Molecular characteristics of community-acquired, methicillin-resistant Staphylococcus aureus isolated from Chinese children

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Keywords
community-acquired methicillin-resistant Staphylococcus aureus; SCCmec; multilocus sequence typing; spa typing; children.

Abstract
The aim of this study was to investigate the molecular characteristics of community-acquired, methicillin-resistant Staphylococcus aureus (CA-MRSA) isolates from Chinese children. Ninety-nine isolates were collected from eight hospitals, and analyzed by multilocus sequence typing, staphylococcal chromosomal cassette mec (SCCmec) type, and spa typing. The Panton–Valentine leukocidin (PVL) gene was also detected. Overall, 14 sequence types (STs) were obtained, and ST59 (58.6%) was found to be the most prevalent, followed by ST1 (8%) and ST338 (8%). We also first registered the new ST1409. SCCmec type IV was the most predominant type at 67.7%, followed by SCCmec type V at 32.3%. SCCmec subtypes IVa, IVc, and IVg were found among the SCCmec type IV strains. Twenty-one spa types were also identified. Four new spa types were found by synchronization with the Ridom SpaServer and referring to the website (http://www.SeqNet.org). ST59-MRSA-IVa with t437 accounted for 40.4% of occurrences, making it the most prevalent clone. The prevalence of PVL genes was 58.6%, and multidrug resistance was observed in 95% of all isolates. This result indicates that CA-MRSA isolates in Chinese children are largely associated with the ST59-MRSA-IV clone, and that the predominant clones of CA-MRSA are spread all over the country.

Introduction
In the early 1990s, community-acquired methicillin-resistant Staphylococcus aureus (CA-MRSA) emerged as a serious health problem worldwide (Grundmann et al., 2006). It is primarily associated with skin soft-tissue infections (SSTIs) in otherwise healthy children or adolescents; it is also associated with severe systemic infections such as sepsis and necrotizing pneumonia. In contrast to hospital-associated MRSA (HA-MRSA), CA-MRSA tends to affect individuals of all ages without the traditional risk factors of MRSA. It is likewise characterized by the existence of staphylococcal chromosomal cassette mec (SCCmec) type IV or V, frequent production of Panton–Valentine leukocidin (PVL), and susceptibility to non-β-lactam antimicrobials (Zetola et al., 2005). In addition, CA-MRSA is genetically heterogeneous (Yamamoto et al., 2006; Baranovich et al., 2007). Infections caused by CA-MRSA strains in children and adults have been reported worldwide and constitute an important public health problem (Vandenesch et al., 2003), but there are few reports on CA-MRSA monitoring among children in China.

Our previous retrospective study showed the results of multilocus sequence typing (MLST) and the spa typing of 29 CA-MRSA isolates from Chinese children from 2005 to 2006 (Zhang et al., 2009). However, the small sample size resulted in inconclusive information about the molecular characteristics of CA-MRSA. In addition, 27.6% of the CA-MRSA isolates were nontypeable, and no data were shown on the prevalence of the PVL gene. This prospective study was started in 2008 and implemented until June 2009. It focuses on an expanded sample of CA-MRSA infection cases to
obtain accurate molecular characteristics of CA-MRSA from children in mainland China, and to investigate whether the epidemiology could be affected by time.

**Materials and methods**

**Bacterial isolates**

An enhanced surveillance of CA-MRSA in children 0–16 years old was conducted over an 18-month period from July 2008 to June 2009. It involved eight regional hospitals distributed in seven cities in China. These cities were located in the northern, southern, eastern, and central regions (Fig. 1). An MRSA case was considered community acquired if it was isolated from an outpatient or an inpatient within 48 h of hospitalization, and if risk factors for HA infections, including recent (within the past year) hospitalization or medical procedure (such as dialysis, surgery, and catheters), were absent. Thus, these patients satisfied the international criteria for CA-MRSA infections as indicated by the Centers for Disease Control and Prevention of the United States (Klevens et al., 2007). Ninety-nine CA-MRSA isolates were collected from 99 different children with informed consent.

The isolates were recovered from several clinical sources, including the sputum (50), pus (34), blood (4), punctate (2), secretions (5), and pharynx swabs (4). During the study period, sputum was obtained for culture from children with pneumonia, and pus from children with SSTIs. The other sources, including blood, punctate, and secretions, were from children with septicemia, hydrothorax, and trauma, respectively. Four strains were obtained from colonization in the pharynx of healthy children. One isolate was collected from each patient. The identities of the *S. aureus* isolates in each hospital were confirmed by colony morphology and the coagulase test. Meticillin resistance was screened by oxacillin and cefoxitin discs, and confirmed by *mecA* PCR. Ninety-nine MRSA strains were collected and were reidentified in the microbiology laboratory of the Beijing Children's Hospital. The presence of *mecA* and *nuc* genes was also verified by PCR.

