ISOLATION AND ANTIBIOTIC SUSCEPTIBILITY OF CEFAZOLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*, COMPARED WITH COAGULASE-NEGATIVE STAPHYLOCOCCI

SATOSHI NAKASHIO, ISAO HARASAWA*,
YUKO SAYAMA and MASAO NAKAMURA

Department of Laboratory Medicine, * Department of Clinical Laboratory,
St. Marianna University School of Medicine, 2-16-1 Sugao, Miyamae-ku,
Kawasaki 213, Japan

(Received May 19, 1987)

Since methicillin- and/or cephem-resistant staphylococci are increasingly recognized as potential human pathogens, the isolation frequency and antibiotic susceptibility of representative strains of cefazolin (CEZ)-resistant staphylococci against 18 antimicrobial agents were investigated in this study. Results for *S. aureus* strains were compared with those for coagulase-negative staphylococci (CNS). Sixty-six of 463 *S. aureus* strains (14.3%) and 31 of 416 CNS strains (7.5%) were CEZ-resistant. These were isolated abundantly from pus, punctate and bile specimens. These isolates showed multiple resistance against at least three of six representative agents (CEZ, PCG, KM, EM, TC, CP). CEZ-resistant CNS isolates were more resistant than those of *S. aureus* against many agents, especially CET, CMZ, CTM, MCIPC and GM. AMK, DOXY, MINO and OFLX were the most active agents and the last two inhibited over 80% of strains in both groups of staphylococci at a concentration of 3.13 μg/ml. In both groups, the predominant coagulase types were II, III and IV, which accounted for over 85%. No apparent relationship was observed between coagulase type and either the source of the isolate or antibiotic susceptibility. Although no significant difference in β-lactamase production was observed between *S. aureus* and CNS isolates, the percentage (93.9%) of β-lactamase-positive isolates among CEZ-resistant *S. aureus* was considerably higher than that (68.2%) of CEZ-sensitive *S. aureus* isolates. Species identification of CNS may help to evaluate differential pathogenic significance and also to guide effective chemotherapy against CNS infections.

Key words : Cefazolin-resistance, *S. aureus*, Coagulase-negative staphylococci

INTRODUCTION

Methicillin- and/or cephem-resistant staphylococci are increasingly recognized as potential pathogens, especially since the third-generation cephalosporins were extensively introduced[1~3]. In Japan, methicillin was first introduced for penicillin G-resistant staphylococci in 1961. It exhibits, however, no activity against Gram-negative rods and its antibacterial activity against Gram-positive cocci-including *Streptococcus pneumoniae* and group A and B streptococci-is weaker than that of penicillin G. Instead of methicillin (preferred in Europe and the USA), cephalosporins, and especially cefazolin or cephalothin, were used in Japan against penicillin G-resistant staphylococci because of their wider spectrum and better activity. Methicillin-resistant staphylococci were first detected in Great Britain in 1961 and thereafter became a [rapidly growing clinical and epidemiological problem all over the world[4].

Recent progress in the taxonomy of staphylococci has led to a wider acceptance of and interest in

the variety of species other than *S. aureus* and *S. epidermidis*[5~7]. Coagulase-negative staphylococci (CNS), formerly regarded as contaminants or only occasionally opportunistic pathogens, are now the subject of increasing interest in various human infections[8,9]. The present study was undertaken to determine the isolation frequency and antimicrobial susceptibility of cefazolin-resistant *S. aureus* strains in comparison with those of CNS strains.

MATERIALS AND METHODS

Strains tested. A total of 879 isolates of staphylococci were used in this study. Most of these had been recently isolated in St. Marianna University Hospital from various clinical specimens including blood, other normally sterile body fluids and tissues, high-colony-count urine, sputum, pus, bile, otopyorrhea, tracheal and oropharyngeal swabs, and others. These were selected because of source, amount of organisms, or both parameters. The isolates were almost all from different patients ; although, in a few cases, isolates from different sites on the same patient collected on different days were included if their biotypes were not the same. Staphylococci were tentatively categorized as *S. aureus* or CNS by colonial and microscopical morphology ; catalase, coagulase and acetoin production ; and mannitol fermentation. The tube coagulase test was performed by inoculating one or two colonies of staphylococci into 0.5 ml of rabbit coagulase plasma containing EDTA (Denka Seiken, Tokyo). The tube was incubated at 35°C and examined for the presence of clot formation at 4 and 24 h. Species identification of CNS was performed initially using the criteria of KLOOS and SCHLEIFER[5~7] and later reconfirmed using the commercially available SP-18 system (Nissui, Tokyo).

