Journal of Microbiology, Immunology and Infection (2013) 46, 382–388

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ORIGINAL ARTICLE

Clinical manifestations and microbiology of acute otitis media with spontaneous otorrhea in children

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Received 4 February 2013; received in revised form 11 March 2013; accepted 1 April 2013

KEYWORDS
Acute otitis media;
Children;
Otorrhea;
Streptococcus pneumoniae;
Taiwan

Background/Purpose(s): In Taiwan, clinical and microbiological data on acute otitis media (AOM) with spontaneous otorrhea in children are limited.
Methods: We retrospectively collected data on children with AOM and spontaneous otorrhea between January 2011 and June 2012. Otorrhea samples were collected using sterile swabs and sent for cultures. Pathogens found were *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pyogenes*, and *Staphylococcus aureus*. Pneumococcal isolates collected from October 2011 to June 2012 were serotyped.
Results: A total of 92 patients were enrolled in the study for demographic and microbiological analysis. Their median age was 2.5 years. After excluding those with lobar pneumonia, 84 patients were included for analysis of clinical manifestation. The mean febrile duration was 6 days. Leukocytosis and C-reactive protein (CRP) level >50 mg/L were noted in 29 (34.5%) patients and 38 (45.2%) patients, respectively. Patients with pneumococcal infection were older ($p = 0.007$) and had more severe symptoms [fever ($p = 0.001$), otalgia ($p = 0.055$), respiratory symptoms ($p = 0.002–0.03$), and higher CRP level ($p = 0.015$)] than children with other bacterial infection. Otorrhea cultures were obtained from 69 (75%) patients, of whom 52 had definitive AOM pathogens. The most common causative pathogen was *S. pneumoniae* (61.5%), followed by *S. aureus* (36.5%). Serotype 19A accounted for two-thirds of pneumococcal isolates and had a high rate of nonsusceptibility to penicillin (66.7%) and ceftriaxone (83.3%).

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http://dx.doi.org/10.1016/j.jmii.2013.04.001

Conclusion: *S. pneumoniae* was found to be the most important source of AOM with spontaneous otorrhea in children and caused more severe symptoms. Serotype 19A, which was usually nonsusceptible to antimicrobial agents, was the most prevalent serotype in these patients.

Introduction

Acute otitis media (AOM) is a common disease in children, and more than 80% of them experience at least one episode of AOM prior to the age of 3 years.[1] The incidence of AOM in Taiwan was reported to be 64.6 cases per 1000 children (33.5 cases per 100 person-years) and mostly noted in children aged 0—2 years.[2] A variety of studies have found that spontaneous otorrhea is one of the complications of AOM that occurs in 3.3—52% of children with AOM.[3—5] Given the difficulty in obtaining children's cooperation for performing tympanocentesis, spontaneous otorrhea provides an easier way to approach the etiology of AOM. In addition to the well-known pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pyogenes*, *and Staphylococcus aureus* was also reported to cause spontaneous otorrhea.[6,7] Chiu et al[8] reported the epidemiological and microbiological characteristics of culture-proven AOM in children of northern Taiwan during 1999—2008, but the serotype data of pneumococcus and data from other hospitals in Taiwan were lacking. Since October 2005, pneumococcal conjugate vaccination (PCV) has been introduced in Taiwan in the private sector. The aim of this study is to analyze the demographics and microbiology, including pneumococcal serotype distribution and antibiotic susceptibility, of patients having AOM and spontaneous otorrhea during January 2011—June 2012 in northern Taiwan.

Materials and methods

Patients

This study was conducted in a 395-bed children hospital in northern Taiwan. The study was approved by the Institutional Review Board of Chang Gung Memorial Hospital. Pediatric inpatients younger than 18 years admitted during January 2011—June 2012 were enrolled in the study. A total of 738 inpatients were diagnosed with AOM, based on the International Classification of Diseases, ninth version, Clinical Modification (ICD-9-CM) code 3810, 3820, or 3829. Repeated cases and patients with chronic otitis media, tympanostomy tube insertion, immunodeficiency, malignancy, and other chronic illness were excluded. Ninety-two patients with spontaneous otorrhea were enrolled for demographic studies and pathogen analysis. Detailed clinical features were obtained from 84 patients after excluding eight patients having necrotizing or lobar pneumonia.

Microbiology

Samples of middle ear fluid was obtained from the ear canal using sterile swabs (Copan sterile plain swabs; Copan Italia, Brescia, Italy) either within 24 hours after otorrhea was diagnosed or within 24 hours after admission. The swabs were then transported to the laboratory in Amies transport medium (Copan Italia, Brescia, Italy), and placed on blood agar whole plate, eosin methylene blue (EMB) whole plate, and Columbia colistin-nalidixic acid (CNA) agar biplate, and cultured at 37°C for 48 hours. Pathogens causing AOM were identified as *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, *S. pyogenes*, and *S. aureus*. Patients with positive *S. pneumoniae* isolates (including those with mixed infection) were categorized as the pneumococcal group and the others as the non-pneumococcal group.

