PL Ho 何栢良
KY Yuen 袁國勇
WS Tse 謝詠詩
TK Ng 伍德強
TL Que 郭德麟
E Lai 黎羚怡
RW Yung 翁維雄

Molecular epidemiology of community-associated methicillin-resistant *Staphylococcus aureus*

Key Messages

1. Community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) strains with diverse genetic backgrounds are emerging in Hong Kong.
2. Intra-familial spread of community-associated MRSA is common.

Introduction

Staphylococcus aureus is a common cause of community- and health care–associated skin and soft-tissue infections (SSTIs), pneumonia, and bacteraemia. Traditionally, methicillin-resistant *S aureus* (MRSA) infections are confined to individuals with established risk factors, for examples: nursing home residents, hospitalised individuals, patients undergoing operations, persons with indwelling medical devices. Since the 1990s, there are increasing reports of MRSA infections in healthy individuals from the community without established risk factors.[1] By means of genotypic studies, most community-associated MRSAs are found to be genetically distinct from the health care–associated MRSA. With few exceptions, the former strains possess the Panton-Valentine leukocidin genes and one of the novel *Staphylococcus* cassette chromosome mec elements (types IV and V). They are sensitive to most antibiotics except β-lactams. Nowadays, community-associated MRSAs are recognised to cause outbreaks in 'closed populations', such as aboriginals, contact sports athletes, inmates of correctional services, military recruits, and children attending day care centres. Recently, they have even been found to spread inside hospitals and are displacing the traditional health care–associated MRSA as the pathogens in nosocomial infections.[2]

Aims and objectives

We evaluated the molecular epidemiology and household transmission of community-associated MRSA in patients who were reported to a monitoring system in Hong Kong from January 2004 to December 2005.

Methods

In January 2004, a monitoring group was formed under the coordination of the Department of Health and the Centre of Infection at the University of Hong Kong, to conduct laboratory-based surveillance for community-associated MRSA. The participating microbiology network included five public and six private hospital laboratories, as well as six stand-alone community laboratories. These laboratories were estimated to provide inpatient and outpatient service to half of the 6.5-million inhabitants of Hong Kong. All participating laboratories were requested to screen the clinical information in the request forms and pay attention to MRSA isolates with a non-multiresistant antibiogram. Suspected community-associated MRSA isolates were referred to the laboratory in the Centre of Infection for molecular testing.

Culture swabs from household contacts were processed as described previously. A broth enrichment step (mannitol-salt medium; Oxoid, Hampshire, UK) was used, followed by plating onto oxacillin (6 μg/mL) blood and mannitol salt agar. The MRSA were characterised by *Staphylococcus* cassette chromosome mec typing, pulsed-field gel electrophoresis and multilocus sequence typing. Polymerase chain reaction was used to detect mecA, Panton-Valentine leukocidin, and erythromycin resistance determinants.[3-5]

Results

From January 2004 to December 2005, 25 episodes of community-associated

Hong Kong Med J 2009;15(Suppl 9):S6-8

Department of Microbiology, The University of Hong Kong, Queen Mary Hospital Compound, Pokfulam Road, Hong Kong SAR, China
PL Ho, KY Yuen, WS Tse, TK Ng, TL Que, E Lai, RW Yung

RFCID project number: HKU-B4-003

Principal applicant and corresponding author:
Dr PL Ho
Department of Microbiology, The University of Hong Kong, Queen Mary Hospital Compound, Pokfulam Road, Hong Kong SAR, China
Tel: (852) 2855 4892
Fax: (852) 2855 1241
E-mail: plho@hkucc.hku.hk

MRSA infections from seven children (aged <16 years) and 16 adults were reported; 14 were Chinese, three were Filipino, and two each were British, Nepalese, and Japanese. The mean age of the patients was 28 (standard deviation [SD], 21; range, 1-91) years. Eight episodes of SSTIs (including six furuncles/carbuncles, one infected chickenpox lesion, and one infected eczema) occurred in the 7 children; one 7-year-old child had two episodes of infection. The 17 episodes of infections in the 16 adults included one bacteraemia complicated by meningitis and 16 SSTIs (11 furuncles/carbuncles, two perianal abscesses, one deep-seated thigh infection, one infected sebaceous cyst, and one scalp abscess).

The 23 patients belonged to 21 unrelated families. Nine families declined screening. A total of 46 household members from the remaining 12 families were assessed. Two community-associated MRSA infections and four carriages were found. In households 3 and 10, more than one person was infected.

