



Original Article

Change in Detection Rate of Methicillin-Resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* and Their Antibiotic Sensitivities in Patients with Chronic Suppurative Otitis Media

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OBJECTIVE: To investigate changes in *Pseudomonas aeruginosa* (PA) and methicillin-resistant *Staphylococcus aureus* (MRSA) and their antibiotic sensitivities over 13 years in patients diagnosed with chronic suppurative otitis media (CSOM).

MATERIALS and METHODS: The current study reports on a retrospective analysis of the outcomes of 2256 outpatients who visited the Department of Otorhinolaryngology clinics of 3 tertiary medical centers and who were diagnosed with chronic otitis media (COM) or chronic cholesteatomatous otitis media (CCOM) from January 2001 to December 2013. Aural discharge was collected from each patient. Infectious bacteria were identified, and their antibiotic sensitivities were determined.

RESULTS: The most frequent age range of patients diagnosed with CSOM was 41 to 50 years. In patients aged more than 30 years, CSOM was more frequent in females than in males, whereas in those aged less than 30 years, it was more frequent in males. Regardless of age, the isolated MRSA strains showed high sensitivity to vancomycin, teicoplanin, and trimethoprim/sulfamethoxazole, whereas the isolated PA strains showed high sensitivity to cefepime, amikacin, and ceftazidime. The isolation rate of MRSA in patients with CSOM slightly decreased over the 13-year study period; however, PA resistance to quinolones and aminoglycosides showed a tendency to increase.

CONCLUSION: Bacteria isolated from patients with CSOM showed little change between 2001 and 2013, whereas their antibiotic resistance showed changes; in particular, increased PA resistance to quinolones was observed. Empirical antibiotic treatment can lead to bacterial resistance, and changes in antimicrobial agents commonly used to treat CSOM should be considered.

KEYWORDS: Chronic otitis media, bacteria, antibiotic sensitivity

INTRODUCTION

Chronic suppurative otitis media (CSOM) is characterized by a perforated tympanic membrane with persistent discharge from the middle ear caused by bacteria, fungi, and viruses, resulting in the inflammation of the mucosal lining. Chronic inflammation of the mastoid cavity and middle ear are characteristic of CSOM; however, the mechanism of chronic infection has not yet been determined^[1]. Without appropriate treatment, CSOM may result in various complications. CSOM can be classified as perforated non-cholesteatomatous chronic otitis media (COM), with perforation of the tympanum, and chronic cholesteatomatous otitis media (CCOM), with cholesteatoma formation regardless of eardrum perforation^[2].

In general, Eustachian tube dysfunction and bacterial infection are the most frequent causes of CSOM; thus, the selection of appropriate antimicrobial agents is an important aspect of its treatment^[3]. The recent abuse of antimicrobial agents, however, has led to changes in the major pathogens causing CSOM and in their antibiotic sensitivities. Many studies have reported that the most frequently detected frequently in patients with CSOM are *Staphylococcus* and *Pseudomonas aeruginosa* (PA); increases in the resistance of these pathogens to antimicrobial agents have made them difficult to treat^[4]. Empirical antibiotic treatment of patients with antibiotic-resistant bacteria, such as quinolone-resistant PA and methicillin-resistant *Staphylococcus aureus* (MRSA), which have been increasingly identified in infectious diseases, may result in treatment failure or complications^[5,6].

We determined the predominant pathogenic strains of CSOM according to patient gender and age distribution and their changes in antimicrobial susceptibility over 13 years from 2001 to 2013. We also investigated changes in the primary pathogens and their antibiotic sensitivities in subgroups of patients diagnosed with COM and CCOM to select appropriate antimicrobial agents for

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primary treatment and to prevent the development of antibiotic-resistant bacteria.

MATERIALS and METHODS

Subjects and Methods

The study population consisted of 2256 outpatients who visited the Department of Otorhinolaryngology clinics of 3 tertiary medical centers from January 2001 to December 2013. All patients were diagnosed with CSOM by medical history taking; physical examination, including otoscopy and tympanometry (Grason-Stadler GSI 33 middle-ear analyzer, Viasys, Conshohocken, PA, USA), pure tone audiometry (Grason-Stadler GSI 61 clinical audiometer, Nicolet Biomedical, Madison, USA), temporal bone computed tomography (General Electric Medical Systems, Milwaukee, USA), and the presence or absence of cholesteatoma on surgery. Based on diagnostic results and clinical findings, the patients were diagnosed as having COM or CCOM.