Between October 2011 and June 2012, pneumococcal isolates from swab cultures were collected, subcultured, and frozen at −70°C. Serogroups were determined by the latex agglutination method (Pneumotest-latex; Statens Serum Institute, Copenhagen, Denmark). The capsular swelling method (Quellung reaction) was then performed using antisera (Pneumococcal factor antisera; Statens Serum Institute) for pneumococcal serotyping. Minimum inhibitory concentrations (MICs) of penicillin and ceftriaxone were determined by E test (AB Biodisk, Solona, Sweden), and susceptibility of vancomycin, levofloxacin, and moxifloxacin was determined by the disc diffusion method. The susceptibility criteria were developed according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.[9] The CLSI nonmeningitis criteria for penicillin susceptibility are defined as follows: susceptible, MIC $\leq$2 μg/mL; intermediately resistant, MIC = 4 μg/mL; and resistant, MIC $\geq$8 μg/mL. The nonmeningitis criteria for ceftriaxone susceptibility are as follows: susceptible, MIC $\leq$1 μg/mL; intermediately resistant, MIC = 2 μg/mL; and resistant, MIC $\geq$4 μg/mL.

Definition

The diagnosis of AOM was made by a pediatrician or an otolaryngologist. The diagnosis of acute mastoiditis was made clinically or radiologically. Patients with mastoiditis may have fever, otalgia or irritability, retroauricular pain, swelling, erythema, and a downward and outward deviation of the auricle. Coalescence or clouding of mastoid air cells is noted in plain radiographs. In computed tomography (CT), the typical findings include haziness or destruction of mastoid outline, and loss of or decrease in the sharpness of bony septa.[10] The duration of four seasons were defined as follows: spring, March—May; summer, June—August; fall, September—November; and winter, December—February. Analyses of pneumococcal conjugate vaccination [any PCV: 7-valent PCV (PCV7), 10-valent PCV (PCV10), or 13-valent PCV (PCV13)] categorized patients into those without vaccination and those receiving $\geq$1 dose. Previous antibiotic use was defined as exposure to antibiotics in the last 2 weeks prior to admission. Leukocytosis was defined as white blood cell (WBC) count $\geq$15,000/μL.

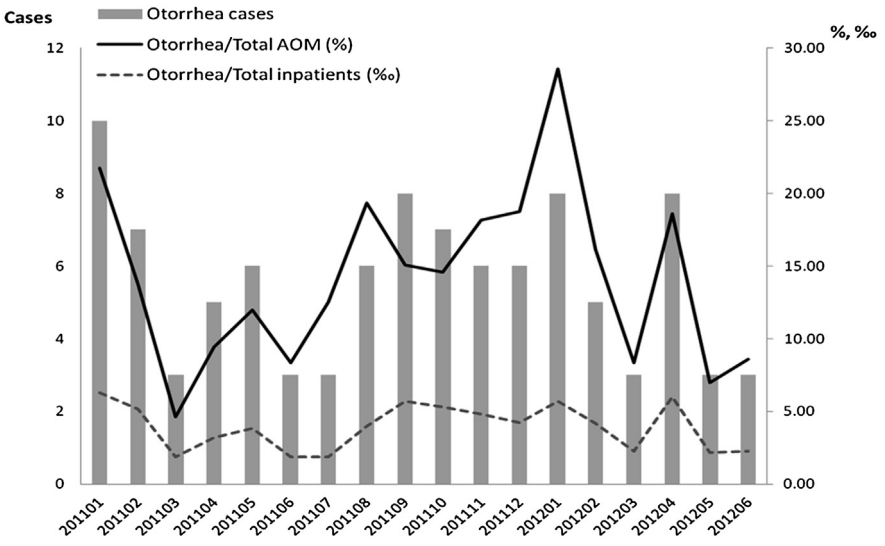

Figure 1. Monthly distribution of inpatients with spontaneous otorrhea.

Statistical analysis

For categorical variable, we used Chi-square test and Fisher's exact test, and the independent *t* test was used for continuous variables. Statistical significance was defined as $p < 0.05$ (2-sided). All analysis were performed using the software SPSS, version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

Epidemiology

A total of 100 inpatients had spontaneous otorrhea during the study period. Fig. 1 shows the monthly distribution of these episodes, and the ratios of the number of spontaneous otorrhea to the number of all-cause admissions (total 25,741 cases) and AOM admissions (total 738 cases). Peaks were observed in January 2012 (28.7% to AOM admission and 5.7‰ to all-cause admission) and January 2011 (21.7% and 6.3‰, respectively). Spontaneous otorrhea occurred more frequently in autumn (17.16% to AOM admission and 5.8‰ to all-cause admission) and winter (18.1% and 4.9‰, respectively) compared to spring and summer (10—11.1% and 2.3—3.3‰, respectively).