***In vitro* susceptibility testing.** Antibiotic susceptibility of isolates was qualitatively determined by the tri-disc method (Eiken, Tokyo) and commercially available semi-automatic analyzer (COBAS BACT, Roche, Tokyo)[10]. The minimum inhibitory concentrations (MICs) were determined basically by the agar dilution method as described by the Japanese Society of Chemotherapy[11] but slightly modified as described by WOODS et al.[12]. Overnight cultures of test organisms were diluted to a density of approximately 10^6 colony-forming units per ml in modified Mueller-Hinton broth (Nissui, Tokyo) and supplied by means of the multiple inocula replicator (Sakuma, Tokyo) to the surface of modified Mueller-Hinton agar (Nissui) plates containing two-fold dilutions of antimicrobial agents. The MICs were determined as the lowest concentrations of antimicrobial agents inhibiting growth after 24 h incubation at 30°C. Results were expressed as the range of MIC (μg/ml), in addition to MIC_{50} and MIC_{80} (the concentrations of antimicrobial agents inhibiting 50% and 80% of the strains tested). A total of 18 antimicrobial agents was tested. The abbreviated forms of their names are used according to the recommendations of the Japanese Society of Chemotherapy. The drugs were kindly supplied by the corresponding organizations. Solutions of antimicrobial agents were freshly prepared for each test.

Coagulase typing and β-lactamase production. Coagulase types of *S. aureus* isolates were determined by the agglutination test using the specific antisera against each type of coagulase (Denka Seiken, Tokyo)[13]. β-lactamase production was examined with a chromogenic cephalosporin, nitrocefin (Cefinase ; BBL Microbiology Systems, Maryland, USA)[14,15].

RESULTS

Antibiotic susceptibility of staphylococci. Antibiotic susceptibility of a total of 879 isolates of staphylococci from clinical specimens was tentatively investigated by the tri-disc method and strains showing susceptibility of "+" or "−" were tentatively categorized as resistant. The percentages of resistant isolates against each of 18 antimicrobial agents are shown in Table 1. In *S. aureus*, the percentages against cefazolin and methicillin were 14.3 and 14.5%, and those against penicillin G and ampicillin exceeded 60%. Percentages of resistant isolates were much higher against third-generation cephalosporins such as latamoxef and cefoperazone than first- and second-generation drugs such as cephalothin, cefmetazole and cefotiam. No resistant isolate against minocycline and ofloxacin was detected. In CNS, percentages of resistant isolates against cefazolin and methicillin were 7.5 and 22.1%. A significant difference in these percentages between strains of *S. aureus* and CNS was observed against cefoperazone and cloxacillin.

Isolation frequency of CEZ-resistant staphylococci. Table 2 summarizes the number of iso-

Table 1. Susceptibility of staphylococci from clinical specimens against 18 antimicrobial agents

Antimicrobial agent	Percentage of resistant isolates		
	S. aureus	CNS*	Total staphylococci
CEZ	14.3	7.5	11.0
CET	3.5	6.3	4.8
CMZ	1.7	7.9	4.7
CTM	4.3	3.4	3.9
LMOX	13.2	20.7	16.7
CPZ	21.0	8.7	15.1
PCG	77.5	58.7	68.6
ABPC	62.0	43.5	53.2
MCIPC	4.3	28.4	15.7
DMPPC	14.5	22.1	18.1
GM	17.7	26.0	21.6
AMK	1.5	2.4	1.9
EM	27.9	30.8	29.2
LCM	21.6	26.7	24.0
CLDM	19.0	22.8	20.8
DOXY	6.7	9.9	8.2
MINO	0	0	0
OFLX	0	0	0

* CNS : coagulase-negative staphylococci.
No. of isolates tested : *S. aureus*, 463
CNS, 416.

