## RESEARCH NOTE

# COMMUNITY-ACQUIRED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* IN A MALAYSIAN TERTIARY CENTRE

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**Abstract.** Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is a pathogen recognized to be distinct in both phenotype and genotype from hospital-acquired MRSA. We have identified CA-MRSA cases in Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia, including their antibiotic susceptibility patterns and genotypic characteristics. Cases were identified during January to December 2009 from routine clinical specimens, where culture and antibiotic susceptibility results yielded pauci-resistant MRSA isolates suspected as being CA-MRSA. The patients' clinical data were collected and their specimens were sent for molecular confirmation and analysis. Five cases of CA-MRSA were identified, which had a multi-sensitive pattern on antibiotic susceptibility tests and were resistant to only penicillin and oxacillin. All cases were skin and soft-tissue infections, including diabetic foot with gangrene, infected scalp hematoma, philtrum abscess in a healthcare worker, thrombophlebitis complicated with abscess and infected bedsore. All five cases were confirmed MRSA by detection of *mecA*. SCC*mec* typing (*ccr* and *mec* complex) revealed SCC*mec* type IV for all cases except the infected bedsore case. Panton-Valentine leukocidin gene was positive in all isolates. As clinical features among methicillin-sensitive *Staphylococcus aureus*, CA-MRSA and "nosocomial CA-MRSA" are indistinct, early recognition is necessary in order to initiate appropriate antibiotics and infection control measures. Continual surveillance of pauci-resistant MRSA and molecular analysis are necessary in order to identify emerging strains as well as their epidemiology and transmission, both in the community and in healthcare setting.

**Keywords:** *Staphylococcus aureus*, community-acquired methicillin-resistance, skin and soft tissue infections, Malaysia

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## INTRODUCTION

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is increasingly recognized as a cause of skin infections and invasive infections among healthy individuals and children in the community, as well as life-threatening sepsis and community-acquired pneumonia (CDC, 1999, Zetola *et al*, 2005). CA-MRSA is a pathogen recognized as being distinct from hospital-acquired (HA) MRSA both in phenotype and genotype. CA-MRSA refers to an MRSA infection with onset in the community from an individual not associated with established MRSA risk factors, such as recent hospitalization, surgery, residence in a long-term care facility, receipt of dialysis, or presence of invasive medical devices (Fridkin *et al*, 2005).

We sought to identify cases of CA-MRSA in Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia, and analyze their antibiotic susceptibility patterns and genotypic characteristics, namely SCC*mec* typing and presence of Panton-Valentine leukocidin (PVL) genes.

## MATERIALS AND METHODS

### Samples

Samples were identified retrospectively from January to December 2009, from routine clinical specimens, where culture and antibiotic susceptibility results yielded pauci-resistant MRSA isolates, which were suspected as being CA-MRSA. The specimens were obtained during the patients' acute clinical presentations. The isolation and identification of *Staphylococcus aureus* were performed in the Microbiology Laboratory by standard bacteriologic culture methods. Antimicrobial susceptibility was determined using disk diffusion method, according to the Clinical Laboratory Standards Institute recommendations and breakpoints for interpretations (CLSI, 2009). Oxacillin (1 g) was used for susceptibility testing of MRSA. *Staphylococcus aureus* ATCC 25923 strain was used as a control strain for disk diffusion testing. The patients' clinical data, including history and clinical presentations, microbiologic investigation results, and antibiotics prescribed and outcomes, were collected.

### Genotyping

Molecular analysis and genotyping were performed at the Institute for Medical Research (IMR), Kuala Lumpur, Malaysia. The isolates were confirmed as MRSA by detection of *mecA* as described by Murakami *et al* (1991) using polymerase chain reaction (PCR). MRSA strain ATCC 49975 was used as the control strain for *mecA* detection. For SCC*mec* typing, chromosomal DNA was extracted from the isolates using a DNeasy kit (Qiagen, Hilden, Germany) according to instructions of the manufacturer, and subjected to PCR using primers specific for SCC*mec* types I to V as described by Ito *et al* (2004) and Lim *et al* (2003). The strains were first screened for *ccr* complex, followed by *mec* complex determination. Detection of PVL-encoding genes was performed as described by Lina *et al* (1999), using ATCC 43300 as a control strain.

