Etiology and Outcome of Community-Acquired Lung Abscess

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Key Words

Community-acquired lung abscess · Etiology · Percutaneous ultrasonography-guided transthoracic needle aspiration · Protected specimen brush

Abstract

Background: Anaerobes are the first and *Streptococcus* species the second most common cause of community-acquired lung abscess (CALA) in the West. The etiologic pathogens of this disease have changed in Taiwan, with *Klebsiella pneumoniae* being reported as the most common cause of CALA. **Objective:** To determine the etiologies of community-acquired lung abscess. **Methods:** We retrospectively reviewed the records of 205 Japanese adult patients with CALA to evaluate etiologies and outcomes. We used not only traditional microbiological investigations but also percutaneous ultrasonography-guided transthoracic needle aspiration and protected specimen brushes. **Results:** Of these 205 patients, 122 had documented bacteriological results, with 189 bacterial species isolated. Pure aerobic, mixed aerobic and anaerobic, and pure anaerobic bacteria were isolated in 90 (73.8%), 17 (13.9%), and 15 (12.3%) patients, respectively. The four most common etiologic pathogens were *Streptococcus* species (59.8%), anaerobes (26.2%), *Gemella* species (9.8%), and *K. pneumoniae* (8.2%). *Streptococcus mitis* was the most common among the *Streptococcus* species. Mean duration of antibiotic administration was 26 days. Six patients

(2.9%, 3 with actinomycosis and 3 with nocardiosis) were treated with antibiotics for 76–189 days. Two patients with anaerobic lung abscess died. **Conclusions:** The first and second most common etiologic pathogens of CALA in our hospital were *Streptococcus* species and anaerobes, respectively. The etiologies in our study differ from those in Taiwan and are similar to those in the West with the exception that *Streptococcus* species were the most common etiologic pathogens in our study whereas anaerobes are the most frequent etiologic pathogens in Western countries. *S. mitis* and *Gemella* species are important etiologic pathogens as well. The identification of *Actinomyces* and *Nocardia* is important in order to define the adequate duration of antibiotic administration.

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Introduction

Prior to the introduction of antimicrobials into clinical practice, one third of the patients with lung abscess died [1]. Antimicrobial use has improved the prognosis, but mortality was estimated at 2.0–38.2% in previous reports published from 1969 to 2005 [2–13], and lung abscess remains an important respiratory disease. Anaerobes comprise 60–80% of lung abscess etiologic pathogens, and anaerobes and microaerophilic streptococci account for the majority of these microorganisms [1].

However, Wang et al. [13] reported *Klebsiella pneumoniae* (33%) to be the most common etiologic pathogen of community-acquired lung abscess (CALA) in Taiwan and concluded that the bacterial etiology of lung abscess has changed. Whether the etiologies in our Japanese hospital differ from those in Taiwan or the West is unknown. In addition, the bacteriological classification of one of the most common etiologic pathogens of lung abscess, the *Streptococcus* species, has been changed. Before 1974, microaerophilic streptococci were included into *Peptococcus* and *Peptostreptococcus* species, and in 1986, the genus *Streptococcus* was split into three genera (*Enterococcus*, *Lactococcus* and *Streptococcus*) [15, 16]. Therefore, the etiologic pathogens of CALA should be investigated on the basis of the present bacteriological classification.

Adequate duration of antibiotic administration for lung abscess has been investigated. *Actinomyces* and *Nocardia* are known as important etiologic pathogens of lung abscess, and these two microorganisms differ from others because they require a longer duration (6 months) of antibiotic administration [17].

In this report, we investigated the causes and outcomes of CALA. We used not only traditional microbiological investigations but also percutaneous ultrasonography-guided transthoracic needle aspiration (PUTA) and protected specimen brushes (PSBs). The incidence of actinomycosis and nocardiosis in CALA was investigated as well.

Methods

Patients

We studied 205 Japanese adult patients with CALA treated from 1994 through 2008. The diagnosis of CALA was established on the basis of clinical symptoms, laboratory data, and findings of imaging studies (a cavity seen on a chest radiograph was confirmed by a chest CT). This study was approved by the institutional review board.