COM was defined as chronic inflammation of the middle ear and mastoid cavity lasting >6-12 weeks and presenting as recurrent ear discharge or otorrhea through a tympanic perforation. CCOM was defined as a pocket or perforation (opening) in the eardrum, often with drainage or deposits of old skin cells on otoscopy. The study protocol was approved by the institutional review board of Kyung Hee University Medical Center.

Samples, Bacterial Culture, and Antimicrobial Susceptibility Tests

An otorrhea sample was collected from each patient on the first day of their hospital visit. After cleansing of the external auditory canal, the otorrhea sample was aseptically collected using sterilized cotton while employing an antiseptic otoscope to prevent contact with the external auditory canal. In addition, discharge and middle ear fluid samples were collected from patients during middle ear surgery, including mastoidectomy, tympanoplasty, and ventilation tube insertion.

Each collected sample was added to Stuart's transport medium and was used to inoculate blood agar medium and fluid thioglycollate medium. All cultures were incubated for at least 24 h at 35 °C, and the resultant bacteria were identified by biochemical tests and gram staining. Antimicrobial susceptibility tests were performed after bacterial recognition, following the guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) [7].

Gram-positive bacteria were evaluated for sensitivity to penicillin, trimethoprim/sulfamethoxazole (TMP/SMX; SPT; co-trimoxazole), clindamycin, erythromycin, vancomycin, tetracycline, teicoplanin, linezolid, ciprofloxacin (CIP), ceftazidime (CAZ), rifampin, and oxacillin. Gram-negative bacteria were evaluated for sensitivity to amikacin (AMK), tobramycin (TOB), gentamicin (GM), ceftazidime (CAZ), cefepime (CFP), CIP, piperacillin (PIP), PIP/tazobactam (PITA), imipenem (IMP), and levofloxacin (LFX). Ten antimicrobial agents were categorized into five classes—aminoglycosides (AMK, GM, TOB), antipseudomonal penicillins (PIP, PITA), cephalosporins (CAZ, CFP), quinolones (CIP, LFX), and carbapenems (IMP)—to evaluate the tendency of PA resistance to antimicrobial agents.

Statistical Analysis

All statistical analyses were conducted using SPSS for Windows, version 16 (IBM Company; Chicago, IL, USA). Cultured bacteria from

Table 1. Gender and age distribution of patients with CSOM

Age (male/female)	Number of cases (%)					
	Under 20 (M/F)	21-30 (M/F)	31-40 (M/F)	41-50 (M/F)	51-60 (M/F)	Over 60 (M/F)
Non-cholesteatomatous	78/52 (5.7%)	73/51 (5.4%)	126/149 (12.4%)	202/263 (20.6%)	166/214 (16.9%)	149/226 (16.6%)
Cholesteatomatous	17/10 (1.1%)	38/18 (2.4%)	47/40 (3.8%)	77/74 (6.6%)	48/54 (4.5%)	33/51 (3.7%)
Total	95/62 (6.9%)	111/69 (7.9%)	173/189 (16.2%)	279/337 (27.3%)	214/268 (21.4%)	182/277 (20.3%)

CSOM: chronic suppurative otitis media; M: male; F: female

various age groups were compared using chi-squared test. Trends in antimicrobial susceptibility over 13 years were assessed by linear association. Statistical significance was defined as p-value less than 0.05.

RESULTS

Bacterial Culture and Major Strains Isolated according to Gender and Age

Culture tests on samples collected from the 2256 patients showed the presence of bacteria in samples from 1705 patients (75.6%), fungi in samples from 59 patients (2.6%), and neither bacteria nor fungi in samples from 492 patients (21.8%). Of the 1749 patients diagnosed with COM, 1309 (74.9%) were positive for bacteria, 46 (2.6%) were positive for fungi, and 394 (22.5%) were negative for both. Of the 507 patients with CCOM, 396 (78.1%) were positive for bacteria, 13 (2.5%) were positive for fungi, and 98 (19.4%) were negative for both.

Table 1 shows the distribution of patients with CSOM according to gender and age. The highest numbers of patients diagnosed with CSOM were aged 41-50 years, followed by those aged 51-60 years. In patients aged over 30 years, CSOM was more frequent in females than in males, whereas in those aged under 30 years, the proportion of males was higher.

