Clinical and Molecular Epidemiology of Invasive *Staphylococcus aureus* Infections in Chinese Children: A Single-center Experience

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Key words: Children; Clinical; Invasive Infection; Molecular; *Staphylococcus aureus*

Staphylococcus aureus is associated with a variety of invasive infection; typically, these infections occur as sepsis, osteomyelitis, endocarditis, and arthritis. China has a relatively high incidence of invasive *S. aureus* disease in children.[1] The present study aimed to provide the demographics, clones, and the antimicrobial susceptibility of *S. aureus* that cause invasive infection in Chinese children.

Invasive *S. aureus* infection refers to *S. aureus* isolated from a normally sterile body site, including blood, pleural effusion, cerebrospinal fluid, joint effusion, and bone marrow, or a skin and soft tissue infection (SSTI) requiring hospital admission for surgical drainage/debridement under general anesthetic and/or intravenous antimicrobial therapy.[2] PCR amplification was used for multilocus sequence typing, agr typing, and *spa* typing. A total of 274 children (≤14 years old) between February 2016 and January 2017 in Beijing Children's Hospital had positive *S. aureus* clinical microbiology reports. Among these 274 children, 30 patients were classified as having invasive *S. aureus* infection; the incidence was 10.9% (30/274). Among these 30 patients, 8 patients were <1 month old, 11 patients between 2 months and 6 years, and 11 patients between 10 years and 14 years; 11 patients were infected by methicillin-resistant *S. aureus* (MRSA) and 19 by methicillin-susceptible *S. aureus* (MSSA); 8 patients suffered from single-site infection, 12 from two-site infection, and 10 from multi-site infection. Twenty-two (22/30) were hospitalized, and five (5/22) of them gave up for treatment, and one (1/5) died immediately.

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Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.219158

As shown in Table 1, MRSA was more likely to cause osteomyelitis than MSSA ($P = 0.03$). Three most common two-site infections were sepsis related to skin soft tissue or pneumonia or osteomyelitis. The multi-site infection was sepsis with osteomyelitis and arthritis, followed by sepsis with osteomyelitis and SSTI. Seven cases (7/30) had produced a total of 15 positive strains that had been collected at a different time or different aseptic sites, so we collected 38 isolates in total. Two agr types were detected, most isolates were agr 1 type (34/38), and 4 of them belonged to agr 2 type. A total of 10 STs were included, thirteen MRSA belonged to ST 59, four MRSA, and 7 MSSA belonged to ST22. The *S. aureus* strains displayed 18 *spa* types, among which t309 (12/38) was the most dominant clone (12/38, 4 MRSA, and 8 MSSA), following by t437 (8/38). Both the resistance rate of *S. aureus* to penicillin and erythromycin was 100%. All isolates resistant to ceffuxin are MRSA with a resistant rate of 47.1%. All isolates were susceptible to linezolid, tigecycline, fusidic acid, mupirocin, and vancomycin.

The invasive *S. aureus* infectious disease is relatively rare, however, it can be very serious and occasionally fatal.[3] In this

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Received: 23-06-2017 **Edited by:** Xin Chen
How to cite this article: Wang LJ, Dong F, Qian SY, Yao KH, Song WQ. Clinical and Molecular Epidemiology of Invasive *Staphylococcus aureus* Infections in Chinese Children: A Single-center Experience. Chin Med J 2017;130:2889-90.

Table 1: Clinical characterization of patients with invasive *S. aureus* infections

Characteristics	Total (n = 30)	MRSA (n = 11)	MSSA (n = 19)	Statistics*	P
Risk factors, *n*					
Hospitalization in previous 12 months	8	5	3	3.75	0.15
Surgery	3	1	2		
Trauma or scalds	1	0	1		
Endotracheal intubation	7	2	5		0.49
Congenital heart disease	1	1	0		
Other congenital diseases	5	3	2		
Symptoms					
Fever (days), median (range)	15.4 (0–90.0)	18.3 (3.0–90.0)	8.1 (0–20.0)	0.41	0.68
Shock, *n*	3	0	3		
Coma, *n*	1	0	1		
Laboratory examination, median (range)					
White cell count-median ($\times 10^9$/L)	13.90 (0.29–30.96)	15.05 (7.61–30.96)	12.76 (0.29–29.11)	0.23	0.63
Percentage of neutrophil (%)	64.80 (6.99–85.8)	64.96 (6.99–85.80)	64.76 (10.30–85.80)	0.00	0.97
Thrombocytopenia ($\times 10^9$/L)	317.5 (24.0–794.0)	415.1 (154.0–794.0)	261.7 (24.0–597.0)	2.25	0.13
C-reactive protein (mg/L)	87.9 (8.0–343.0)	69.4 (9.0–190.0)	98.4 (8.0–343.0)	0.12	0.73
Duration of Hospitalization (days), median (range)	23.7 (0–106.0)	19.9 (0–39.0)	25.9 (12.0–106.0)	0.06	0.81
Intensive Care Unit admission, *n*	10	4	6		0.70
Duration of Intensive Care Unit (days), median (range)	11.7 (0–106.0)	8.0 (0–32.0)	13.8 (0–106.0)	0.17	0.68
Infection site, *n*					
Sepsis	26	11	15		0.14
Osteomyelitis	11	7	4		0.03
Necrotizing fasciitis	8	3	5		
Pneumonia	7	1	6		0.17
Arthritis	4	2	2		
Endocarditis	3	2	1		
Meningitis	2	0	2		

*Chi-square test or Fisher's exact test. *S. aureus*: *Staphylococcus aureus*; MRSA: Methicillin-resistant *S. aureus*; MSSA: Methicillin-susceptible *S. aureus*.

study, we collected 30 cases within 1 year; the incidence was 10.9%. Eight of the patients were <1 month old, indicating that more than 25% of the invasive *S. aureus* infection in Chinese children are neonates. In this study, a higher proportion of MRSA osteomyelitis was observed compared with MSSA; and 22 patients suffered from two or multi-sites infection. When infection refers to multiple organs, invasive *S. aureus* infection should be considered. Empiric therapy like anti-MRSA antibiotics should be in consideration.[4] There were no isolates resistant to linezolid, tigecycline, fusidic acid, mupirocin, and vancomycin. In this study, the best way for patients with arthritis and/or osteomyelitis was vacuum sealing drainage.

Two MRSA strain types predominated (ST59 and ST22) and together accounted for all MRSA strains identified. This study showed that ST22 was present in both the invasive MRSA and MSSA isolates, so we should pay attention to this clone in case that it may be the replacement of ST59 clone. We found a diverse range of MSSA STs causing disease; the observed strain diversity indicated that host factors might be as important as the bacterial genetic profile in children.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given consent for images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

This work was supported by grants from the National Natural Science Foundation of China (No. 81571948) and Beijing Natural Science Foundation (No. 7172075).

Conflicts of interest

There are no conflicts of interest.

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