**DNA extraction**

Using a DNA extraction kit (Saibaisheng, China), DNA was extracted and used as the template in all PCRs described in the following section.

**MLST and data analysis**

MLST was performed as described in a previous study (Enright et al., 2000). The PCR fragments were purified and sequenced using an ABI 3700 sequencer. The seven housekeeping gene sequences were compared with known alleles from the MLST database (http://saureus.mlst.net), and the allelic profiles [sequence types (STs)] were determined based on this database. Clustering of related STs, which were defined as clonal complexes (CCs), was determined using EBURST (based on related STs).

**SCCmec typing and subtyping**

All isolates and subtypes, the *SCCmec* types and *SCCmecIV* isolates, respectively, were determined using a multiplex PCR assay described in 2007 (Milheiroco et al., 2007a, b). The prototypes of *SCCmec* types I–V for the isolates and *SCCmecIV* subtypes for the subtypes (donated by Ito) were used as quality controls.

**Spa typing**

Spa typing was performed as described in previous studies (Koreen et al., 2004). Purified *spa* PCR products were sequenced, and short sequence repeats were designated with a random string of alphabetical letters according to a website for *spa* typing (http://www.ridom.de/spaserver).

**PVL gene detection**

Oligonucleotide primers were designed according to the published sequences of the PVL genes (Lina et al., 1999). The identities of the PCR products were then confirmed by sequencing using an ABI 3700 sequencer.

**Antimicrobial susceptibility testing**

Antimicrobial susceptibility profiles were determined in accordance with the guidelines of the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS). The antimicrobial agents were obtained from Sigma: penicillin,
oxacillin, cefuroxime, clindamycin, ciprofloxacin, chloramphenicol, erythromycin, gentamicin, rifampin, tetracycline, trimethoprim-sulfamethoxazole, and vancomycin. The breakpoints of CLSI were used for minimum inhibitory concentration (MIC) interpretation. Staphylococcus aureus ATCC 29213 was used as the quality control in each set of tests.

**Statistical analysis**

Categorical variables were compared using the $\chi^2$-test. Statistical analysis was carried out using the software spss 13.0, and the level of significance was fixed at $\alpha = 5\%$.

**Results**

**MLST results**

All 99 CA-MRSA isolates were used for MLST analysis, and 14 ST types were obtained. Clustering analysis using the **EBURST** program showed that these STs belonged to 11 CCs. The most prevalent ST was ST59, which belongs to CC59, constituting 58.6% (58/99) of all isolates and existing in all cities. ST338, which also belongs to CC59 and shows single locus variants to ST59, was found to be the second most common ST (8/99; 8%), discovered in the southern region of China. Further, we found four ST910 type strains that belong to CC30 and show single locus variants to ST905, as we reported previously. A new ST type, ST1409, which belongs to CC5 and shows single locus variants to ST906 and ST5, was first registered as ID 2939 in the database. It was isolated from a child with pneumonia. In addition, we found three rare types of ST1349, which were only isolated in pharynx swabs from healthy children in Beijing. The other ST types were ST1, ST88, ST509, ST398, ST239, ST217, and ST45 (Table 1).

**SCCmec types**

All 99 MRSA isolates were analyzed through SCCmec typing. Two types (types IV and V) were found. Of these, the most common was type IV, which was found in 67 isolates (67/99, 67.7%), while type V was found in 32 isolates (32/99, 32.3%).

From the 67 type IV isolates, three SCCmec subtypes were found: IVa, IVc, and IVg. The most common type was type IVa (52/67, 77.6%), followed by type IVc (8/67, 11.9%). Two SCCmecIVg subtypes were also found, whereas five isolates (5/67, 7.5%) could not be subtyped.

**Spa type of CA-MRSA**

The typing of all isolates yielded 21 spa types. Four new spa types were found by synchronizing with the Ridom SpaServer and referring to the website (http://www.SeqNet.org): t3590, t5348, t5349, and t5350. Two typical livestock-associated types t034 were found in children living in the countryside. The most predominant spa type was t437 (62/99, 62.6%). The other spa types were t1081, t375, t127, t002, t318, t062, t441, t309, t114, t1861, t3485, t1764, t653, t030, and t045.