Table 2. Isolation frequency of CEZ-resistant staphylococci from clinical specimens

Clinical specimen	*Staphylococcus aureus*				Coagulase-negative staphylococci			
	No. of isolates tested (A)	No. of resistant isolates (C)	C/A(%)	C/D(%)	No. of isolates tested (A)	No. of resistant isolates (C)	C/A(%)	C/D(%)
T.O. swab*	66	3	4.5	4.5	23	2	8.7	6.5
Sputum	89	9	10.1	13.6	36	3	8.3	9.7
Punctate	28	7	25.0	10.6	24	2	8.3	6.5
Pus	118	30	25.4	45.5	58	8	13.8	25.8
Bile	0	0	0	0	6	2	33.3	6.5
Urine	38	5	13.2	7.6	148	10	6.8	32.3
Feces	18	4	22.2	6.1	15	1	6.7	3.2
Otopyorrhea	48	3	6.3	4.5	35	2	5.7	6.5
Others	58	5	8.6	7.6	71	1	1.4	3.2
Total	463 (B)	66 (D)			416 (B)	31 (D)		

* T.O. swab : tracheal and oropharyngeal swab.

lates of staphylococci and the sources from which they were recovered. The isolation frequency of CEZ-resistant isolates varied widely according to the specimens. A total of 66 (14.3%) isolates of CEZ-resistant *S. aureus* were detected from 463 strains of *S. aureus*, and 31 (7.5%) isolates of CEZ-resistant CNS from 416 strains of CNS. The isolation frequency of CEZ-resistant *S. aureus* was higher in punctate, pus and feces than in the other specimens. On the other hand, the isolation fre-

Table 3. Multiple-antibiotic resistance of CEZ-resistant staphylococci

Type of multiple-resistance		No. of isolates (%) showing multiple-resistance	
		S. aureus	Coagulase-negative staphylococci
3	CEZ, PCG, KM	34 (51.5)	3 (9.7)
4	CEZ, PCG, KM, EM	13 (19.7)	16 (51.8)
	CEZ, PCG, KM, TC	2 (3.0)	1 (3.2)
5	CEZ, PCG, KM, EM, TC	17 (25.8)	2 (6.5)
	CEZ, PCG, KM, EM, CP	0	7 (22.6)
6	CEZ, PCG, KM, EM, TC, CP	0	2 (6.5)

Table 4. MIC distribution of CEZ-resistant *Staphylococcus aureus* against 18 antimicrobial agents

Antimicrobial agent	Minimum inhibitory concentration (μg/ml)													
	0.025	0.05	0.10	0.20	0.39	0.78	1.56	3.13	6.25	12.5	25	50	100	>100
CEZ									12	28	14	5	3	4
CET						4	24	20	4	2	6		6	
CMZ								26	29	6	5			
CTM							1	30	21	4	2	6		2
LMOX										7	34	16	1	8
CPZ									2	14	35	4	5	6
PCG							1		2	1	5	17	29	11
ABPC							2		2	1	6	32	22	1
MCIPC					20	25	7	4	2	2	1			5
DMPPC							3	1	33	14	5	2	2	6
GM			2	8	1		5	11	17	9	4	8	1	
AMK						16	32	7	11					
EM					7			25	5	1				28
LCM				1	2	33							2	28
CLDM		9	26	1										30
DOXY			34	4	2	2		1		23				
MINO				24	18	2	22							
OFLX		1	3	6	2	3	19	32						

No. of isolates tested : 66.

quency of CEZ-resistant CNS strains was higher in bile and pus.

Multiple antibiotic resistance of CEZ-resistant staphylococci. Multiple antibiotic resistance of CEZ-resistant staphylococci was investigated against cefazolin, penicillin G, kanamycin, erythromycin, tetracycline and chloramphenicol as representatives by the tri-disc method. All the isolates tested showed multiple resistance to more than three of the six agents. All CEZ-resistant staphylococci showed cross-resistance to penicillin G and kanamycin. Multiple resistance to cefazolin, penicillin G and kanamycin was highest (51.5%) among *S. aureus* isolates, while multiple resistance to four agents (cefazolin, penicillin G, kanamycin and erythromycin) was highest (54.8%) among CNS isolates (Table 3). A significant difference in multiple resistance between CEZ-resistant *S. aureus* and CNS isolates was observed. None of the CEZ-resistant *S. aureus* isolates showed multiple resistance to all six agents. Thirty-four (51.5%) isolates of *S. aureus* showed multiple resistance to cefazolin, penicillin G and kanamycin, while only 3 (9.7%) isolates of CNS did (Table 3). Seventeen (54.8%) isolates of CNS showed multiple resistance to cefazolin, penicillin G, kanamycin and erythromycin or tetracycline.