Study Design

Case records of adult patients with CALA were retrospectively reviewed. The following data were recorded: age at diagnosis, underlying disease, risk factors, prior antibiotic use, symptoms, radiographic location of the lung abscess, methods for diagnosing etiology, etiologic microorganisms, complications, treatment and outcome. Patients with CALA distal to the occlusion due to lung cancer were excluded from this study.

Aerobic culture was performed with the usual media. Anaerobic culture was performed with 3 media: Gifu Anaerobic Medium Semisolid 'Nissui' (Nissui Pharmaceutical Co., Ltd., Japan), Brucella HK agar with hemolyzed rabbit blood and defibrillated sheep blood (Kyokuto Pharmaceutical Industrial Co., Ltd., Japan), and Anaero Pack® (Mitsubishi Gas Chemical Company,

Inc., Japan). Identification of Gram-positive cocci was performed with the Vitek® 2 GP Card (Sysmex bioMérieux Co., Ltd., Japan), identification of streptococci was with the api® 20 Strep system (Sysmex bioMérieux Co., Ltd., Japan), and anaerobes were identified with the Rapid™ ANA II System (Thermo Fisher Scientific Remel Products, USA).

Data Analysis

Uncontaminated specimens included lung tissue samples obtained by PUTA, pleural effusion, blood culture, intraoperative specimens and autopsy specimens. PUTA was performed according to the methods of Yang et al. [18]. Expecterated sputum, lavage fluid from bronchoscopic examinations and PSB specimens were not regarded as uncontaminated specimens. PSB was performed according to the methods of Hammond et al. [9] and has been used from 1997.

All aerobic and anaerobic microorganisms cultured from uncontaminated specimens were considered pathogenic. The following microorganisms cultured from contaminated specimens were considered pathogenic: all aerobic and anaerobic microorganisms cultured from PSB specimens, or aerobic microorganisms cultured from purulent sputum sample or lavage fluid from bronchoscopic examinations with a compatible result from the Gram stain. Sputum has undergone quality testing. Sputum data were only evaluated when the Gram stain test revealed >25 granulocytes and <10 epithelial cells per low-power field. Results of semi-quantitative cultures were expressed as 1+ to 5+. Moderate to heavy growth (4+ to 5+) on sputum culture was considered as pathogenic. Normal oral floras, such as *Streptococcus* species or *Gemella* species, were excluded. In this report, we defined all microorganisms isolated from both uncontaminated and contaminated specimens meeting the above criteria as etiologic pathogens unless otherwise noted. For comparisons between groups, the χ^2 test or Fisher's exact test was used for continuous variables.

Results

Patient Characteristics and Risk Factors

Patient age was 59.3 ± 12.2 years (mean $\pm$ SD) (table 1). Of the 205 patients, 16.6% were alcohol drinkers, 61% had periodontal disease, and 22.9% had diabetes mellitus.

Symptoms and Radiographic Location

Patients had symptoms for 31.2 ± 41.8 days (mean $\pm$ SD). Lesion location included the right upper lobe in 35.1%, the left upper lobe in 19.0%, and both lungs in 8.0% of cases (table 2). No patients required admission to an intensive care unit.

Diagnostic Methods and Results

PSB was performed in 87 patients (table 3), and microorganisms were isolated in 71 (81.6%). PUTA was performed in 40 patients, and microorganisms were isolated

Table 1. Baseline characteristics and risk factors of 205 patients with CALA

Characteristics and risk factors	Value
Age, mean $\pm$ SD, years	59.3 $\pm$ 12.2
Male	168 (82.0)
Prior antibiotic use	98 (47.8)
Smoking history	155 (75.6)
Alcoholism	34 (16.6)
<i>Underlying disease</i>	
None	38 (18.5)
Prior lung illness	28 (13.7)
Chronic obstructive pulmonary disease	7 (3.4)
Bronchiectasis	7 (3.4)
Asthma	5 (2.4)
Old pulmonary tuberculosis	3 (1.5)
Others	8 (3.9)
Extrapulmonary condition	155 (75.6)
Periodontal disease	125 (61.0)
Diabetes mellitus	47 (22.9)
Prior operation of digestive system	22 (10.7)
Malignancy	17 (8.3)
Old cerebral infarction	13 (6.3)
Chronic liver disease	13 (6.3)
Seizures	2 (1.0)
Steroid use	1 (0.5)
Others	26 (12.7)

Data are expressed as number of patients and percentages (in parentheses) unless otherwise indicated.

in 28 (70.0%). No complications occurred in patients undergoing PSB, and pneumothorax or empyema did not occur in patients undergoing PUTA. Prior antibiotic treatment had no impact on the sensitivity for PSB (73.5% if antibiotics were taken vs. 87.8% if no antibiotics were taken; $p = 0.929$), and no impact on the sensitivity for PUTA (70.6% vs. 73.9%; $p = 0.8159$).