An analysis of the relationship between the 29 isolates was performed using pulsed-field gel electrophoresis. At a cut off of >80% similarity, the dendrogram divided all but one of the isolates into three pulsed-field type clusters (designated as HKU100 to HKU300) [Table]. Infections and carriages in the same families were caused by MRSA isolates with identical pulsed-field type. HKU100 was the largest cluster, with 18 isolates throughout Hong Kong. This cluster included isolates from persons of Chinese, Nepalese, Filipino, and British origins. In the multilocus sequence typing analysis, HKU100 isolates were found to belong to the ST30 (2-2-2-2-6-3-2) group. All HKU200 isolates were recovered from persons of Chinese origin. Unlike HKU100 isolates, the geographic sources of HKU200 isolates were more restricted. Four of the five isolates were recovered from patients residing in districts close to the border with mainland China. The only patient whose residential address was not close to the border had a travel history to mainland China 1 month before the onset of infection. Furthermore, the HKU200 cluster included the two isolates from household 12 with frequent travel history to mainland China. HKU200 isolates had three antibiogram patterns. They had an ST59 allelic profile (19-23-15-2-19-20-15) or its single locus variant (19-23-15-48-19-20-15, designated as ST338). All five isolates of HKU300 were recovered from one Japanese family. Interestingly, the isolates exhibited different susceptibility to gentamicin and tetracycline, resulting in three different antibiogram patterns. Three HKU300 isolates were found to have an ST8 allelic profile (3-3-1-1-4-4-3). The singleton isolate had an ST8 allelic profile.

Table. *Staphylococcus* cassette chromosome mec (SCCmec) types and Panton-Valentine leukocidin (PVL) positivity according to dendrogram grouping

Dendrogram groups (no. of isolates)	*ccr* gene complex	Loci present	SCCmec type	No. of PVL positive/total
HKU100 (18)	2	D	IV	17/18
HKU200 (5)	5	EF	V	5/5
HKU300 (5)	2	DG	IVA	0/5
Singleton (1)	2	D	IV	1/1

Discussion

There are multiple lineages of community-associated MRSA (ST30-IV, ST59-V, and ST8-IV/IVA) in Hong Kong. These lineages differed from the major clones of MRSA that account for most health care–associated MRSAs in this locality.[5]

Our community-associated MRSA strains could have been introduced from other areas through international travel, as Hong Kong has over 10-million visitors annually. HKU200 isolates may have a link to mainland China because all were recovered from individuals whose addresses were close to the border with mainland China or with a history of frequent cross-border travel.

Community-associated MRSA infections could spread among household contacts of individuals. In each household, transmission of the same MRSA strain was confirmed by pulsed-field gel electrophoresis analysis. Although spread of MRSA among household contacts of persons with community-associated MRSA has been previously reported,[6] our study is the first to document the magnitude of this risk. Intrafamilial transmission of community-associated MRSA raises issues such as whether household screening should be routinely arranged, with a view to decolonise the carriers.

Nine (39%) of the 23 isolates from the index patients were recovered from individuals of non-Chinese origins. Therefore, certain ethnic groups in Hong Kong could be at a higher risk for community-associated MRSA infections.

Conclusions

Multiple lineages of community-associated MRSA, including the widespread ST30-IV Southwest Pacific clone, are spreading in the Hong Kong community. Intrafamilial transmission of community-associated MRSA may remain under-recognised unless household screening is conducted. More studies should be conducted to understand the transmission dynamics of community-associated MRSA in non-familial settings.

Acknowledgements

This project forms part of a series of studies commissioned by the Food and Health Bureau of the Hong Kong SAR Government and was funded by the Research Fund for the Control of Infectious Diseases. The results of this study have been reported in the following publications:

1. Ho PL, Cheung C, Mak GC, et al. Molecular epidemiology

and household transmission of community-associated methicillin-resistant *Staphylococcus aureus* in Hong Kong. Diagn Microbiol Infect Dis 2007;57:145-51.

2. Ho PL, Wong MP, Lai EL, Chan KH, Chiu SS. DNA typing of cytological samples for retrospective identification of an early case of Panton-Valentine leukocidin-positive, community-associated methicillin-resistant *Staphylococcus aureus* pneumonia. J Clin Microbiol 2008;46:2457-8.

References

1 Vandenesch F, Naimi T, Enright MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* carrying Panton-Valentine leukocidin genes: worldwide emergence. Emerg Infect Dis 2003;9:978-84.

2 Zetola N, Francis JS, Nuermberger EL, Bishai WR. Community-acquired methicillin-resistant *Staphylococcus aureus*: an emerging threat. Lancet Infect Dis 2005;5:275-86.

3 Jarraud S, Mougel C, Thioulouse J, et al. Relationships between *Staphylococcus aureus* genetic background, virulence factors, agr groups (alleles), and human disease. Infect Immun 2002;70:631-41.

4 Ho PL; Hong Kong intensive care unit antimicrobial resistance study (HK-ICARE) Group. Carriage of methicillin-resistant *Staphylococcus aureus*, ceftazidime-resistant Gram-negative bacilli, and vancomycin-resistant enterococci before and after intensive care unit admission. Crit Care Med 2003;31:1175-82.

5 Que TL, Ho PL, Yip KT, et al. Three-year study of targeted screening for methicillin-resistant *Staphylococcus aureus* at hospital admission. Eur J Clin Microbiol Infect Dis 2003;22:268-70.

6 Faden H, Ferguson S. Community-acquired methicillin-resistant *Staphylococcus aureus* and intrafamily spread of pustular disease. Pediatr Infect Dis J 2001;20:554-5.