Susceptibility of CEZ-resistant staphylococci. Susceptibility of CEZ-resistant *S. aureus* isolates against 18 antimicrobial agents is compared

Table 5. MIC distribution of CEZ-resistant coagulase-negative staphylococci against 18 antimicrobial agents

Antimicrobial agent	Minimum inhibitory concentration (μg/ml)													
	0.025	0.05	0.10	0.20	0.39	0.78	1.56	3.13	6.25	12.5	25	50	100	>100
CEZ									7	1	2	5	6	11
CET				1		4	1	2	1	1	3	1	13	4
CMZ						1			1	7	11	10	1	
CTM						1	1	4	3	4	1	4	10	3
LMOX									2		1	3	5	20
CPZ							1	3	1	5	2	2	1	16
PCG											3	9	12	7
ABPC									1	1	7	8	14	
MCIPC						2						1		28
DMPPC									2		2	3	5	19
GM	3					1		1	3	2	7	10	1	3
AMK				2	1	4	1	10	5	4	2	2		
EM			1		1				2		7	2		18
LCM					8	2				1	3			17
CLDM		9	2	4			1							15
DOXY			3	5	4	14			1	3	1			
MINO			2	11	13	1		2	2					
OFLX				1	13	14	3							

No. of isolates tested: 31.

Table 6. Susceptibility of CEZ-resistant staphylococci against 18 antimicrobial agents

Antimicrobial agent	*Staphylococcus aureus*			Coagulase-negative staphylococci		
	MIC range	MIC_{50}*	MIC_{80}*	MIC range	MIC_{50}*	MIC_{80}*
CEZ	6.25->100	12.5	25	6.25 ->100	100	100
CET	0.78- 100	3.13	12.5	0.20 ->100	100	100
CMZ	3.13- 25	6.25	6.25	0.78 - 100	25	50
CTM	1.56->100	6.25	12.5	0.78 ->100	50	100
LMOX	12.5 ->100	25	50	6.25 ->100	100	100
CPZ	6.25->100	25	50	1.56 ->100	100	100
PCG	1.56->100	100	100	25 ->100	100	100
ABPC	1.56->100	50	100	6.25 - 100	50	100
MCIPC	0.39->100	0.78	3.13	0.78 ->100	100	100
DMPPC	1.56->100	6.25	25	6.25 ->100	100	100
GM	0.10- 100	6.25	12.5	0.025->100	25	50
AMK	0.78- 6.25	1.56	3.13	0.20 - 50	3.13	12.5
EM	0.39->100	6.25	100	0.10 ->100	100	100
LCM	0.20->100	0.78	100	0.39 ->100	100	100
CLDM	0.05->100	0.10	100	0.05 ->100	1.56	100
DOXY	0.10- 12.5	0.10	12.5	0.10 - 25	0.78	0.78
MINO	0.20- 1.56	0.39	1.56	0.10 - 6.25	0.39	0.39
OFLX	0.05- 3.13	1.56	3.13	0.10 - 1.56	0.78	0.78

* $MIC_{50,80}$: MIC (μg/ml) required to inhibit 50 and 80% of the isolates, respectively.

with those of CEZ-resistant CNS in Tables 4 and 5. The MIC range, MIC_{50} and MIC_{80} are also shown in Table 6. In general, CEZ-resistant CNS isolates were more resistant than CEZ-resistant *S. aureus* isolates against many agents. Amikacin, doxycycline, minocycline and ofloxacin were the most active agents, inhibiting 80% of the strains of both CEZ-resistant *S. aureus* and CNS at a concentration of 12.5 μg/ml. A significant difference in susceptibility between CEZ-resistant *S. aureus* and

Table 7. β-lactamase production of staphylococci

Species	CEZ-resistant		CEZ-sensitive	
	No. of isolates tested	No. of β-lactamase positive isolates (%)	No. of isolates tested	No. of β-lactamase positive isolates (%)
S. aureus	66	62 (93.9)	44	30 (68.2)
CNS*	31	26 (83.9)	35	27 (77.1)
Total	97	88 (90.7)	79	57 (72.2)

* CNS : coagulase-negative staphylococci.