**Prevalence of the PVL gene**

All isolates were analyzed for the presence of the PVL gene. We found 58 PVL-positive isolates (58/99, 58.6%). More instances of PVL-positive isolates emerged from strains of children with skin and subcutaneous tissue infection than from children without these infections (82.4% vs. 44.6%, $\chi^2 = 13.015, P < 0.01$). In addition, more instances of PVL-negative isolates emerged from strains of children with pneumonia compared with other children (61.4% vs. 27.3%, $\chi^2 = 11.631, P < 0.01$). There was no obvious difference between the median age of the PVL-positive and PVL-negative patients (2.8 years vs. 2 years).

**Molecular characteristics of prevalent clones**

In this study, the most common clones were ST59-MRSA-IVa and ST59-MRSA-V with t437, accounting for 40.4% and 13.1% of occurrences, respectively. The PVL-positive ST59-MRSA-IVa with t437 isolates were more common in Beijing than in other cities (59.1% vs. 14.3%, $\chi^2 = 18.704, P < 0.01$). In addition, we also found ST338-MRSA-V with the t437 clone, which accounted for 5% of the total isolates.

ST1-MRSA-IV with t127 was the second most common clone, accounting for 6% of the total isolates. ST1-MRSA-IVg was only found in Shenzhen, and ST1-MRSA-IVc was only found in Shanghai.

Furthermore, ST910, which was previously reported to be present only in Shanghai, was likewise found in Wenzhou and Beijing in this study. ST1349-MRSA-IVc, a clone that we may need to pay more attention to, was only found in healthy children living in Beijing (Table 1).

**Antimicrobial susceptibility**

All MRSA isolates were found to be resistant to penicillin, cefuroxime, oxacillin, and erythromycin, but susceptible to vancomycin. The resistance rates to other antimicrobial drugs tested were 87.9% (87/99) to clindamycin, 57.6% (57/99) to tetracycline, 42.4% (42/99) to gentamicin, 41.4% (41/99) to chloramphenicol, 31.3% (31/99) to ciprofloxacin, 30.3% (30/99) to sulfamethoxazole and trimethoprim, and 14.1% (14/99) to rifampicin. The isolates from Chongqing and Shenzhen were all found to be susceptible to trimethoprim-sulfamethoxazole (Table 2).

The ST types of the CA-MRSA isolates and their respective antibiotic resistance profiles are listed in Table 1. There
were 34 antibiogram patterns among the 99 isolates studied. The most prevalent multiresistant antibiotics group (10%) includes erythromycin, tetracycline, clindamycin, and chloramphenicol. The resistance rate to three or more nonlactam antibiotics was 95%, whereas that to more than four, five, and six nonlactam antibiotics was 65.7%, 41.4%, and 28.3%, respectively. The multiresistance rate (resistant to more than three nonlactam antibiotics) of ST59-MRSA-IVa with spa437 clone was 90%, which shows no obvious difference from the others. There was no apparent association between the CCs and the antibiogram patterns. Interestingly, there was a significant difference in the ciprofloxacin resistance rate between the SCCmecIVc isolates and other isolates (75% vs. 37.9%, \(\chi^2 = 7.72, P < 0.05\)). The two SCCmecIVg isolates were sensitive to chloramphenicol, rifampicin, tetracycline, and trimethoprim-sulfamethoxazole. The MIC\(_{50}\) of every antibiotic is summarized in Table 2.

### Discussion

Our data revealed that ST59-MRSA-IVa and ST59-MRSA-V with spa 437 were the most predominant clones of CA-MRSA in Chinese children. These clones exist in all cities, covering most areas in China and constituting 53.5% of all isolates. In our previous study, the ST910-MRSA-IV clone was found only in Shanghai, whereas ST59 was found in the southern region. In this study, however, the ST910-MRSA-IV clone occurred in more areas. ST59-MRSA-IVa was the

### Table 1. Molecular characteristics of CA-MRSA isolates recovered in China and their respective antibiotic resistance profiles