Among 92 patients undergoing demographic analysis, the median age was 2.5 years. Fifty-two percent of them were 2—5 years old, and 35% were less than 2 years. The male-to-female ratio was 1.5. Eleven patients (12%) had previous episodes of AOM. Among 90 patients with available history of pneumococcal vaccination, 29 (32%) had ≥1 dose of any type of PCV, and only three received ≥1 dose of PCV13. Recent antibiotic exposure was reported in 37% of patients.

Clinical manifestations

After excluding those with lobar pneumonia, 84 patients were enrolled in the study for analysis of clinical manifestations and laboratory data (Table 1). Seventy-four patients (88.1%) had fever, with a median duration of 6 days (range, 1—20 days). Spontaneous otorrhea occurred at a median of 4 days following fever (range, −6 to 16 days). The median duration of hospitalization was 5 days. In only one-quarter of patients, bilateral ears were involved. Leukocytosis and high C-reactive protein (CRP) level (>50 mg/L) were noted in 34.5% and 45.2% of patients, respectively. Eight patients (9.5%) had complications. Three had pneumococcal bacteremia, two mastoiditis, one mastoiditis with cholesteatoma, and the remaining two periauricular cellulitis.

Microbiology

Among the 92 inpatients with spontaneous otorrhea, 69 (75%) had otorrhea cultures, and 52 were found to be culture positive (Table 2). *S. pneumoniae* accounted for 61.5% of all pathogens, followed by *S. aureus* (36.5%), *S. pyogenes* (3.8%), *M. catarrhalis* (1.9%), and *H. influenzae* (1.9%). Mixed infections were observed in five patients (9.6%): *S. pneumoniae* plus *S. aureus* in three, *S. pneumoniae* plus *H. influenza* in one, and *S. aureus* plus *S. pyogenes* in one. Other bacteria isolated from these patients included the following: four *Propionibacterium acnes*, two *Klebsiella pneumoniae*, two viridans streptococci, two *Acinetobacter baumannii*, two *Peptostreptococcus* spp., two *Corynebacterium* spp., one *Pseudomonas aeruginosa*, and one β-hemolytic streptococcus (group non-ABD). Among the 32 *S. pneumoniae* isolates, 10 (31.3%) were intermediately resistant and one (3.1%) was highly resistant to penicillin. Furthermore, 27 (84.3%) were intermediately resistant and two (6.3%) highly resistant to ceftriaxone. All isolates were susceptible to vancomycin, levofloxacin, and moxifloxacin.

We collected 28 isolates of *S. pneumoniae* from patients with spontaneous otorrhea for serotyping: 16 specimens from inpatients and 12 from outpatients. Serotypes 19A and 19F accounted for 64.3% (18/28) and 25% (7/28) of isolates, respectively (Fig. 2). As to the antibiotic susceptibility of serotype 19A, 11 (61.1%) were intermediately resistant and one (5.6%) was highly resistant to penicillin, and 15 (83.3%) were intermediately resistant and none was highly resistant

Table 1 Clinical manifestations of the 84 patients with spontaneous otorrhea

	Case no.	%
Symptoms and signs		
Fever	74	88.1
Highest temperature (°C)	39.41 ± 0.65	
Fever duration (d)	6 ± 0.3.3	
Otorrhea onset following fever (d)	4.34 ± 3.51	
Ear pain/ear rubbing	49	58.3
Cough	65	77.4
Rhinorrhea/nasal obstruction	60	71.4
Nausea/vomiting	8	9.5
Diarrhea	7	8.3
Unilateral	63	75
Laboratory data		
Peak WBC (×1000/μL)	14.09 ± 5.34	
Segment (%)	57.37 ± 17.17	
Lymphocyte (%)	31.24 ± 14.58	
Band (%)	0.51 ± 1.35	
Leukocytosis (WBC ≥15,000/μL)	29	34.5
Peak CRP (n = 83, mg/L)	62.99 ± 56.6	
High CRP (>50 mg/L)	38	45.2
Associated diagnosis		
Upper respiratory tract	14	16.7
Flu/flu-like illness	5	6
Sinusitis	10	11.9
Lower respiratory tract[a]	15	17.9
Acute gastroenteritis	6	7.1
Febrile convulsion	2	2.4
Complications	8	9.5
Mastoiditis[b]	3	3.6
Bacteremia	3	3.6
Periauricular cellulitis	2	2.4
Hospitalization duration (d)	4.95 ± 2.28	

[a] Lobar pneumonia and necrotizing pneumonia have been excluded.
[b] One had concomitant cholesteatoma.
Data presented as mean ± SD unless otherwise stated.
CRP = C-reactive protein; SD = standard deviation; WBC = white blood cell.