Documented Bacterial Findings

Etiologic microorganisms were isolated in 122 of the 205 patients (59.5%) and comprised 187 bacteria (table 4). Among these 122 patients, infection by a single microorganism occurred in 75 (61.5%), and infection by two microorganisms occurred in 35 (28.7%). Pure aerobic infection occurred in 90 patients (73.8%), mixed aerobic and anaerobic infection occurred in 17 (13.9%), and pure anaerobic infection occurred in 15 (12.3%). There were no differences in pathogen frequency between the patients with and without periodontal disease (data not shown).

Table 2. Symptoms and radiographic location in 205 patients with CALA

	Value
<i>Symptoms</i>	
Duration, mean $\pm$ SD, days	31.2 $\pm$ 41.8
Fever	167 (81.5)
Cough	114 (55.6)
Sputum	114 (55.6)
Chest pain	76 (37.1)
Bloody sputum	45 (22.0)
Anorexia	37 (18.0)
General malaise	25 (12.2)
Weight loss	17 (8.3)
Asymptomatic	4 (2.0)
<i>Radiographic location</i>	
Right upper lobe	72 (35.1)
Right middle lobe	7 (3.4)
Right lower lobe	32 (15.6)
Left upper lobe	39 (19.0)
Left lower lobe	27 (13.1)
Right multiple lobes	8 (3.9)
Left multiple lobes	4 (2.0)
Bilateral	16 (8.0)

Data are expressed as number of patients and percentages (in parentheses) unless otherwise indicated.

Table 3. Diagnostic methods and results in 205 patients with CALA

Diagnostic method	Episodes studied	Diagnostic studies, n
PSB culture	87	71 (81.6%)
Culture of PUTA specimens	40	28 (70.0%)
Pleural effusion culture	18	5 (27.8%)
Sputum culture	144	15 (10.4%)
Blood culture	44	2 (4.5%)
Bronchial lavage fluid culture	41	9 (22.0%)
Culture of surgical material (lung or brain abscess)	5	3 (60.0%)
Culture of autopsy specimen	1	1 (100.0%)

Documented Bacterial Findings from Uncontaminated Specimens

In total, 53 microorganisms were isolated from uncontaminated specimens of 38 patients, of whom 13 experienced (34.2%) mixed infection. Of these 53 isolated microorganisms, *Streptococcus* species were the most com-

Table 4. Bacteriological findings in 122 patients with documented bacteriological results

	Patients
Number of isolated bacteria	
One	75 (61.5%)
Two	35 (28.7%)
Three	8 (6.6%)
Four	2 (1.6%)
Five	2 (1.6%)
Isolated bacteria	
Pure aerobic ¹	90 (73.8%)
Mixed aerobic and anaerobic	17 (13.9%)
Pure anaerobic ²	15 (12.3%)

¹ Of 90 patients with pure aerobic infections, 25 were polymicrobial.

² Of 15 patients with pure anaerobic infections, 5 were polymicrobial.

mon (23 patients, 60.5%), followed by anaerobes (16 patients, 42.1%), *Gemella* species (5 patients, 13.2%), *Staphylococcus aureus* (2 patients, 5.3%), *Haemophilus influenzae* (2 patients, 5.3%), and others (5 patients, 13.2%).

Aerobic Bacteria Isolated in 107 Patients

One hundred forty-one strains of aerobic bacteria were isolated in 107 patients. The most common pathogens were *Streptococcus* species. The incidence of other etiologic pathogens in the 122 patients was as follows: *Gemella* species, 9.8%; *K. pneumoniae*, 8.2% (table 5). Compared to the patients without diabetes mellitus, a trend towards a significantly larger proportion of patients with isolated *K. pneumoniae* was observed for the patients with diabetes mellitus (2.6% vs. 12.8%; $p = 0.083$).