<table>
<thead>
<tr>
<th>MLST-CC</th>
<th>MLST allele no.</th>
<th>Spa type</th>
<th>IVa</th>
<th>IVc</th>
<th>IVg</th>
<th>IV(NT)</th>
<th>V</th>
<th>Predominant antibiotic resistance profile (no. of isolates)</th>
<th>No. of isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST59-CC59</td>
<td>19-23-15-2-19-20-15</td>
<td>t437</td>
<td>40</td>
<td>2</td>
<td>1</td>
<td>13</td>
<td>ELY (7)</td>
<td>&lt; 58</td>
<td></td>
</tr>
<tr>
<td>ST338-CC59</td>
<td>19-23-15-48-19-20-15</td>
<td>t437</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>ELYH (4)</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>ST1-C1</td>
<td>1-1-1-1-1-1-1</td>
<td>t127</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>ELY (1)</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST910-CC30</td>
<td>109-2-2-2-6-3-2</td>
<td>t318</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>TELG (1)</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST45-CC45</td>
<td>10-14-8-6-10-3-2</td>
<td>t1081</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>ECGY (2)</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST5-CC5</td>
<td>1-4-1-12-1-10</td>
<td>t002</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>ELGY (1)</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST88-CC88</td>
<td>22-214-12-23-14-3</td>
<td>t5348</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>ECLH (1)</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST1349-singletons</td>
<td>14-210-45-2-7-110-2</td>
<td>t5350</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>TECL GY H (2)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST398-CC398</td>
<td>3-35-19-20-20-26-39</td>
<td>t034</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>ELYH (1)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST509-CC509</td>
<td>1-26-28-18-18-33-37</td>
<td>t375</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>ECLH (1)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST239-CC8</td>
<td>2-3-1-1-4-4-3</td>
<td>t030</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>TEC RGY (1)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST217-CC22</td>
<td>7-6-1-5-8-5-6</td>
<td>t309</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>ECLY (1)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST965-CC5</td>
<td>1-4-1-119-1-10</td>
<td>t062</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>TECL GY H (1)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST1409-CC5</td>
<td>1-4-1-1-19-1-10</td>
<td>t653</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>TELGH (1)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

T, sulfamethoxazole-trimethoprim; E, erythromycin; C, ciprofloxacin; L, clindamycin; R, rifampicin; G, gentamicin; Y, tetracycline; V, vancomycin; H, chloramphenicol.

### Table 2. Results of the susceptibility testing of the CA-MRSA strains

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Resistant strains (%)</th>
<th>MIC(_{50})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>99 (100)</td>
<td>16</td>
</tr>
<tr>
<td>Oxacillin</td>
<td>99 (100)</td>
<td>32</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>99 (100)</td>
<td>64</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>99 (100)</td>
<td>&gt; 256</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>42 (42.4)</td>
<td>2</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>14 (14.1)</td>
<td>0.008</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>31 (31.3)</td>
<td>1</td>
</tr>
<tr>
<td>Sulfamethoxazole-trimethoprim</td>
<td>30 (30.3)</td>
<td>1</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>87 (87.9)</td>
<td>&gt; 256</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0 (0.0)</td>
<td>0.5</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>41 (41.4)</td>
<td>16</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>57 (57.6)</td>
<td>16</td>
</tr>
</tbody>
</table>
most nationally prevalent type. This may indicate that epidemic clones have, over time, become disseminated throughout the country.

International surveillance studies revealed that nearly 70% of HA-MRSA isolates belonged to five major pandemic clones, namely, the Iberian (ST247-MRSA-IA), Brazilian (ST239-MRSA-III), Hungarian (ST239-MRSA-III), New York/Japan (ST5-MRSA-II), and pediatric (ST5-MRSA-IV) (Campanile et al., 2009) clones. ST239 was probably the most globally common clone, being frequently recorded throughout China, many other Asian countries, and much of Europe and South America (Aires de Sousa et al., 2003; Ko et al., 2005; Chongtrakool et al., 2006). However, CA-MRSA clones were found to be continent-specific. For instance, clones with ST1 and ST8 are mostly found in the United States and Canada (Gilbert et al., 2006), whereas clones with ST80 are mostly found in Europe. In addition, clones ST30 are found worldwide (Wijaya et al., 2006). In 2004, ST59 was reported to be predominant in Taiwan (Wang et al., 2004). In 2006, a study in Hong Kong reported isolates sharing characteristics with the major CA-MRSA clone in Taiwan (Ho et al., 2007). Furthermore, the same strain might have been brought into Singapore from Taiwan through international travel in 2005 (Hsu et al., 2005). Our findings reveal that the predominant ST59, which belongs to CC59 and is found in mainland China, was the same as that in Taiwan, but was different from other countries.

However, most PVL-positive CA-MRSA ST59 clones in Taiwan belong to SCCmecIV, which contains a ccrC recombinase gene variant (ccrC2) and mec complex C2 (Boyle-Vavra et al., 2005). In our study, the majority of these clones belong to SCCmecIV, and the others to SCCmecV. We did not find any SCCmecIV isolates, which may indicate that the background of CA-MRSA ST59 clones in mainland China is different from Taiwan. In addition, we found ST338 in the southern region of China, which belongs to CC59 and shows single locus variants to ST59. ST59 could have undergone a minor variation after its gradual spread to China.