Table 2 AOM pathogens isolated from 52 children with spontaneous otorrhea

Bacteria	Isolate n (%)
Streptococcus pneumoniae	32 (61.5)
Streptococcus pyogenes	2 (3.8)
Moraxella catarrhalis	1 (1.9)
Haemophilus influenzae	1 (1.9)
Methicillin-resistant *Staphylococcus aureus*	12 (23.1)
Methicillin-sensitive *S. aureus*	7 (13.5)
Mixed infection	5 (9.6)
S. pneumoniae + *S. aureus*	3
S. pneumoniae + *H. influenzae*	1
S. aureus + *S. pyogenes*	1

AOM = acute otitis media.

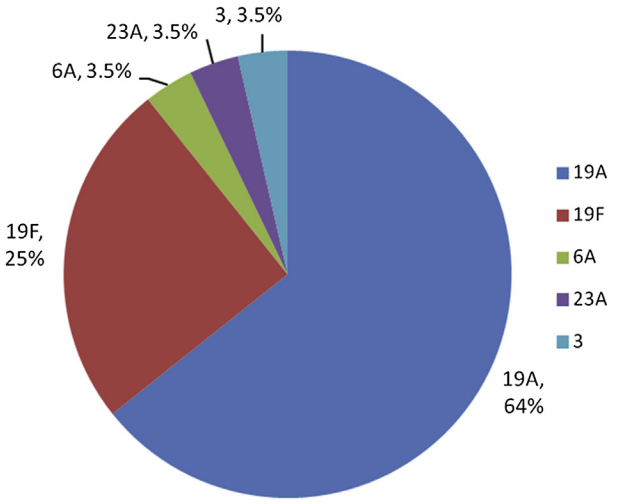

Figure 2. Serotype distribution of *Streptococcus pneumoniae* isolated from 28 patients with spontaneous otorrhea.

to ceftriaxone. All these isolates were susceptible to vancomycin, levofloxacin, and moxifloxacin.

Comparison between AOM caused by *S. pneumoniae* and other pathogens

The comparison of demographic characteristics is listed in Table 3. The two groups were similar with respect to male gender, underlying diseases, previous AOM history, antibiotic exposure, siblings, and pneumococcal vaccination status. The median age of the nonpneumococcal group was less than that of the pneumococcal group, but it did not reach statistical significance. Classification of these patients into three age groups (0–2 years, 2–5 years, and >5 years) revealed that half of the cases from the pneumococcal group were between 2 and 5 years of age, whereas 77.8% of patients from the nonpneumococcal group were less than 2 years old (p = 0.007).

As to the comparison of clinical manifestations between the two groups (Table 4), all patients in the pneumococcal group but only 61% of those in the nonpneumococcal group had fever (p = 0.001). Otalgia or ear rubbing was noted in more patients in the pneumococcal group (62% vs. 33%), but only equivocally significant difference was found (p = 0.055). Respiratory tract infection symptoms (cough and rhinorrhea/nasal obstruction) were statistically more common in the pneumococcal group, and bilateral otorrhea occurred in 44.8% of them, compared to 5.6% in the nonpneumococcal group (p = 0.004). However, there was no significant difference in the peak temperature, fever duration, and otorrhea onset date following fever between the two groups. Moreover, peak CRP level was significantly higher in the pneumococcal group (p = 0.015). No difference was observed when comparing complications and hospitalization duration between the two groups.

Discussion

To our knowledge, only a few studies have discussed AOM pathogens and pneumococcal serotypes in recent years in

Table 3 Comparison of demographics between patients with pneumococcal infection and others

	Pneumococcal group ($n = 32$)	Nonpneumococcal group ($n = 18$)	p
Male	18 (56.3)	12 (66.7)	0.470
Age			
Mean ± SD (y/o)	2.92 ± 2.16	1.96 ± 2.92	0.189
Median (range)	2.45 (0.58–12.25)	0.83 (0.13–10.42)	
0–2 y old	12 (37.5)	14 (77.8)	0.007
2–5 y old	18 (56.3)	2 (11.1)	
>5 y old	2 (6.3)	2 (11.1)	
Underlying disease	4 (12.5)	1 (5.6)	0.642
Previous AOM	2 (6.3)	1 (5.6)	1.000
Pneumococcal vaccination			
Any PCV[a]	13/31 (41.9)	7/18 (38.9)	0.834
Any PCV7[b]	9/27	3/15	0.485
Any PCV13[b]	0/27	2/15	0.122
With sibling	18 (56.3)	10 (55.6)	0.962
Previous antibiotic use	14/26 (53.8)	5/17 (29.4)	0.115

[a] Any PCV: patients having ≥1 dose of pneumococcal conjugate vaccine; data of pneumococcal vaccination were available for 31 patients and 18 patients, respectively.