Streptococcus Species Isolated in 73 Patients

Eighty-five strains of *Streptococcus* species were isolated in 73 of the 122 patients with identified etiologic pathogens: 24 patients with *Streptococcus mitis*, 17 with *S. constellatus*, 16 with *S. salivarius*, and 5 with *S. intermedius* (table 6).

Anaerobic Bacteria Isolated in 32 Patients

Forty-six strains of anaerobes were identified in 32 of the 122 patients with identified etiologic pathogens: 10 patients with *Peptostreptococcus* species, 9 with *Prevotella* species, 7 with *Veillonella* species, and 7 with *Fusobacterium* species (table 7).

Table 5. Aerobic bacteria isolated from 107 patients with CALA

Bacteria	Isolates, n
<i>Streptococcus</i> species	85
<i>Gemella</i> species ¹	12
<i>Klebsiella pneumoniae</i>	10
<i>Pseudomonas aeruginosa</i>	6
<i>Haemophilus influenzae</i>	5
<i>Staphylococcus aureus</i>	3
<i>Nocardia</i> species	3
<i>Neisseria</i> species	3
<i>Lactococcus cremoris</i>	2
<i>Escherichia coli</i>	2
<i>Enterococcus faecalis</i>	2
<i>Haemophilus parainfluenzae</i>	1
<i>Haemophilus parahaemolyticus</i>	1
<i>Staphylococcus warneri</i>	1
<i>Enterobacter aerogenes</i>	1
<i>Sphingomonas paucimobilis</i>	1
<i>Serratia marcescens</i>	1
<i>Corynebacterium</i> species	1
<i>Leuconostoc</i> species	1
Total	141

¹ *Gemella* species included *G. haemolysans* (n=6), *G. morbilorum* (n = 5), and unidentified *Gemella* species (n = 1).

Complications, Treatments and Outcomes

Empyema was seen in 11 and brain abscess in 2 patients. Ampicillin/sulbactam was administered as empirical therapy in 101 (49.3%) of the 205 patients (table 8). Forty-two (21.0%) patients received second-, third-, or fourth-generation cephalosporin, with or without clindamycin, and 34 (16.6%) patients received piperacillin, with or without clindamycin. Twenty-three (11.2%) patients received carbapenem, and 5 received fluoroquinolone. Twelve patients who were initially treated with ampicillin/sulbactam subsequently received other antibiotics because initial antibiotic treatments were ineffective. Three patients who were initially treated with second- or third-generation cephalosporin received carbapenem, and 1 patient initially treated with piperacillin subsequently received carbapenem. Duration of antibiotic administration was 26 ± 20 days (mean $\pm$ SD). The 3 patients with actinomycosis and the 3 with nocardiosis received antibiotics for 76–189 days. One hundred ninety-five (95.1%) patients improved with antibiotic administration alone, 3 (1.5%) improved with chest tube drainage (because the amount of the pleural effusion of the other 8 patients with empyema were small to moderate and medical manage-

Table 6. *Streptococcus* species isolated from 73 patients with CALA

Bacteria	Isolates, n
<i>Streptococcus mitis</i>	24
<i>Streptococcus constellatus</i>	17
<i>Streptococcus salivarius</i>	16
<i>Streptococcus intermedius</i>	5
<i>Streptococcus parasanguis</i>	4
α -Hemolytic <i>Streptococcus</i>	4
<i>Streptococcus sanguis</i>	3
<i>Streptococcus pneumoniae</i>	3
<i>Streptococcus oralis</i>	2
<i>Streptococcus anginosus</i>	2
<i>Streptococcus bovis</i>	1
<i>Streptococcus acidominimus</i>	1
<i>Streptococcus morbillorum</i>	1
Group G β -hemolytic <i>Streptococcus</i>	1
γ -Hemolytic <i>Streptococcus</i>	1
Total	85

Table 7. Anaerobic bacteria isolated from 32 patients with CALA

Bacteria	Isolates, n
<i>Peptostreptococcus</i> species	10
<i>Prevotella</i> species	9
<i>Veillonella</i> species	7
<i>Fusobacterium</i> species	7
<i>Actinomyces</i> species	3
<i>Eikenella corrodens</i>	3
<i>Bacteroides capillosus</i>	1
<i>Propionibacterium acnes</i>	1
<i>Eubacterium</i> species	1
<i>Peptococcus</i> species	1
<i>Porphyromonas</i> species	1
Unidentified Gram-positive rod	1
Unidentified Gram-negative bacillus	1
Total	46