Staphylococci were isolated from 998 (58.1%) patients; of these, 47% were males and 53% were females. The most commonly affected age group consisted of patients aged 41 to 50 years, while the least affected age group included those under 20 years old (Table 2). PA was isolated from 460 (26.9%) patients; of these, 44% were males and 56% were females. Similar to patients infected with *Staphylococcus aureus*, the most commonly affected age group was aged 41 to 50 years, whereas the least affected age group was under 20 years old (Table 3).

Antimicrobial Susceptibility Tests

Methicillin-resistant *Staphylococcus aureus* strains isolated from 181 patients showed 100% sensitivity to teicoplanin and vancomycin and 92.2% sensitivity to co-trimoxazole. These strains, however, showed low sensitivity to other antimicrobial agents, in particular, 100% resistance to penicillin, tetracycline, ceftazidime, and oxacillin. Bacteria isolated from patients with CSOM showed particularly low sensitivity to erythromycin, CIP, and rifampin.

Methicillin-susceptible *Staphylococcus aureus* (MSSA) strains isolated from 625 patients showed 100% sensitivity to teicoplanin and vancomycin, 95.3% sensitivity to co-trimoxazole, and 18-60% sensitivity

Table 2. *Staphylococcus* cultured from patients with CSOM according to age

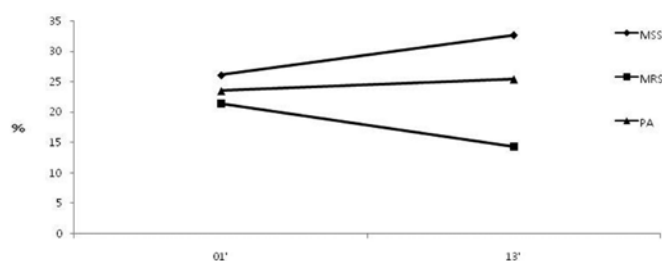
Age (male/female)	Number of cases					
	Under 20 (M/F)	21-30 (M/F)	31-40 (M/F)	41-50 (M/F)	51-60 (M/F)	Over 60 (M/F)
COM						
MRSA	2/0 (0.2%)	5/6 (1.1%)	9/12 (2.1%)	17/20 (3.7%)	14/17 (3.1%)	20/25 (4.5%)
MSSA	19/15 (3.4%)	27/11 (3.8%)	39/31 (7.0%)	52/90 (14.2%)	51/55 (10.6%)	47/62 (10.9%)
CNS	2/2 (0.4%)	4/4 (0.8%)	13/18 (3.1%)	16/15 (3.1%)	13/12 (2.5%)	16/15 (3.1%)
CCOM						
MRSA	0/0 (0%)	1/1 (0.2%)	1/4 (0.5%)	5/8 (1.3%)	3/5 (0.8%)	4/5 (0.9%)
MSSA	3/5 (0.8%)	4/7 (1.1%)	11/13 (2.4%)	15/18 (3.3%)	14/18 (3.2%)	6/12 (1.8%)
CNS	1/1 (0.2%)	7/1 (0.8%)	5/8 (1.3%)	17/7 (2.4%)	6/2 (0.8%)	2/3 (0.5%)
Total	26/23 (4.9%)	48/30 (7.8%)	78/86 (16.4%)	122/158 (28.1%)	101/109 (21.1%)	95/122 (21.7%)

CSOM: chronic suppurative otitis media; COM: chronic non-cholesteatomatous otitis media; CCOM: chronic cholesteatomatous otitis media; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-susceptible *Staphylococcus aureus*; CNS: coagulase-negative *Staphylococcus*; M: male; F: female

Table 3. *Pseudomonas aeruginosa* cultured from patients with CSOM according to age

Age (male/female)	Number of cases					
	Under 20 (M/F)	21-30 (M/F)	31-40 (M/F)	41-50 (M/F)	51-60 (M/F)	Over 60 (M/F)
COM						
<i>Pseudomonas</i>	19/9 (6.1%)	11/8 (4.1%)	23/50 (15.8%)	48/47 (20.7%)	28/41 (15.0%)	24/54 (16.9%)
CCOM						
<i>Pseudomonas</i>	5/2 (1.5%)	13/6 (4.1%)	7/7 (3.1%)	14/13 (5.9%)	6/9 (3.3%)	6/10 (3.5%)
Total	24/11 (7.6%)	24/14 (8.2%)	30/57 (18.9%)	62/60 (26.5%)	34/50 (18.2%)	30/64 (20.4%)