[b] PCV7, PCV13: seven-valent and 13-valent pneumococcal conjugate vaccine; data available for 27 patients and 15 patients. None of them received 10-valent pneumococcal conjugate vaccine.

Data are presented as *n* (%) unless otherwise stated.

AOM = acute otitis media; PCV = pneumococcus conjugate vaccination; SD = standard deviation.

Taiwan. Similar to AOM, spontaneous otorrhea occurs more often in winter months.[11] The age of AOM peaks between 6 months and 18 months of age.[12] However, in this study the median age of spontaneous otorrhea was older (median 2.5 years, approximately half between 2 years and 5 years of age). Approximately three-quarters (52 cases) of the patients were defined as culture positive. Patients with pneumococcal infection were older and had more severe symptoms (fever, otalgia, bilateral ear involvement, and higher CRP level in more patients). Pneumococcal infection accounted for the majority (two-thirds) of the causative pathogens, and the most common serotype was 19A with high antibiotic resistance.

In the current study, the most common pathogens in spontaneous otorrhea were found to be *S. pneumoniae* and *S. aureus*. Some earlier studies suggested that only four well-known pathogens, including *S. pneumoniae*, *M. catarrhalis*, *H. influenzae*, *and S. pyogenes*, cause otorrhea; meanwhile, *S. aureus* was thought to be only a contaminant.[8,13–15] *S. aureus* is more related to chronic otitis media, but its role in AOM is still unknown.[16] Heslop and Ovesen[17] recovered *S. aureus* from 8–21% of cases with acute ear infections (AOM, mastoidismus, and acute mastoiditis). In recent years, AOM caused by methicillin-resistant *S. aureus* have been reported.[18,19] Brook and Gober[20] compared otorrhea specimens from spontaneous draining AOM and those from aspiration of the remaining middle ear effusion; they found that *S. aureus* did exist in aspirate specimens and *S. pneumoniae*, *S. pyogenes*, and *S. aureus* were predominant in otorrhea specimens. In a subsequent study, *S. aureus*, including methicillin-resistant *S. aureus*, was found to be significantly more common in patients with otorrhea after routine pneumococcal vaccination in the United States.[6] We therefore considered *S. aureus* as a possible pathogen for AOM with otorrhea and enrolled these patients for further analysis.

Chiu et al[8] reported the epidemiology and microbiology in pediatric patients with culture-proven AOM in Taiwan between 1999 and 2008, and the most common pathogens of spontaneous otorrhea were *S. pneumoniae* (65.9%), nontypeable *H. influenzae* (18.6%), and *S. pyogenes* (6.2%). Our result also showed a similar percentage of *S. pneumoniae*. After the introduction of PCV, *H. influenzae* became more prevalent in AOM; by contrast, the incidence of *S. pneumoniae* infection became less.[21] PCV has been introduced in Taiwan since October 2005, but not yet included in the National Immunization Program; therefore, the change in microbiology of AOM needs further observation.

AOM caused by *S. pyogenes* is characterized by older age with higher rates of tympanic perforation and mastoiditis in children.[15,22] *S. pyogenes* accounted for 5.7–29% of all pathogens in spontaneous otorrhea.[13,15] In this study, only two patients (3.8%) were found to have *S. pyogenes* infection, with one of them having mastoiditis. The lower rate of *S. pyogenes* infection and higher morbidity are compatible with the results of previous studies.[13,15]

We also analyzed the serotype distribution of pneumococcal isolates from patients with otorrhea. Serotype 19A accounted for two-thirds of the isolates available. After the wide use of PCV7, 19A became the major cause of invasive pneumococcal disease (IPD) in the world.[23–25] Emergence of multidrug-resistant serotype 19A was reported in Korea and Israel prior to the introduction of PCV7, suggesting that the capsular switch driven by PCV7 was not the only reason for the emergence of 19A.[26,27] PCV-related serotype replacement, antibiotic selection pressure, and genetic changes in *S. pneumoniae* lead to the rise of serotype 19A globally.[26–28] In Taiwan, serotype 19A has been noted as an emerging serotype and has become the most prevalent cause for IPD since 2009 (affecting 43.4% of children ≤5 years in 2011) (data from Taiwan Center for Disease Control). The emergence of serotype 19A in Taiwan is similar to that in Korea because of high antibiotic selective pressure and suboptimal vaccine coverage.[29] In addition to causing IPD, serotype 19A has been reported as the main serotype of *S. pneumoniae* in AOM in the post-PCV7 era.[21,23,30,31] In one study on the epidemiology of spontaneous otorrhea after PCV7 in Greece, the proportion of serotype 19A isolates increased from 2% in 2006 to 25% in 2008.[15] Serotype 19A appears to have higher AOM potential than other nonvaccine serotypes.[32] Children with AOM also have a higher risk of 19A nasopharyngeal colonization, as reported in a national study in France.[33] These studies indicate the prominence and importance of serotype 19A not only in IPD, but also in AOM and nasopharyngeal colonization.