ST1-MRSA-IV with two spa types, t127 and t114, was the second most predominant clone in this study. This strain, which is predominant in the United States and the United Kingdom, has not been reported in Japan, Hong Kong, or Taiwan (Chen & Huang, 2005; Lo et al., 2006). In this study, ST1-MRSA-IV clones came from children with SSTIs and pneumonia. The two SCCmecIV isolates in our findings were only found in the ST1 types. This may indicate that CA-MRSA was transmitted into China from far distant countries, a process that may affect transmission.

As we have already mentioned, the most prevalent ST type in many countries is ST30, which belongs to CC30. It was first reported in Australia, New Zealand, and West Samoa, and was later found in Singapore and parts of Europe and the US (Hsu et al., 2006). In this study, we did not find any ST30 isolates in China. However, we found ST910 throughout China, which also belongs to CC30. This clone is closely related to ST30 and may have undergone minor variations after its gradual spread from the Southwest Pacific region into China (Enright et al., 2000).

Most worldwide CA-MRSA belong to SCCmecIVa and SCCmecV; ST80-MRSA-IVc was found in the UK in 2008 (Otter et al., 2009). In this study, most CA-MRSA isolates belong to SCCmecIVa. We first found SCCmecIVa and SCCmecIVg in China, which belong, respectively, to five ST types and one ST type. Except for three ST1349-MRSA-IVc isolates taken from healthy children, the other SCCmecIVc and SCCmecIVg isolates were from two children with pneumonia and SSTIs. This means that the genetic background of CA-MRSA in China is varifom.

In this study, four new spa types were found for the first time; of these, two of the new ones (t5590, t5350) belong to ST338. This demonstrates that the variation is progressing in China. It should be noted that ST398 with t034 is a typical livestock-associated spa type. In Europe, patients carrying this spa type are usually in contact with a major animal reservoir of these MRSA, mostly pigs (Kock et al., 2009). In the current work, we first reported ST398 with t034 strains in Chinese children with pneumonia who lived in the countryside, which may indicate that CA-MRSA might be transmitted from animals to children in China. Such a discovery requires further attention and research.

As reported previously, PVL is a bicomponent exotoxin that causes dermal necrosis and possesses particular cytolytic activity against neutrophils and monocytes. PVL-positive CA-MRSA is often associated with SSTIs (Kaplan, 2006). In this study, most PVL-positive strains were associated with SSTIs in Chinese children, which is consistent with previous reports.

CA-MRSA strains were resistant to β-lactams, but were found to be susceptible to other antibiotics in many countries (Zetola et al., 2005). However, the CA-MRSA ST59 clone, which shows resistance to four non-β-lactams including gentamicin, has been reported in Taiwan (Takano et al., 2008). In addition, the US reported an increase in the proportion of CA-MRSA isolates resistant to ciprofloxacin in this period (P < 0.01) (Como-Sabetti et al., 2009). In this study, the multiresistant rate of CA-MRSA was high in Chinese children. The most prevalent multiresistant antibiotics group included erythromycin, tetracycline, clindamycin, and chloramphenicol. These findings may be explained by the high rate of antibiotic use in the Chinese community (Aires de Sousa et al., 2003), and they are indicative of the presence of strong selective pressure from antimicrobial use in the community. The findings may also indicate that a transfer of drug resistance from hospitals to the community may occur soon in China. Interestingly, as mentioned previously, there was a significant difference in
the ciprofloxacin resistance rate between the SCCmecIVc and other SCCmecIV subtype isolates. In addition, the two SCCmecIVa isolates were also found to be sensitive to chloramphenicol, rifampin, tetracycline, and trimethoprim-sulfamethoxazole, suggesting that the antibiotic resistance profile of CA-MRSA may be related to the SCCmec subtypes or certain prevalent clones.

This study revealed the recent molecular characteristics of CA-MRSA in Chinese children and compared them with our previous study. The ST59 clone, which is prevalent in Taiwan, is spreading in mainland Chinese communities. Moreover, ST59-MRSA-IVa with spa 437, first identified in this study, is the most predominant clone from Chinese pediatric cases whose multiresistant rate is high. The predominant clones of CA-MRSA have been disseminating all over the country, which may make its control more difficult. In an era of increasing CA-MRSA, appropriate measures need to be taken to prevent, if possible, the further spread of these strains in the community and in hospitals.

This study has some limitations. The MRSA isolates were all obtained from large tertiary pediatric hospitals, and we have no information about the western and remote districts in China. More toxin genes included in CA-MRSA strains should be detected in further studies.

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