CSOM: chronic suppurative otitis media; COM: chronic non-cholesteatomatous otitis media; CCOM: chronic cholesteatomatous otitis media; M: male; F: female

**Figure 1.** Annual proportions of *Staphylococcus* and *Pseudomonas aeruginosa* isolates in patients with CSOM from 2001 to 2013

to other antimicrobial agents except for penicillin. Coagulase-negative *Staphylococcus* (CNS) strains isolated from 190 patients showed 100% sensitivity to teicoplanin and vancomycin, similar to the findings for MRSA, as well as 70% sensitivity to clindamycin. However, isolated CNS strains showed 20-50% sensitivity to other antimicrobial agents, with $\geq 90\%$ resistance to penicillin and tetracycline (Table 4).

Pseudomonas aeruginosa strains isolated from 471 patients showed 81.7% sensitivity to CFP and AMK, as well as relatively high sensitivities to aztreonam (71.3%), CAZ (69.6%), and IMP (52.2%). These strains, however, showed low sensitivity to quinolone antimicrobial agents, including LFX (9.8%) and CIP (38.4%), and to aminoglycoside antimicrobial agents such as TOB (28.1%) and GM (29.3%) (Table 5). The antibiotic resistances of *Staphylococcus* and PA did not differ with respect to age and gender.

Annual Isolation Rates and Trends of Bacterial Strains in Each OM Group

Regardless of CSOM subtype, the isolation rates of MSSA were the highest (30-40%), followed by PA (15-30%) and MRSA (10-25%), with no significant changes in relative isolation rates over the 13-year study period. Strains from patients with COM and CCOM indicated similar patterns. The prevalence rate of MRSA generally decreased from 2001 (21.4%) to 2013 (14.9%), while the that of MSSA tended to increase; the PA isolation rate was relatively unchanged (Figure 1). Among the PA isolates, however, there was a significant increase in resistance to aminoglycosides over time, from 31.1% in 2001 to 54.5% in 2013, and resistance to quinolones, from 16.2% in 2001 to 65.3% in 2013. The levels of PA resistance to IMP and antipseudomonals increased slightly over 13 years. COM and CCOM showed similar patterns (Figure 2). The overall rates of non-susceptibility of MRSA to various antimicrobial agents were unchanged over the 13-year period, while all MRSA strains were susceptible to teicoplanin and vancomycin (Figure 3).

DISCUSSION

Chronic suppurative otitis media refers primarily to chronic inflammation of the middle ear and mastoid cavity, with a perforated tympanic membrane and drainage. CCOM has been found to occur when keratinized squamous epithelium invades the middle ear and destroys nearby tissues. CCOM may also be involved in the severity and maintenance of inflammation [8].

Because the primary causes of CSOM are Eustachian tube dysfunction and bacterial infection, many studies have investigated the pri-