Serotype 19A is known to show a high level of antimicrobial resistance. In this study, the nonsusceptible rates of pneumococcal 19A isolates were observed to be 66.6% to

Table 4 Comparison of clinical manifestations between patients with pneumococcal infection and others

	Pneumococcal group (n = 29)	Nonpneumococcal group (n = 18)	p
Symptoms and signs			
Fever	29 (100)	11 (61.1)	0.001
Highest temperature (°C)	39.31 ± 0.69	39.07 ± 0.73	0.354
Fever ≥39°C	20 (69.0)	7 (38.9)	1.000
Fever duration (d)	6.03 ± 3.24	5.91 ± 4.37	0.921
Otorrhea onset day following fever (d)	3.97 ± 3.61	4 ± 4.65	0.980
Ear pain/ear rubbing	18 (62.1)	6 (33.3)	0.055
Cough	26 (89.7)	11 (61.1)	0.030
Rhinorrhea/nasal obstruction	25 (86.2)	8 (44.4)	0.002
Nausea/vomiting	1 (3.4)	1 (5.6)	1.000
Diarrhea	2 (6.9)	2 (11.1)	0.631
Bilateral otorrhea	13 (44.8)	1 (5.6)	0.004
Laboratory test			
Peak WBC (×1000/μL)	13.93 ± 5.67	14.46 ± 3.94	0.730
Leukocytosis (WBC ≥15,000)	11 (37.9)	6 (33.3)	0.750
Peak CRP (mg/L)	71.92 ± 63.26	33.98 ± 38.16	0.015
High CRP (>50 mg/L)	14 (48.3)	4 (23.5)	0.097
Associated diagnosis			
Upper respiratory tract	4	0	
Flu/flu-like illness	3	0	
Sinusitis	4	1	
Lower respiratory tract[a]	5	3	
Acute gastroenteritis	2	2	
Outcome			
Complications[b]	1 (3.4)	3 (16.7)	0.150
Hospitalization duration (d)	5.28 ± 2.31	4.33 ± 2.64	0.200

[a] Lobar pneumonia and necrotizing pneumonia have been excluded.
[b] Complications in pneumococcal group: one bacteremia; complications in nonpneumococcal group: two mastoiditis and one periauricular cellulitis.
Data are presented as n (%) or mean ± SD.
CRP = C-reactive protein; SD = standard deviation; WBC = white blood cell.

penicillin and 83.3% to ceftriaxone, using the nonmeningitis criteria. The antibiotic resistance of *S. pneumoniae* in Taiwan has increased gradually in recent years. Nonsusceptibility to ceftriaxone among invasive isolates has increased significantly since 2005, reaching 76.4% by the meningitis criteria and 21.3% by the nonmeningitis criteria in 2007 among invasive isolates from children aged 2–4 years.[29,34] An analysis of the drug susceptibility of pneumococcal 19A isolates from children with IPD during 2005–2007 in Taiwan revealed that 78% of *S. pneumoniae* were nonsusceptible to penicillin by nonmeningitis criteria. ST320 accounted for the majority of these 19A isolates.[35] In Taiwan and some Asian countries, the high prevalence of multidrug-resistant ST320 may explain the high nonsusceptibility rate of 19A.[36] The higher nonsusceptibility rate in this study may explain why the patients with AOM progressed to spontaneous otorrhea despite initial antimicrobial therapy in local medical offices.

This study has certain limitations. This is a retrospective study, and therefore not all patients with spontaneous otorrhea had pus cultures. Only 75.4% of them were culture positive. The possible explanations for negative culture in some patients include previous antibiotic exposure, viral infection only, and lower number of bacteria present in the specimens. It is also difficult to address the treatment issue because of the retrospective nature of this study. Furthermore, the way to obtain cultures from external auditory canal was simple and useful, but some of the pathogens might still have been missed.[20]

In conclusion, *S. pneumoniae* remained the most common etiologic agent responsible for AOM with spontaneous otorrhea. Serotype 19A was the most common serotype for AOM with otorrhea in Taiwan, where PCV has been used only in the private sector. *S. pneumoniae*, serotype 19A in particular, was also observed to exhibit high nonsusceptibility to penicillin and ceftriaxone. Because it is difficult to perform tympanocentesis in children, sterile swab sampling for spontaneous otorrhea is an alternative way to know the etiology of severe AOM, which can be used to guide the treatment.

