Methicillin-resistant *Staphylococcus aureus* in Nosocomial Infections in the Surgical ward and Operating Room

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**ABSTRACT**

In this study 214 strains of *Staphylococcus aureus* were isolated from clinical specimens on the surgical ward from 1983 to 1988 and in addition, 62 airborne strains were collected in the operating room. Highly methicillin-resistant strains of *S. aureus* (H-MRSA, MIC > 100 µg/ml) were not detected in 1983 showing a significant increase in frequency by 1987 accounting for about 60% of MRSA (MIC ~ 12.5 µg/ml). Countermeasures instituted in 1987 such as the use of disinfectant chlorhexidine alcohol significantly decreased the frequency of MRSA and H-MRSA isolates in 1988. In our study of coagulase type, MRSA type IV strains were predominant until 1984, whereas after 1986 type II was prevalent.

All airborne strains collected in the operating room were methicillin-sensitive *S. aureus*, with type VII currently epidemic. We therefore concluded that cross infection with MRSA took place on the surgical ward rather than in the operating room.

**Key words:** Nosocomial infection, *Staphylococcus aureus*, Operating room, Surgical patients

Methicillin-resistant strains of *Staphylococcus aureus* (MRSA) were first reported in 1961, soon after the clinical use of that antibiotic. Following the introduction of the third-generation cephalosporins in Japan in 1982, MRSA began to increase. Since MRSA now occupies a prominent position among nosocomial infections, we studied by coagulase typing strains of *S. aureus* isolated from clinical specimens on the surgical ward and airborne organisms collected in the operating room.

**MATERIALS AND METHODS**

1) Bacterial strains. Studied were 214 strains of *S. aureus* isolated from clinical specimens on the surgical ward from 1983 to 1988: 153 were isolated from intra-abdominal drains, 27 from skin and soft tissue, 20 from sputum, 8 from blood, 4 from urine and 2 from bile. An additional 62 strains of airborne bacteria were collected in the operating room in 1988.

2) Antibiotic minimum inhibitory concentration (MIC) determination. Antibiotic sensitivity was evaluated by MIC according to the standard method of the Japan Society of Chemotherapy. MICs of methicillin (DMPPC, Banyu Japan Co. Ltd., Tokyo, Japan), clexacillin (MCIPC, Meiji, Seika Co. Ltd., Tokyo, Japan), cefmetazole (CMZ, Sankyo Co. Ltd., Tokyo, Japan), imipenem (IPM, Banyu Japan, Co. Ltd., Tokyo, Japan), amikacin (AMK, Meiji Seika Co. Ltd., Tokyo, Japan), gentamicin (GM, Essex Nippon Co. Ltd., Tokyo, Japan), minocycline (MINO, Lederle Jahanan Co. Ltd., Tokyo, Japan), ofloxacin (OFLX, Daiichi Seiyaku Co. Ltd., Tokyo, Japan) were measured. Methicillin resistance was defined as an MIC equal to or more than 12.5 µg/ml while highly methicillin-resistant (H-MRSA) was defined as an MIC greater than 100 µg/ml.

3) Coagulase typing of *S. aureus*. Clinical isolates were cultured at 37°C for 3 days in heart infusion broth (Eikenn KK) and centrifuged at 3,000 rpm for 30 min. 0.1 ml of anticoagulant sera (type I–VIII) was added to 0.1 ml of the supernatant and incubated at 37°C for 1 hour. The coagulase typing of *S. aureus* was determined by the corresponding coagulase antiserum which inhibited the coagulation of normal rabbit plasma.

4) β-lactamase detection. The sensitivity of the acid-metry disk method is lower than that of nitrocefin method. Therefore, we evaluated the isolates for highly penicillinase production using the acid-metry disk method. One drop of a 0.01 mol phosphate buffer pH 7.0 was added to the β-lactamase detection disk (Nippon Seibutsu Zairyou center) which contained penicillin G and cefazolin as substrates. β-lactamase
RESULT

1) Isolation of MRSA and H-MRSA among the total *S. aureus* strains, 1983-1988 (Fig. 1).

H-MRSA, which was not detected in 1983 was present to a minor extent (<10%) in 1984 and 1985 and showed a significant increase in 1986-1987 accounting for about 60% of the total MRSA in 1987. With the medical staff’s awareness of this prevalence of MRSA on the ward, countermeasures against cross infection such as disinfection with chlorhexidine alcohol were instituted. This was followed in 1988 by a significant decrease in the frequency of infection by MRSA and H-MRSA.

2) Antibiotic susceptibility of H-MRSA (Fig. 2).

The highly resistant strains of *S. aureus* tended to be resistant not only to methicillin but also to other β-lactam antibiotics, while they were sensitive to GM, MINO and OFLX.