Table 4. Antibiotic susceptibility patterns of *Staphylococcus* isolates

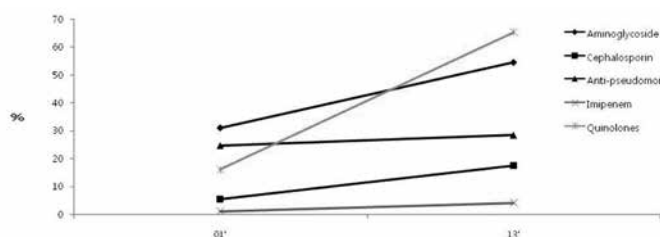
	SPT	CL	PC	EM	VAN	TCP	TC	CIP	LZ	CFT	RFP	OX
COM												
MRSA (147)	131 (89.1)	85 (58.4)	1 (0.7)	3 (2.2)	147 (100)	147 (100)	0 (0)	2 (1.5)	44 (29.9)	1 (0.7)	53 (35.8)	0 (0)
MSSA (499)	476 (95.3)	249 (49.9)	29 (5.8)	190 (38.0)	499 (100)	499 (100)	67 (13.4)	215 (42.8)	159 (31.8)	185 (37.1)	189 (37.8)	498 (99.7)
CNS (130)	93 (71.5)	85 (65.0)	11 (8.3)	49 (37.5)	129 (99.2)	130 (100)	16 (12.5)	49 (37.5)	46 (35.0)	51 (39.2)	44 (34.1)	65 (57.9)
CCOM												
MRSA (37)	31 (83.7)	16 (44.4)	0 (0)	10 (25.9)	37 (100)	37 (100)	0 (0)	10 (25.9)	14 (37.8)	0 (0)	18 (48.6)	0 (0)
MSSA (126)	122 (96.8)	69 (54.7)	9 (7.5)	36 (28.3)	126 (100)	126 (100)	25 (19.8)	59 (47.2)	50 (39.6)	50 (39.6)	50 (39.6)	125 (99.2)
CNS (60)	45 (75.0)	42 (70.0)	7 (12.0)	26 (44.0)	60 (100)	59 (98.3)	10 (16.0)	28 (46.0)	27 (45.0)	29 (38.0)	22 (36.0)	53 (51.1)
Total												
MRSA (184)	162 (88.0)	101 (54.9)	1 (0.5)	13 (7.1)	184 (100)	184 (100)	0 (0)	12 (6.5)	58 (31.5)	1 (5.4)	71 (38.5)	0 (0)
MSSA (625)	598 (95.6)	318 (50.8)	38 (6.1)	226 (36.2)	625 (100)	625 (100)	92 (14.7)	273 (43.6)	134 (33.4)	235 (37.6)	239 (38.2)	623 (99.6)
CNS (190)	138 (72.6)	127 (66.8)	18 (9.4)	75 (39.4)	189 (99.4)	189 (99.4)	26 (13.6)	77 (40.5)	73 (38.4)	80 (42.1)	66 (34.7)	118 (62.1)

COM: chronic non-cholesteatomatous otitis media; CCOM: chronic cholesteatomatous otitis media; SPT: trimethoprim/sulfamethoxazole (TMP/SMX, co-trimoxazole); CL: clindamycin; PC: penicillin; EM: erythromycin; VAN: vancomycin; TCP: teicoplanin; TC: tetracycline; CIP: ciprofloxacin; LZ: linezolid; CFT: cefoxitin; RFP: rifampin; OX: oxacillin; AOM: acute otitis media; OME: otitis media with effusion; CSOM: chronic suppurative otitis media; MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-susceptible *Staphylococcus aureus*; CNS: coagulase-negative *Staphylococcus*

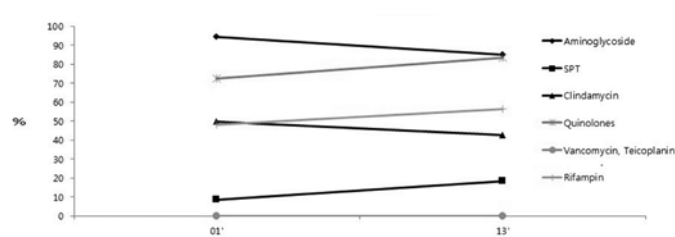
Table 5. Antibiotic susceptibility patterns of *Pseudomonas aeruginosa* isolates

	SPT	CL	PC	EM	CTX	PITA	TET	CFP	CIP	CFT	RFP	IMP	AK	GM	AZM	CAZ	PIP	TOB	CO	LFX
COM																				
(362)	66	26	10	37	14	129	2	300	152	23	0	193	295	110	257	256	169	106	50	41
	(18.2)	(7.2)	(2.9)	(10.1)	(4.0)	(35.7)	(0.6)	(83.0)	(42.1)	(6.3)	(0)	(53.3)	(81.6)	(30.3)	(70.9)	(70.6)	(46.7)	(29.4)	(13.8)	(11.2)
CCOM																				
(98)	21	7	0	9	1	28	1	76	25	4	1	47	80	25	71	64	46	23	21	4
	(21.6)	(7.2)	(0)	(9.6)	(1.2)	(28.9)	(1.2)	(77.1)	(25.3)	(3.6)	(1.2)	(48.2)	(81.9)	(25.3)	(72.3)	(65.1)	(1.2)	(22.9)	(21.7)	(3.6)
Total																				
(460)	87	33	10	46	15	157	3	376	177	27	1	240	275	135	328	320	215	129	71	45
	(18.9)	(7.2)	(2.2)	(10)	(3.3)	(34.1)	(0.7)	(81.7)	(38.4)	(5.9)	(0.2)	(52.2)	(81.5)	(29.3)	(71.3)	(69.6)	(46.7)	(28.1)	(15.4)	(9.8)

