Jpn. J. Infect. Dis., 54, 2001

Laboratory and Epidemiology Communications

Molecular Epidemiology of Methicillin-Resistant *Staphylococcus aureus* Infections in a Newborn Nursery, a Neonatal Intensive Care Unit, and a General Pediatrics Ward

Namiko Mori, Tomoko Fujino, Hiroshi Uchida, Hirofumi Miyazawa, Shigeki Minoura, Akihiko Kawana, Hisashi Kawahata, Michiko Gotoh, Tatsumi Yonamine, Fumiko Yamanishi, Tadatoshi Kuratsuji, Koichiro Kudo, Oichirou Kobori, Yoshio Yazaki and Teruo Kirikae*

International Medical Center of Japan, Toyama 1-21-1, Shinjuku-ku, Tokyo 162-8655

Communicated by Hiroshi Yoshikura

(Accepted October 10, 2001)

Nosocomial infection caused by methicillin-resistant *Staphylococcus aureus* (MRSA) is a serious problem in perinatal, neonatal, and pediatric medicine. Genome typing using pulsed-field gel electrophoresis (PFGE) is a powerful tool for investigating the source, transmission, and spread of MRSA.

In June 2001, an MRSA outbreak occurred involving a neonatal intensive care unit (NICU), a newborn nursery, and a general pediatrics ward in a hospital with 925 beds. These three wards are on the same floor. The NICU had five beds and the pediatric ward had 27 beds. One baby each in the newborn (B3) and in the NICU (N1) had conjunctivitis. One baby (N3) in the NICU had pneumonia. Two children (C2 and C3) in the general pediatrics ward had sepsis and otitis media. MRSA was isolated from eye mucus (from B3 and N1), the pharynx (from N3 and C2), and otorrhea (from C3) of these children. MRSA was also isolated from umbilical (from B1), vaginal (from B2), pharynx (from N2) and nasal (from C1) swabs, and the tip of a stomach tube (from N4). A total of ten isolates were obtained and coded as an isolate group 4N4S0601. Six MRSA isolates with two different PFGE patterns (patterns A4 and B) had been obtained from the same wards in December 2000 (isolate group HOSP1200) (1).

The all isolates 4N4S0601 were tested for chromosomal DNA typing (PFGE) by using a contour-clamped homogeneous electric field system (CHEF Mapper™: Bio-Rad Laboratories, Hercules, Calif., USA). They were also tested for antibiotic resistance (WalkAway™: Dade Behring, Deerfield, Ill., USA), enterotoxin serotyping (SET-RPLA: Denka Seiken Co., Tokyo), toxic shock syndrome toxin-1 (TSST-1) production (TST-RPLA: Denka Seiken), and coagulase serotyping (Denka Seiken).

PFGE patterns of *Sma*I DNA digests for isolate 4N4S0601 are shown in Fig.1. Band-based cluster analysis of these patterns (Molecular Analyst™: Bio-Rad) revealed five PFGE, patterns A4, A13, B, L, and K. A4, A13, and B shared a similarity of more than 75% (Fig. 2). Sensitivity to antibiotics is shown in Table 1. There were four different patterns. Patterns a and a' were different only in the level of minocycline (MINO) sensitivity. All isolates except No. 859 produced enterotoxin type C and TSST-1. All except Nos. 859 and 864 produced type II coagulase (Table 2).

All three MRSA isolates from the newborn nursery (Nos.

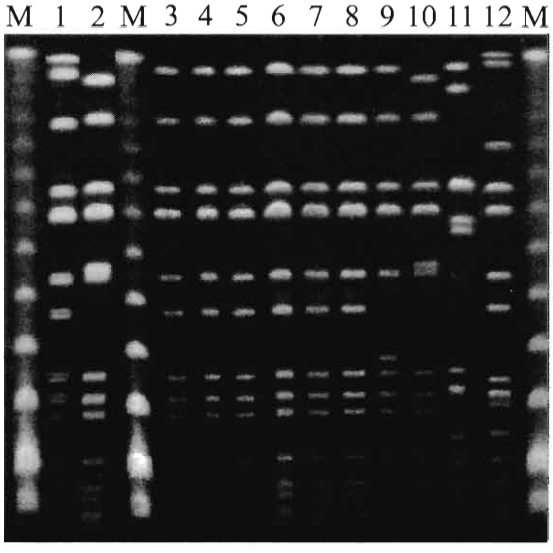

Fig. 1. Pulsed-field gel electrophoresis of *Sma*I-digested genomic DNA from MRSA isolates.
PFGE analysis of HOSP1200 isolates of Nos. 719 (lane 1) and 592 (lane 2), and 4N4S0601 isolates of Nos. 856 (lane 3), 858 (lane 4), 862 (lane 5), 861 (lane 6), 866 (lane 7), 867 (lane 8), 860 (lane 9), 863 (lane 10), 864 (lane 11) and 859 (lane 12). M: low range PFG Marker.