Table 8. Species identification of coagulase-negative staphylococci

Species	CEZ-resistant isolates (%)	CEZ-sensitive isolates (%)
S. epidermidis	5 (16.1)	44 (84.6)
S. haemolyticus	22 (71.0)	5 (9.6)
S. cohnii	1 (3.2)	2 (3.8)
S. sciuri ss. *lentus*	2 (6.5)	0
S. intermedius	1 (3.2)	0
S. capitis	0	1 (1.9)
Total	31	52

Table 9. Coagulase-typing of *Staphylococcus aureus*

Coagulase-type	CEZ-resistant isolates (%)	CEZ-sensitive isolates (%)
I	0	0
II	30 (45.5)	30 (56.6)
III	13 (19.7)	10 (18.9)
IV	20 (30.3)	6 (11.3)
V	2 (3.0)	3 (5.7)
VI	0	0
VII	1 (1.5)	4 (7.5)
VIII	0	0
Total	66	53

CNS isolates was observed especially against cephalothin, cefotiam and methicillin.

Wide variations in MIC distribution of CEZ-resistant *S. aureus* and CNS isolates were found to lincomycin, clindamycin and erythromycin. For example in CEZ-resistant *S. aureus* isolates to clindamycin, 30 (45.5%) of 66 isolates were evaluated as highly resistant with MICs over 100 μg/ml, while the remaining isolates were evaluated as highly sensitive with MICs less than 0.2 μg/ml.

β-lactamase production of staphylococci. β-lactamase production detected by Cefinase disc is presented in Table 7. No significant difference in β-lactamase production was observed between *S. aureus* and CNS isolates. However, the percentage of β-lactamase-positive isolates among CEZ-resistant *S. aureus* was rather higher, especially than that of CEZ-sensitive *S. aureus*. No significant difference in coagulase type was observed between 66 isolates of CEZ-resistant *S. aureus* and 53 isolates of comparable CEZ-sensitive *S. aureus*. The most common coagulase type was II, accounting for 45.5% of CEZ-resistant *S. aureus* and for 56.6% of CEZ-sensitive *S. aureus*. The coagulase types which accounted for over 85% of both CEZ-resistant and -sensitive *S. aureus* were II, III and IV.

Species identification of CNS. Species identification of CEZ-resistant CNS isolates was performed and the results compared with 52 isolates of arbitrarily selected CEZ-sensitive CNS in Table 8. Twenty-two CEZ-resistant isolates (71%) were identified as *S. haemolyticus*, while 44 CEZ-sensitive isolates (84.6%) were identified as *S. epidermidis* and only 5 (9.6%) as *S. haemolyticus*. A pilot series showed that five isolates arbitrarily selected from 49 isolates of *S. epidermidis* (10.2%) were CEZ-resistant, while 22 of arbitrarily selected 27 isolates of *S. haemolyticus* (81.5%) were CEZ-resistant. Although there were not enough of the other individual species to make a meaningful comparison, *S. haemolyticus* isolates were more resistant to β-lactam agents than *S. epidermidis* isolates. From these findings, precise species identification of CNS as a routine procedure would appear to be clinically important.

DISCUSSION

Recent studies have shown a high incidence of resistance in routine isolates of CNS in comparison with *S. aureus* isolates[8,9,16]. In the present study,

CEZ-resistant CNS isolates were overall more resistant than *S. aureus* isolates against many antimicrobial agents and also showed high multiple resistance to six representative antimicrobial agents. COHEN and colleagues[17,18] demonstrated that aminoglycoside resistance in CNS is plasmid-mediated and that the plasmids can be passed from CNS to *S. aureus*, probably by conjugation as well as transduction. Multiple-resistant CNS strains may act as reservoirs of resistance for *S. aureus* strains.