COM: chronic non-cholesteatomatous otitis media; CCOM: chronic cholesteatomatous otitis media; SPT: trimethoprim/sulfamethoxazole (TMP/SMX, co-trimoxazole); CL: clindamycin; PC: penicillin; EM: erythromycin; CTX: cefotaxime; PITA: piperacillin/tazobactam; TET: cefotetan; CFP: cefepime; CIP: ciprofloxacin; CFT: cefoxitin; RFP: rifampin; IMP: imipenem; AK: amikacin; GM: gentamicin; AZM: aztreonam; CAZ: ceftazidime; PIP: piperacillin; TOB: tobramycin; CO: colistin; LFX: levofloxacin

**Figure 2.** Trend of isolation of antibiotic-resistant *Pseudomonas aeruginosa* strains in patients with CSOM from 2001 to 2013

many pathogens in patients with CSOM and the use of antibiotics to treat CSOM. Due to the overuse and misuse of antibiotics in the treatment of various infectious diseases and the increasing frequency of antibiotic resistant bacteria, empirical antibiotic therapy may delay appropriate treatment regimens, causing secondary complications. Thus, if CSOM patients have concurrent symptoms, particularly otorrhea, the otorrhea sample should be cultured to identify causative

**Figure 3.** Trend of isolation of antibiotic-resistant MRSA strains in patients with CSOM from 2001 to 2013

bacteria, with appropriate antibiotic therapy according to the results of antibiotic sensitivity testing.

The bacterial isolation rate in patients with COM and CCOM is approximately 80%, regardless of otorrhea [9]. Similarly, we were able to isolate bacteria from 75.5% of the patients with CSOM. In addition to pathogenic bacteria, the normal flora that always exist in the exter-

nal auditory canal include *S. auricularis*, *S. epidermidis*, *S. capitis*, and *Corynebacterium* [10, 11]. We found that the rates of isolation of pathogenic bacteria, including PA, MRSA, and MSSA, were high. This result indirectly confirms that the sample collection was in accordance with standards for bacteriologic examination and that the likelihood of sample contamination with the normal flora in the external auditory canal was low. CSOM has mostly been found among children and young adults in developing countries and lower socioeconomic groups. This may be due to their low resistance to infection and their relatively short and straight Eustachian tubes. In this study, however, the most frequent age group of patients with CSOM (27.3%) was 41 to 50 years. The incidence rate of CSOM according to age and the bacterial detection rate of MRSA and PA showed similar patterns. We assumed that specific bacteria in a particular age group did not cause CSOM. PA isolates were found in teenaged patients, whereas MRSA was rare; this finding was different from that observed in developing countries [12].

In this study, females were more commonly affected than males, similar to findings in Singapore [13]. Other studies, however, have shown the opposite trend, likely due to geographical variations. Males are generally regarded to be more vulnerable to infection than females. The reason for this is that androgens in males and estrogens in females modulate host immunity, and these sex steroids affect disease resistance genes and behaviors [14]. Although one epidemiologic study reported a slightly higher male predominance in patients with cholesteatoma irrespective of age [15], we found that the incidence of CSOM was slightly lower in males than in females, suggesting that gender predominance is associated with gender differences in immune responses. This hypothesis, however, requires further verification, such as the measurement of serum immunoglobulin concentrations in males and females with cholesteatoma. In addition, advanced age was shown to be a significant predictor of antibiotic-resistant community-associated bloodstream infection [16]. In this study, the incidence of CSOM tended to increase; however, there were no age-associated differences in antibiotic resistance.

The isolated MSSA strains showed 100% sensitivity to the antimicrobial agents teicoplanin and vancomycin, intermediate sensitivity (50%) to CIP, and low sensitivity ($\leq 40\%$) to other antimicrobial agents. MSSA strains isolated from patients with CSOM and CCOM had sensitivities of 20–60%. These findings indicate that regardless of CSOM subtype, isolated MSSA strains have high sensitivity to teicoplanin, vancomycin, and co-trimoxazole and intermediate sensitivity to CIP; however, they have low sensitivity to other antimicrobial agents such as erythromycin and amoxicillin.