3) Changes in coagulase type, 1983-1988 (Fig. 3).

MRSA type IV strains were predominantly isolated until 1984. After 1986 most MRSA belonged to type II.

In contrast, type II was rare in community-acquired infection, and type IV occupied the most prominent position.
MRSA in nosocomial infections

Fig. 5. Antibiotic susceptibility of coagulase types II and IV methicillin-resistant *S. aureus* to aminoglycosides. About 80% of type II MRSA were sensitive to gentamicin though almost all types of this strain were resistant to amikacin.

Fig. 6. Antibiotic susceptibility of *S. aureus* isolated from the surgical ward and operating room. All airborne strains isolated from the operating room were methicillin sensitive.

Predominantly MRSA type IV strains were isolated prior to 1984. Type II was apparent in 1984, and after 1986, most MRSA were type II. By 1988, most strains were coagulase type II and IV.

4) Coagulase types of *S. aureus* isolated from infected lesions at time of admission vs. from postoperative infections, 1983-1988 (Fig. 4).

Type II accounted for 70.3% of the *S. aureus* isolated from postoperative infections. In contrast, type II was rare in community acquired infection, and type IV occupied the most prominent position.

5) Frequency of highly penicillinase-producing strains of coagulase types II and IV MRSA.

Of the type IV MRSA strains, 80.6% were highly penicillinase-producing strains whereas only 40.0% of the type II strains produced penicillinase, a statistically significant difference (p<0.01).

6) Antibiotic susceptibility of coagulase types II and IV.

Type II MRSA tended to be highly resistant to methicillin, and 97% were type II. Type II strains were more sensitive than type IV to minocycline and ofloxacin, but were less sensitive to methicillin. About 30% of type II MRSA were sensitive to gentamicin though almost all this type of strains were resistant to amikacin (Fig. 5). These gentamicin-sensitive, amikacin-resistant strains were detected in our institution beginning in the latter half of 1986.

7) Antibiotic susceptibility and coagulase types of *S. aureus* isolated from the surgical ward and the operating room (Fig. 6, 7).

All airborne strains isolated from the operating room were methicillin sensitive. Although type II strains occupied the prominent position in the infection which occurred in surgical ward, type VII strains were currently epidemic in the operating room.
DISCUSSION

In any study of nosocomial infection, it is important to demonstrate whether the infection originated within the hospital or outside it. There are two reasons why we regard MRSA as a nosocomial pathogen. First, in our evaluation of coagulase types we demonstrated that type II was epidemic. Second, with the countermeasures against nosocomial infection we observed a decrease in the frequency of MRSA.

The failure of povidone iodine to reduce the prevalence of MRSA in our institution led us to choose another antiseptic solution. It was recently reported that MRSA’s sensitivity to povidone iodine is unexpectedly low. Even at low concentrations chlorhexidine has a persistent antibacterial effect whereas povidone iodine solutions lack such activity. We therefore chose chlorhexidine-alcohol as the antiseptic solution for use in our facility beginning in 1987.

Most strains of MRSA were coagulase types II and IV. Type IV strains were those predominantly isolated until 1984, whereas after 1989 type II clearly predominated. Type II strains were frequently isolated from postoperative infections although type IV strains were commonly isolated from patients having infections on admission. Therefore, it is reasonable to assume that type II MRSA was responsible for nosocomial infections that originating on our ward, with type IV introduced into the ward by patients infected in other settings.

The suggested mechanism for resistance in MRSA is an alteration of penicillin-binding-protein (PBP), a key enzyme in cell wall synthesis and the target for β-lactams. Most MRSA contain a PBP 2′ that has a low affinity for most β-lactam antibiotics. It is said that methicillin-resistance is not mediated by the penicillinase plasmid. Therefore, it is possible that type II strains of which only 40.0% were highly penicillinase-producing strains contain a PBP 2′.

MRSA produced modifying enzymes against aminoglycosides (AGs). The AGs-resistant MRSA strains are said to be divided into two main groups: one resistant to gentamicin, tobramycin and amikacin, and the other sensitive to gentamicin, but resistant to both tobramycin and amikacin. MRSA strains of the latter group were not detected in Japan until 1983. This type of MRSA now seems to be reported with increased frequency.

To determine precisely where in the surgical department cross-infection takes place, we compared the strains isolated from the surgical ward with those collected in the operating room. However, MRSA could not be found in the operating room. Notably, the coagulase type epidemic in the operating room was type VII, whereas type II strains were important as nosocomial infections on the ward. We therefore conclude that in our setting, cross infection with MRSA primarily occurred on the ward, not in the operating room.

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REFERENCES