Table 8. First-line antibiotics, failure rate, second-line antibiotics and outcome in 205 patients with CALA

First-line antibiotics	Patients	Failure rate	Second-line antibiotics ¹	Death
Ampicillin/sulbactam	101	12 (11.9%)	carbapenem (n = 10) 4th-generation cephalosporin (n = 1) fluoroquinolone (n = 1)	1 (1.0%)
1st-, 2nd-, 3rd-generation cephalosporin $\pm$ clindamycin	42	3 (7.1%)	carbapenem (n = 3)	1 (2.4%)
Piperacillin $\pm$ clindamycin	34	1 (2.9%)	carbapenem (n = 1)	0
Carbapenem	23	0	0	0
Fluoroquinolone	5	0	0	0

¹ n represents number of patients.

ment with antibiotics was effective, these patients did not require tube drainage), 1 (0.5%) improved with additional drainage of a brain abscess, and 4 (2.0%) underwent pulmonary surgery. Of these 4 patients, 3 underwent pulmonary resection because the lesion did not shrink, and lung cancer could not be excluded. The 4th patient underwent pulmonary resection because recurrent hemoptysis developed. We did not insert any drainage tube into the abscess cavity. Two (1.0%) patients died of lung abscess. The etiologic pathogens in these 2 patients were investigated by PUTA and autopsy and were identified as anaerobes.

Discussion

We reviewed etiology and outcome in 205 Japanese adult patients with CALA. Etiologies were identified in 122 patients (59.5%). The *Streptococcus* species were the most common and anaerobes the second most common etiologic pathogens. These etiologic pathogens were also the first and second most common pathogens identified in uncontaminated specimens. Wang et al. [13] reported that *K. pneumoniae* was the most common etiologic pathogen of CALA in Taiwan and was identified in 33% of the cases. In our study, *K. pneumoniae* accounted for

8.2% of CALA. The etiologic pathogens in our study differ from those in Taiwan and are similar to those in the West with the exception that *Streptococcus* species were the most common etiologic pathogens in our study whereas anaerobes are the most frequent etiology in the West.

Periodontal disease, a known risk factor for lung abscess, was present in 61% of patients in this study. We compared the etiology with and without periodontal disease and found no difference in pathogen frequency. Diabetes mellitus, also a known risk factor, was found in 22.9% of patients and was the second most common underlying disease. Wang et al. [13] reported that diabetes mellitus was an important risk factor associated with *K. pneumoniae* lung abscess; 31% of patients in their study had diabetes mellitus. We also found that *K. pneumoniae* was detected somewhat more often in patients with diabetes mellitus.

Before 1970, mainly aerobic cultures of sputum had been used to identify the etiology of lung abscess. Therefore, the etiology could not be identified in many cases [1]. In the 1970s, transtracheal aspiration was introduced into clinical practice, and anaerobic culture was begun [3], resulting in an increase in etiologic organisms identified. Presently, however, we do not use this procedure, nor is it in general use [1]. Next, PSB emerged. This technique, which we use, was designed to avoid contamination from the upper respiratory tract. However, it is reported that a low level of contamination can occur even with PSB [19]. True etiologic microorganisms are cultured at a high concentration, whereas contaminating microorganisms are cultured at a low concentration [19, 20]. Unfortunately, we did not perform quantitative cultures from the PSB specimens, so the number of bacteria in our study is unknown. However, previous reports have regarded all bacteria cultured from PSB specimens as the etiologic pathogens [9, 21, 22] and we have done the same. PUTA is also used to identify the etiology of infections, and contamination from the upper respiratory tract can be completely avoided. In our hospital, when the lesion is attached to the chest wall, PUTA is applied. PSB is performed in other situations. Sensitivity was 81.6% for PSB and 70% for PUTA in the present study.