It is still uncertain whether methicillin-resistant staphylococci always show cross-resistance to cephalosporins[9,16]. Although it is generally agreed that *S. aureus* strains that are resistant to penicillinase-resistant penicillins (such as methicillin or cloxacillin) can also automatically be regarded as resistant to cephalosporins, this cross-resistance has not been a consistent finding for CNS strains. In the present study, some cephalosporins showed considerable activity against some of the methicillin- and cefazolin-resistant CNS strains. Since β-lactams have an unpredictable activity against staphylococci, especially the CNS species, these agents should probably not be used in "blind" therapy of serious staphylococcal infections regardless of *in vitro* susceptibility testing.

No significant difference was observed in β-lactamase production between CEZ-resistant and -sensitive staphylococci in this study, although KONNO et al.[19] and ROSDAHL et al.[14,20] demonstrated a close relationship between β-lactamase production and susceptibility to antibiotics and also phage typing. This discrepancy may in part be attributed to the strains used, the level of antibiotic consumption for clinical use, and the methods of β-lactamase detection and susceptibility testing[15].

With the increasing frequency and clinical importance of CNS strains, species identification can help in furthering our understanding of the microbiology of these organisms and their role in infectious diseases[8,9,16]. More specifically, increased antibiotic resistance among CNS strains should be differentiated into increased frequency of *S. haemolyticus* or other distinct species and a generalized increase in antibiotic resistance among all species. More information on the pathogenic role of each species would lead to a better understanding of the clinical significance of CNS strains.

References

1) COLLINS, J K MADER J T and KELLY M T: Resistance of methicillin-resistant *Staphylococcus aureus* to third-generation cephalosporins. J Infect Dis 147 : 591, 1983
2) SHIMADA, K ADACHI K TANAKA K KAMIJOH H SASAKI M HATAKEYAMA T INAMATSU T and URAYAMA K: Multiply resistant *Staphylococcus aureus* ; increasing frequency of isolation and their susceptibility to 41 antimicrobial agents. Chemotherapy 31 : 835～841, 1983
3) WATANABE, A OIZUMI K SASAKI M AONUMA S ONUMA K ONO R HONDA Y and KONNO K: Studies on multiple-resistant *Staphylococcus aureus* (I). Comparison of antibiotic sensitivity and β-lactamase producing activity of *Staphylococcus aureus* isolated from sputum in 1982 and 1985. Chemotherapy 34 : 859～868, 1986
4) BARBER, M: Methicillin-resistant staphylococci. J Clin Pathol 14 : 385～393, 1961
5) KLOOS, E W and SCHLEIFFER K H: Isolation and characterization of staphylococci from human skin. II. Description of four new species : *Staphylococcus warneri*, *Staphylococcus capitis*, *Staphylococcus hominis*, and *Staphylococcus simulans*. Int J Syst Bacteriol 25 : 62～79, 1975
6) SCHLEIFFER, K H and KLOOS E W: Isolation and characterization of staphylococci from human skin. I. Amended description of *Staphylococcus epidermidis* and *Staphylococcus saprophyticus* and descriptions of three new species : *Staphylococcus cohnii*, *Staphylococcus haemolyticus*, and *Staphylococcus xylosus*. Int J Syst Bacteriol 25 : 50～61, 1975
7) KLOOS, E W and SCHLEIFFER K H: Simplified scheme for routine identification of human *Staphylococcus* species. J Clin Microbiol 1 : 82～88, 1975
8) NICOLLE, L E HOBAN S A and HARDING G K: Characterization of coagulase-negative staphylococci from urinary tract specimens. J Clin Microbiol 17 : 267～271, 1983
9) GILL, V J SELEPAK S T and WILLIAMS E C: Species identification and antibiotic susceptibilities of coagulase-negative staphylococci isolated from clinical specimens. J Clin Microbiol 18 : 1314～1319, 1983
10) NAKASHIO, S KIKUGAWA I NARIKAWA S NAKAMURA M MIYAMOTO T OURA H IROKAWA C SAKAMA S and HARASAWA I: Evaluation of COBAS BACT (Roche) in antimicrobial susceptibility testing. Rinsho to Biseibutsu