Empirical antibiotics, such as CIP, have been reported to be effective against various gram-positive and gram-negative bacteria that cause CSOM [17]. However, we found that MSSA strains isolated over the 13-year study period showed altered antibiotic sensitivity profiles. Our findings indicate that the use of amoxicillin and CIP as primary empirical antibiotics in patients with CSOM should be reviewed.

The culture positive isolation rate of MRSA from aural discharge samples has been reported to decrease in patients with CSOM since the early 2000s [18]. This finding was contrary to our expectation that infections caused by MRSA would rapidly increase due to the misuse of an-

tibiotics. The decreased isolation rate of MRSA is likely due to increased concerns about infections caused by antibiotic resistant bacteria, isolation of infected patients, and improved personal hygiene, all of which are efforts designed to prevent bacterial transmission. We found that the isolation rate of MRSA in all patients with CSOM over the 13-year study period decreased from 2001 (21.4%) to 2013 (14.9%).

As MRSA is resistant to methicillin and other antibiotics, it cannot be effectively treated by conventional antibiotics alone. We found that regardless of CSOM subtype, most isolated MRSA strains showed 100% sensitivity to teicoplanin and vancomycin and 90% sensitivity to TMP/SMX; however, they showed low sensitivity ($<10\%$) to other antibiotics. Antibiotics effective in treating MRSA give rise to more complications than those effective against MSSA, suggesting that the former may carry a higher risk of morbidities related to these complications [19]. Thus, it is important to select antibiotics with sufficient antimicrobial effects to treat patients with CSOM.

Pseudomonas aeruginosa is a bacterial species that is difficult to treat as it does not have particular environmental or nutritional requirements to grow and is highly resistant to conventional antibiotics [20]. In addition, PA strains isolated from different individuals have different antibiotic sensitivities, emphasizing the importance of simultaneous bacterial identification and antibiotic sensitivity testing to identify appropriate antibiotics. We found that the isolated PA strains had $\geq 70\%$ sensitivity to CFP, AK, and CAZ but that they were resistant to GM, TOB, and quinolone antibiotics such as CIP and LFX. These findings were similar in the CSOM and CCOM groups. Thus, in patients thought to have otorrhea caused by PA, empirical antibiotics conventionally used to treat otorrhea are unlikely to achieve appropriate treatment outcomes.

The levels of PA resistance to CFP and CAZ have increased from 2001 to 2013. This increases the difficulty of choosing appropriate antibiotics. PA resistance to aminoglycosides and quinolones showed a tendency to increase continually; on the other hand, the resistance of PA to other antibiotics has not changed. Because PA is innately resistant to antibiotics, the resistance to quinolones and aminoglycosides of domestic PA strains with otorrhea may be strengthened by hereditary features or the abuse of these medications. Quinolones are a critical group of antibiotics widely used in diverse infectious diseases in adults, including respiratory, urinary tract and bone and joint infections, due to their excellent spectra of activity, good tissue penetration, and convenient administration routes. The empirical treatment of patients with CSOM by quinolones without antibiotic susceptibility tests or cultures may reinforce resistance to quinolones. This seems to result in quinolones no longer being primary antibiotics to CSOM.

In conclusion, the analysis of changes in bacterial isolation rates in patients with CSOM and the antibiotic sensitivities of these bacteria over a 13-year study period showed that the bacteria responsible for each type of CSOM changed little over time. However, the antibiotic resistance of these bacteria was altered, with a marked increase in PA strains resistant to quinolones. The replacement of antibiotics primarily used to treat CSOM and quinolone use, in general, should be considered.

Ethics Committee Approval: Ethics committee approval was received for this study from the Institutional Review Board of Medical Center.

Informed Consent: This study was a retrospective analysis about pus culture. This kind of study did not need to be informed consent.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - S.G.Y.; Design - S.G.Y., S.H.K.; Supervision - S.G.Y., S.H.C.; Funding - S.G.Y., M.G.K.; Materials - M.G.K., S.G.Y.; Data Collection and/or Processing - S.H.K., M.G.K., S.S.K.; Analysis and/or Interpretation - S.H.K.; Literature Review - S.H.K., S.H.C.; Writing - S.H.K., S.G.Y.; Critical Review - S.S.K., S.H.C.

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