSTIs in the community and is also replacing traditional MRSA strains in hospitals on a larger scale.[23] Bearing in mind the fact that full epidemiological investigations are performed on only a small proportion of MRSA cases, it is likely that the true extent of CA-MRSA is underestimated. Such infections are now regarded as a serious public health issue affecting many aspects of our social life, second only to HIV/AIDS in scope and importance.[23] □

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