References

1. Vergison A, Dagan R, Arguedas A, Bonhoeffer J, Cohen R, Dhooge I, et al. Otitis media and its consequences: beyond the earache. *Lancet Infect Dis* 2010;**10**:195–203.
2. Wang PC, Chang YH, Chuang LJ, Su HF, Li CY. Incidence and recurrence of acute otitis media in Taiwan's pediatric population. *Clinics (Sao Paulo)* 2011;**66**:395–9.

3. Ilia S, Galanakis E. Clinical features and outcome of acute otitis media in early infancy. *Int J Infect Dis* 2013;**17**:e317—20.
4. Joki-Erkkila VP, Pukander J, Laippala P. Alteration of clinical picture and treatment of pediatric acute otitis media over the past two decades. *Int J Pediatr Otorhinolaryngol* 2000;**55**: 197—201.
5. Klein JO. The burden of otitis media. *Vaccine* 2000;**19**(Suppl. 1):S2—8.
6. Brook I, Gober AE. Bacteriology of spontaneously draining acute otitis media in children before and after the introduction of pneumococcal vaccination. *Pediatr Infect Dis J* 2009;**28**: 640—2.
7. Marchisio P, Bianchini S, Baggi E, Fattizzo M, Galeone C, Torretta S, et al. A retrospective evaluation of microbiology of acute otitis media complicated by spontaneous otorrhea in children living in Milan [Published online ahead of print Dec 05 2012]. *Infection*. Available at:, http://link.springer.com/article/10.1007%2Fs15010-012-0371-1; 2012 [accessed 25.03.13].
8. Chiu NC, Lin HY, Hsu CH, Huang FY, Lee KS, Chi H. Epidemiological and microbiological characteristics of culture-proven acute otitis media in Taiwanese children. *J Formos Med Assoc* 2012;**111**:536—41.
9. Clinical and Laboratories Standards Institute (CLSI). *Performance standards for antimicrobial susceptibility testing; 21st Informational supplement. M100-S21*. Wayne, PA, USA: Clinical and Laboratory Standard Institute; 2011.
10. Wald ER, Conway JH. Mastoiditis. In: Long SS, editor. *Principles and practice of pediatric infectious diseases*. 4th ed. Philadelphia: Elsevier; 2012. p. 223—4.
11. Rosenfeld RM, Culpepper L, Yawn B, Mahoney MC. Otitis media with effusion clinical practice guideline. *Am Fam Physician* 2004;**69**(2776):2778—9.
12. Ting PJ, Lin CH, Huang FL, Lin MC, Hwang KP, Huang YC, et al. Epidemiology of acute otitis media among young children: a multiple database study in Taiwan. *J Microbiol Immunol Infect* 2012;**45**:453—8.
13. Chiang-Ni C, Wu AB, Liu CC, Chen KT, Lin YS, Chuang WJ, et al. Emergence of uncommon *emm* types of *Streptococcus pyogenes* among adult patients in southern Taiwan. *J Microbiol Immunol Infect* 2011;**44**:424—9.
14. Grevers G, Wiedemann S, Bohn JC, Blasius RW, Harder T, Kroeniger W, et al. Identification and characterization of the bacterial etiology of clinically problematic acute otitis media after tympanocentesis or spontaneous otorrhea in German children. *BMC Infect Dis* 2012;**12**:312.
15. Stamboulidis K, Chatzaki D, Poulakou G, Ioannidou S, Lebessi E, Katsarolis I, et al. The impact of the heptavalent pneumococcal conjugate vaccine on the epidemiology of acute otitis media complicated by otorrhea. *Pediatr Infect Dis J* 2011;**30**: 551—5.
16. Brook I. Otitis media: microbiology and management. *J Otolaryngol* 1994;**23**:269—75.
17. Heslop A, Ovesen T. Severe acute middle ear infections: microbiology and treatment. *Int J Pediatr Otorhinolaryngol* 2006;**70**:1811—6.
18. Brook I. Recovery of methicillin resistant *Staphylococcus aureus* from a child with acute otitis media. *Pediatr Infect Dis J* 2008;**27**:372—3.
19. Al-Shawwa BA, Wegner D. Trimethoprim-sulfamethoxazole plus topical antibiotics as therapy for acute otitis media with otorrhea caused by community-acquired methicillin-resistant *Staphylococcus aureus* in children. *Arch Otolaryngol Head Neck Surg* 2005;**131**:782—4.