12 : 337～342, 1985
11) GOTO, S KAWAKITA T KOZAKAI N MITSUHASHI S NISHINO T OSAWA N and TANAMI H: Methods for determination of minimum inhibitory concentration (MIC). Chemotherapy 29 : 76～79, 1981
12) WOODS, L G HALL G S RUTHERFORD I PRATT K J and KNAPP C C: Detection of methicillin-resistant *Staphylococcus epidermidis*. J Clin Microbiol 24 : 349～352, 1986
13) NAKASHIO, S KIKUGAWA I NAKAMURA M HARASAWA I YANAGAWA C TANAKA Y ASHIKAWA K and MAEDA N: Serotype and antibiotic susceptibility of *Staphylococcus aureus* and *Pseudomonas aeruginosa* isolated from burned patients, with special reference to hospital infection. Kansenshogaku Zasshi 60 : 222～230, 1986
14) ROSDAHL, V T and ROSENDAL K: Correlation of penicillinase production with phage type and susceptibility to antibiotics and heavy metals in *Staphylococcus aureus*. J Med Microbiol 16 : 391～399, 1983
15) SELEPAK, T S and WITEBSKY F G: β-lactamase detection in nine staphylococcal species. J Clin Microbiol 20 : 1200～1201, 1984
16) HAMILTON-MILLER, J M T and ILEFFE A: Antimicrobial resistance in coagulase-negative staphylococci. J Med Microbiol 19 : 217～226, 1985
17) COHEN, M L WONG E S and FALKOW S: Common R-plasmids in *Staphylococcus aureus* and *Staphylococcus epidermidis* during a nosocomial *Staphylococcus aureus* outbreak. Antimicrob Agents & Chemother 21 : 210～215, 1982
18) WEINSTEIN, R A KABINS S A NATHAN C SWEENEY H M JAFFE H W and COHEN S: Gentamicin-resistant staphylococci as hospital flora : epidemiology and resistance plasmids. J Infect Dis 145 : 374～382, 1982
19) KONNO, M UBUKATA K YAMASHITA N MATSUSHITA M KAWAKAMI S MASUDA M and MONOGUCHI R: Relationship between resistant pattern to antibiotics and phage type of methicillin-resistant *Staphylococcus aureus*. Kansenshogaku Zasshi 59 : 1029～1040, 1985
20) FROMODT-MOLLER, N ROSDAHL V T SORENSEN G HARTZEN S H and BENTZON M W: Relationship between penicillinase production and *in vitro* activity of methicillin, oxacillin, cloxacillin, dicloxacillin, flucloxacin, and cephalothin against strains of *Staphylococcus aureus* of different phage patterns and penicillinase activity. J Antimicrob Chemother 18 : 27～33, 1986

Cefazolin 耐性 *Staphylococcus aureus* の検出状況と薬剤感受性 —coagulase-negative staphylococci との比較

中塩哲士・原沢 功・佐山裕子・中村正夫
聖マリアンナ医科大学臨床検査医学教室*

近年 methicillin あるいは cephem 剤耐性 staphylococci の臨床材料からの検出が漸増していることから，CEZ を代表薬剤として耐性菌の検出状況および18薬剤に対する感受性を検討した。*S. aureus* の成績と coagulase-negative staphylococci (CNS) の成績を比較した。*S. aureus* 463株中66株 (14.3%)，CNS 416株中31株 (7.5%) の CEZ 耐性菌が検出された。検体別には膿，穿刺液，胆汁から高頻度に分離された。これらの株は，代表とした6系統薬剤 (CEZ, PCG, KM, TC, CP, EM) のうち少なくとも3系統薬剤以上に同時に交差耐性を示した。多くの薬剤，特に CET, CMZ, CTM, MCIPC, GM に対して CNS 株は *S. aureus* 株より高度の耐性を示した。AMK, DOXY, MINO, OFLX が優れた抗菌力を示し，特に後者の2薬剤は 3.13 μg/ml の濃度で両群ともに80%以上の菌株の増殖を阻止した。両群ともに coagulase 型はII，IIIおよびIV型が多く，85% 以上を占めた。Coagulase 型と由来検体あるいは薬剤感受性との間に相関性は認められなかった。*S. aureus* 株と CNS 株の間に β-lactamase 産生能で差異はなかった。β-lactamase 産生株の割合は CEZ 耐性 *S. aureus* において 93.9%，CEZ 感受性 *S. aureus* において 68.2% であった。CNS の菌種同定はこれらの菌群の病原的意義を明らかにし，併せて効果的な化学療法を進めるうえで必要と考えられた。

* 川崎市宮前区菅生 2-16-1