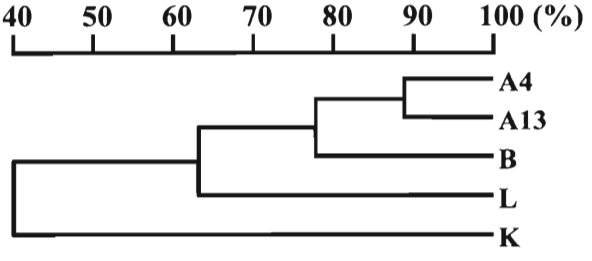

Fig. 2. Band-based cluster analysis of PFGE patterns of these outbreak isolates and the isolation dates of MRSA with each PFGE patterns.

*Corresponding author: Fax: +81-3-3202-7364, E-mail: tkirikae@ri.imcj.go.jp

Table 1. Antibiotic pattern classfied by antibiotic pattern of 18 antibiotics against MRSA

Antibiotic pattern	Antibiotics							
	FOM	LVFX	GM	ABK	MINO	ST	VCM	TEIC
a	R	R	S	S	I	S	S	S
a'	R	R	S	S	S	S	S	S
b	R	R	R	S	S	S	S	S
c	S	I	R	S	I	S	S	S

All isolates were resistant to PCG, MPIPC, ABPC, CEZ, CTM, CFDN, FMOX, IPM, EM, CLDM.
PCG: benzyl-penicillin, MPIPC: oxacillin, ABPC: ampicillin, CEZ: cefazolin, CTM: cefotiam, CFDN: cefdinir, FMOX: flomoxef, IPM: imipenem/cilastatin, EM: erythromycin, CLDM: clindamycin, FOM: fosfomycin, LVFX: levofloxacin, GM: gentamicin, MINO: minocycline, ABK: arbekacin, ST: streptomycin, VCM: vancomycin, TEIC: teicoplanin, R: resistant, S: susceptible, I: intermediate.

Table 2. Phenotypic and genotypic characterization of *S. aureus* isolates in June 2001 (4N4S0601)

Ward	Child	Isolate No.	Source	Symptom	PFGE pattrn	Antibiotic pattern	Enterotoxin	TSST-1	Coagulase
newborn nursery	B1	856	umbilicus	carrier	A4	a'	C	+	II
	B2	858	vagina	carrier	A4	a	C	+	II
	B3	862	eye mucus	conjunctivitis	A4	a	C	+	II
NICU	N1	861	eye mucus	conjunctivitis	A4	a	C	+	II
	N2	863	pharynx	carrier	B	a'	C	+	II
	N3	866	pharynx	pneumonia	A4	a	C	+	II
	N4	867	stomach tube	carrier	A4	a	C	+	II
general pediatrics	C1	859	nasal cavity	carrier	L	c	B	–	VIII
	C2	860	pharynx	sepsis	A13	a	C	+	II
	C3	864	otorrhea	otitis media	K	b	C	+	III

856, 858, and 862) and three of four isolates from the NICU (Nos. 861, 866, and 867) had almost the same character (Table 2). They all produced enterotoxin type C, TSST-1, and type II coagulase, and had the same PFGE pattern of *Sma*I DNA digests and almost the same spectrum of antibiotics susceptibility. These isolates were identical in PFGE pattern to an isolate in the previous outbreak, HOSP1200 isolate No. 592. Another isolate, No. 863, from the NICU had a pattern identical to an isolate of HOSP1200 (No. 719) in the previous outbreak. Three isolates from the general pediatrics ward had characters different from other MRSAs isolated from the newborn nursery or NICU. These results indicate the outbreak in the newborn nursery and the NICU was brought about by clonal expansion of MRSA which had caused an outbreak in the same wards in December 2000. The MRSA infections in the general pediatrics ward were probably unrelated to the outbreak in 2000. Babies in the newborn nursery and the NICU were examined by doctors in one team but cared for by nurses belonging to two different teams. Children in the general pediatrics ward were examined by doctors of another different team and cared for by nurses belonging to the team taking care of the NICU. The MRSA in the newborn nursery and the NICU, therefore, appeared to be transmitted by doctors but not by nurses.

REFERENCE

1. Fujino, T., Mori, N., Kawana, A., Kawabata, H., Kuratsuji, T., Kudo, K., Kobori, O., Yazaki, Y. and Kirikae, T. (2001): Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* in a Tokyo hospital in 2000. Jpn. J. Infect. Dis., 54, 91-93.