## RESULTS

Five cases of CA-MRSA were identified, with all cases being skin and soft-tissue infections (Table 1). All isolates had multi-sensitive patterns upon antibiotic susceptibility tests (sensitive to fucidic acid, erythromycin, rifampicin, gentamicin, vancomycin, teicoplanin, clindamy-

Table 1
Summary of community-acquired methicillin-resistant *Staphylococcus aureus* infections in UKMMC during year 2009.

| Case | Clinical history | Specimen | Antibiotic treatment | Outcome |
|---|---|---|---|---|
| **Case 1:** Diabetic foot with gangrene | 77-year-old Chinese lady, diabetes mellitus, hypertension, recurrent stroke, bedridden, resident in old folks home. | Wound swabs from gangrenous foot ulcers. | IV amoxycillin-clavulanate, then IV vancomycin. | Good post-operative recovery. MRSA-free at 2 months. |
| **Case 2:** Infected scalp hematoma | 1-year-old Pakistani boy, scalp swelling after a fall at home. | Pus from incision and drainage. | IV cloxacillin, then IV vancomycin. Discharged with oral azithromycin. | Recovered and discharged. No further follow-up. |
| **Case 3:** Philtrum abscess in a healthcare worker | 24-year-old Malay nurse, ruptured acne and swelling at upper lip and philtrum. | Pus from incision and drainage. | IV cloxacillin, then IV vancomycin. | Lesions resolved, remain MRSA-free at 1 month. |
| **Case 4:** Thrombophlebitis complicated with abscess | 38-year-old Malay lady, intestinal obstruction, adhesiolysis. Post-op had recurrent right cubital fossa thrombophlebitis. | Pus from incision and drainage. | IV amoxycillin-clavulanate, then discharged on oral ampicillin-sulbactam. | Discharged from hospital after 3 days. Full culture and sensitivity results reported a day after discharge. MRSA-free at 2 and 6 months. |
| **Case 5:** Infected bedsore | 57-year-old Indian lady, hypertension, stroke, bedridden, resident in old folks home. | Wound swabs and debrided tissue from bedsore. | IV vancomycin | Discharged after 2 weeks, to continue wound dressing at nursing home. |

IV, intravenous

cin, chloramphenicol, ciprofloxacin and mupirocin), and were resistant only to penicillin and oxacillin.

All five cases were confirmed MRSA by detection of *mecA* by PCR. SCC*mec* typing and PVL gene detection showed that all five positive samples were positive for the latter gene and positive for SCC*mec* type IV in 4 samples, with one being refractory to typing.

## DISCUSSION

CA-MRSA differs from HA-MRSA in terms of epidemiology, antibiotic susceptibility patterns and clinical virulence. Most CA-MRSA were reported to carry Scc*mec* types IV and V.

In a nasal culture survey among healthy Malaysian carriers, 3% carriage rate were found for MRSA, with one isolate being SCC*mec* type IVa and positive for PVL toxin gene and two isolates having SCC*mec* type V (Mariana *et al*, 2008).

In an analysis of unusually multi-sensitive MRSA in a Malaysian tertiary care center from 2002 to 2007, 9 isolates of multi-sensitive CA-MRSA were found to carry SCC*mec* type IV, of which 5 are PVL positive and 7 being classified as nosocomially acquired (Sam *et al*, 2008). Antimicrobial susceptibility tests of 14 CA-MRSA isolates from various clinical specimens, collected from October 2006 to February 2007 in another tertiary hospital in Malaysia, showed multi-drug resistance to more than 3 classes of antibiotics (Neela *et al*, 2008).These findings differed from the current study and that of Sam *et al* (2008).

In another study with 628 MRSA isolates from 9 Malaysian hospitals between November 2006 and June 2008, 20 isolates were SCC*mec* type IV while 608 were SCC*mec* type III. Nine out of these 20 isolates fit the clinical description of CA-MRSA, being skin and soft tissue infections, with 8 positive for PVL toxin gene, while 11 were clinically HA-MRSA from various sites including blood (Norazah *et al*, 2009).

In an epidemiologic study in Hong Kong of 298 patients with skin and soft tissue infections, 13 out of 125 (10%) *S. aureus* isolates and 12 out of 241 (5%) abscesses were attributed to PVL-positive CA-MRSA (Ho *et al*, 2008). Presence of PVL gene in *S. aureus* isolates has been associated with primary skin infections (Lina *et al*, 1999) and severe necrotizing pneumonia (Lina *et al*, 1999; Gillet *et al*, 2002).

In our study, case 2 was due to CA-MRSA as it fits the description of a community-acquired infection since the patient had no known history of hospital admission, association with a healthcare facility or other predisposing factors for MRSA. Cases 1, 3, 4 and 5 had CA-MRSA genotype in the presence of risk factors for hospital-acquired or nosocomial MRSA, namely, residents of a long-term care facility (cases 1 and 5), a healthcare worker (case 3) and a post-operative patient (case 4).

A multinational study on the epidemiology of *S. aureus* in Asian countries indicated that various MRSA clones have spread between community and hospitals as well as between countries (Song *et al*, 2011). Based on clinical findings, the boundaries among methicillin-sensitive *S. aureus*, CA-MRSA and "nosocomial CA-MRSA" may be indistinct, but molecular criteria may help. Proper identification is important as the antibiotic options are different.

Continual surveillance of pauci-resistant MRSA and molecular analysis are necessary in order to identify emerging strains as well as their epidemiology and transmission, both in the community and in healthcare setting.

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