20. Brook I, Gober AE. Reliability of the microbiology of spontaneously draining acute otitis media in children. *Pediatr Infect Dis J* 2000;**19**:571—3.
21. Coker TR, Chan LS, Newberry SJ, Limbos MA, Suttorp MJ, Shekelle PG, et al. Diagnosis, microbial epidemiology, and antibiotic treatment of acute otitis media in children: a systematic review. *JAMA* 2010;**304**:2161—9.
22. Segal N, Givon-Lavi N, Leibovitz E, Yagupsky P, Leiberman A, Dagan R. Acute otitis media caused by *Streptococcus pyogenes* in children. *Clin Infect Dis* 2005;**41**:35—41.
23. Lai CY, Huang LM, Lee PY, Lu CY, Shao PL, Chang LY. Comparison of invasive pneumococcal disease caused by serotype 19A and non-19A pneumococci in children: More empyema in serotype 19A invasive pneumococcal disease. *J Microbiol Immunol Infect* 2012 Oct 2. [Epub ahead of print].
24. Kaplan SL, Barson WJ, Lin PL, Stovall SH, Bradley JS, Tan TQ, et al. Serotype 19A is the most common serotype causing invasive pneumococcal infections in children. *Pediatrics* 2010; **125**:429—36.
25. Dagan R, Klugman KP. Impact of conjugate pneumococcal vaccines on antibiotic resistance. *Lancet Infect Dis* 2008;**8**: 785—95.
26. Choi EH, Kim SH, Eun BW, Kim SJ, Kim NH, Lee J, et al. *Streptococcus pneumoniae* serotype 19A in children, South Korea. *Emerg Infect Dis* 2008;**14**:275—81.
27. Dagan R, Givon-Lavi N, Leibovitz E, Greenberg D, Porat N. Introduction and proliferation of multidrug-resistant *Streptococcus pneumoniae* serotype 19A clones that cause acute otitis media in an unvaccinated population. *J Infect Dis* 2009;**199**: 776—85.
28. Pillai DR, Shahinas D, Buzina A, Pollock RA, Lau R, Khairnar K, et al. Genome-wide dissection of globally emergent multi-drug resistant serotype 19A *Streptococcus pneumoniae*. *BMC Genomics* 2009;**10**:642.
29. Hsieh YC, Lin PY, Chiu CH, Huang YC, Chang KY, Liao CH, et al. National survey of invasive pneumococcal diseases in Taiwan under partial PCV7 vaccination in 2007: emergence of serotype 19A with high invasive potential. *Vaccine* 2009;**27**:5513—8.
30. Rodgers GL, Arguedas A, Cohen R, Dagan R. Global serotype distribution among *Streptococcus pneumoniae* isolates causing otitis media in children: potential implications for pneumococcal conjugate vaccines. *Vaccine* 2009;**27**:3802—10.
31. Casey JR, Adlowitz DG, Pichichero ME. New patterns in the otopathogens causing acute otitis media six to eight years after introduction of pneumococcal conjugate vaccine. *Pediatr Infect Dis J* 2010;**29**:304—9.
32. Shouval DS, Greenberg D, Givon-Lavi N, Porat N, Dagan R. Site-specific disease potential of individual *Streptococcus pneumoniae* serotypes in pediatric invasive disease, acute otitis media and acute conjunctivitis. *Pediatr Infect Dis J* 2006;**25**: 602—7.
33. Cohen R, Levy C, Bonnet E, Thollot F, Boucherat M, Fritzell B, et al. Risk factors for serotype 19A carriage after introduction of 7-valent pneumococcal vaccination. *BMC Infect Dis* 2011;**11**:95.
34. Chiu CH, Su LH, Huang YC, Lai JC, Chen HL, Wu TL, et al. Increasing ceftriaxone resistance and multiple alterations of penicillin-binding proteins among penicillin-resistant *Streptococcus pneumoniae* isolates in Taiwan. *Antimicrob Agents Chemother* 2007;**51**:3404—6.
35. Janapatla RP, Hsu MH, Du JF, Hsieh YC, Lin TY, Chiu CH. Sequence types and antimicrobial susceptibility of invasive *Streptococcus pneumoniae* isolates from a region with high antibiotic selective pressure and suboptimal vaccine coverage. *Pediatr Infect Dis J* 2010;**29**:467—9.
36. Shin J, Baek JY, Kim SH, Song JH, Ko KS. Predominance of ST320 among *Streptococcus pneumoniae* serotype 19A isolates from 10 Asian countries. *J Antimicrob Chemother* 2011;**66**: 1001—4.