Streptococcus species were the most common etiologic pathogens in our study patients. Many Gram-positive cocci formerly classified as *Peptostreptococcus* have been reclassified as *Streptococcus* [23], and this may be a reason for the first and second most common etiologic microorganisms in our study being opposite to those reported in the previous study in the West. It was reported that of the

Streptococcus species, *Streptococcus milleri* is the most common etiologic pathogen of lung abscess [24–26]. However, the name ‘*Streptococcus milleri* group’ has not been used recently [16], therefore each species was counted separately in our study. The finding that *S. mitis* is an etiologic pathogen of lung abscess was first reported in 1994 [27]. In our study, *S. mitis* was the most common organism in the 73 patients in whom *Streptococcus* species were isolated.

Peptostreptococcus species, *Fusobacterium* species, *Prevotella* species, and *Veillonella* species have been reported to be the most common etiologic microorganisms of lung abscess due to anaerobes [1, 7–9, 13], and the results of the present study are consistent with these reports.

Gemella haemolysans and *G. morbillorum* are Gram-positive cocci and are commensals of the oral cavity of healthy people. *G. morbillorum* was classified into the *Streptococcus* species before 1988 and had been called *S. morbillorum*. This microorganism was a reported cause of lung abscess [28], but in a previous study that investigated the etiologies of lung abscess, this microorganism was not included as an etiologic pathogen, except by Peña Griñan et al. [7]. The first report of *G. haemolysans* as an etiologic pathogen of lung abscess was published in 2000 [29]. In our study, the *Gemella* species were the third most common etiologic pathogens. In our hospital, the Vitek® 2 GP Card is used to identify bacteria when Gram-positive cocci are isolated, and if identification of bacteria fails, we use the api® 20 STREP system. *Gemella* species can be easily isolated with these modalities.

The duration of antibiotic administration in previous reports was estimated to be from 28 to 48 days [11, 22, 30] and was consistent with our results. The 3 patients with nocardiosis and the 3 with actinomycosis required antibiotic administration for 76–189 days. Wang et al. [13] reported an incidence of nocardiosis in lung abscess of 4.4%, and Mansharamani et al. [11] reported the incidence of actinomycosis to be 8.8%. Although their incidence may have been somewhat low, these microorganisms required a longer duration of antibiotics administration; thus it is important to properly identify these microorganisms.

Patients requiring surgical procedures account for 5.1–41.2% of all patients with lung abscess [5–7, 11–13]. Pulmonary resection is required in patients with failure to improve, suspicion of cancer and hemoptysis. Surgical procedures required in our study included drainage of empyema in 3 patients, pulmonary resection in 4 patients (suspicion of cancer in 3 and hemoptysis in 1), and drain-

age of a brain abscess in 1 patient (3.9%). No patients failed to improve.

Mortality from lung abscess is reported to be from 2.0 to 38.2% [2–13]. In our study, mortality was only 1.0%. Patient profiles, pathogens and administered antibiotics may be reasons for this low mortality. Only 2 patients died in the present study, and we were unable to investigate the prognostic factors related to their deaths.

One limitation of the present study is that it was retrospective, and the etiology of CALA could not be fully investigated. A second limitation is that contaminated specimens that were not cultured anaerobically were included. Considering this, we investigated results obtained in uncontaminated specimens. We found that the three leading etiologic pathogens of CALA in uncontaminated specimens were the same as those that included contaminated and uncontaminated specimens. However, results including contaminated specimens showed a 26.2% incidence of anaerobes as the cause whereas the incidence increased to 42.1% when limited to results obtained from uncontaminated specimens alone. Therefore, the 26.2% incidence of anaerobes may be too low. Additionally, our hospital did not perform drug sensitivity testing for anaerobes, and patients with unknown etiologies were included in our study. The 16 (7.8%) patients in whom the administered antibiotics were changed include patients

with unknown etiologies or patients in whom the pathogens were anaerobes; therefore, we could not investigate the reason why the primary antibiotics were changed.

In conclusion, the three leading etiologic pathogens of CALA were *Streptococcus* species, anaerobes, and *Gemella* species. *S. mitis* was the most common of the *Streptococcus* species. Because these three bacterial species belong to the normal flora of the oral cavity, we cannot determine from expectorated sputum whether these microorganisms were the etiologic pathogens. To identify the etiology of CALA, PUTA or PSB is required to avoid contamination from the upper respiratory tract. Long-duration antibiotic administration was required to treat lung abscesses due to *Actinomyces* and *Nocardia*. Identification of these microorganisms is important in order to choose the proper antibiotics and adequate duration of administration.

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