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ORIGINAL ARTICLE

Clinical Characteristics of Lung Abscess Caused by *Streptococcus Constellatus* Infection

YouMing Zhu, Jie Jiang, Tao Jiang, TingTing Hu, YiLing Gan

Department of Respiratory and Critical Care Medicine, the First Affiliated Hospital of Chongqing Medical and Pharmaceutical College, Nanan District, Chongqing, P.R. China

SUMMARY

Background: **This study aimed to understand the clinical characteristics of pulmonary abscess caused by *Streptococcus constellatus* infection.**

Methods: **The clinical manifestations, laboratory examination, drug sensitivity, chest CT manifestations, and treatment and prognosis of patients with pulmonary abscess caused by *Streptococcus constellatus* infection were retrospectively collected and analyzed.**

Results: **A total of 9 cases of pulmonary abscess caused by *Streptococcus constellatus* infection were confirmed; one case was confirmed by traditional cultures, while metagenomic next-generation sequencing (mNGS) confirmed the other 8 cases. All of the 9 patients had different degrees of cough, sputum, fever, chest pain, and/or dyspnea, and the physical examination showed fast breathing, reduced respiratory sound, or moist rales on the affected side. In laboratory tests, 8 patients had elevated white blood cells and hypoproteinemia upon admission. Blood gas analysis showed an oxygenation index < 300. The antimicrobial susceptibility testing results in 1 patient with culture-confirmed pathogen diagnosis showed that *Streptococcus constellatus* was susceptible to ampicillin, penicillin G, cefotaxime, ceftriaxone, cefepime, meropenem, chloramphenicol, linezolid, levofloxacin, and vancomycin and resistant to tetracycline and clindamycin. Relevant antibiotic resistance genes were not detected by mNGS in the 8 patients with negative culture and positive mNGS results. A chest CT showed lung consolidation or cavity formation in 9 patients admitted to the hospital, and 5 patients had pleural effusion. 3 cases were admitted to the respiratory intensive care unit (RICU) and 6 cases were admitted to the general ward. There were 3 cases of nasal catheter oxygen inhalation, 1 case of mask oxygen inhalation, and 5 cases of non-invasive ventilator assisted ventilation. All patients received penicillin or respiratory quinolones anti-infection therapy, and 3 cases were treated with a thoracic closed drainage tube. All patients were discharged from the hospital after improvement, and the hospital stay was 15 - 23 days.**

Conclusions: **Patients with pulmonary abscess caused by *Streptococcus constellatus* infection have an urgent condition and rapid progression. It is helpful to use mNGS combined with traditional culture as soon as possible to identify the pathogenic bacteria. Penicillin antibiotics should be the first choice for pulmonary abscess caused by a suspected *Streptococcus constellatus* infection. If a patient´s condition worsens during the treatment, especially for patients who have lesions involving the interlobar fissure or pleura, compressive atelectasis caused by pleural fluid formation or an increase in the amount of pleural effusion needs to be highly suspected.**

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Correspondence:
Dr. YiLing Gan
Department of Respiratory and Critical Care Medicine
The First Affiliated Hospital of Chongqing Medical and Pharmaceutical College
No. 301, Nancheng Avenue, Nanan District
Chongqing, 400060
P.R. China

Phone/Fax: + 86 2361929135
Email: 307323601@qq.com

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KEYWORDS

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INTRODUCTION

Lung abscess is a suppurative lesion of the lung tissue caused by various pathogenic infections, which is characterized by a localized necrosis and suppuration within the lung tissue and the formation of cavities (more than 2 cm) [1]. For a long time, anaerobic bacteria and microaerophilic *streptococci* have been generally considered to be the predominant pathogens that cause lung abscess. Based on pathogen detection in lung abscess, a previous study showed that lung abscess is mainly caused by pathogens such as *streptococci*, *Staphylococcus aureus*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* [2]. Although patients with lung abscesses have a good prognosis after an aggressive anti-infection therapy and puncture drainage, lung abscess can lead to death without treatment [3]. Pathogen detection is a prerequisite for targeted treatment of lung abscess. Currently, clinical microbial pathogen detection is still dominated by traditional methods such as culture, staining microscopy, and polymerase chain reaction (PCR) assay, which have limitations such as long culture cycles and a low sensitivity. Traditional culture is the gold standard of pathogen detection, but has a low positive rate, especially in patients who have been treated with broad-spectrum antibiotics before sampling [4]. Metagenomic next-generation sequencing (mNGS) is an untargeted DNA/RNA sequencing technique that enables the simultaneous detection of viruses, bacteria, fungi, and parasites in clinical samples [5-7]. mNGS has made a revolution in the mode of pathogen identification and is commonly used in clinical practice [5,7]. Traditional cultures are usually negative in patients with lung abscess, and there is also a possibility of missed detection in a clinical setting, so that the management of lung abscess is mainly based on empirical therapy [8-10]. In our hospital, we used mNGS to detect pathogens in lung abscess, and found that lung abscess was caused by *Streptococcus constellatus* infection in some patients. Currently, lung abscess due to *Streptococcus constellatus* has been rarely reported [11-13]. Therefore, this study aimed to retrospectively analyze the clinical characteristics of lung abscess caused by *Streptococcus constellatus* infection.

MATERIALS AND METHODS

Study population

Patients with a confirmed diagnosis of lung abscess, who were hospitalized in the Department of Respiratory and Critical Care Medicine of the First Affiliated Hospital of Chongqing Medical and Pharmaceutical College from January 2021 to November 2023, were enrolled in the study and retrospectively analyzed.

The inclusion criteria included: 1) patients who were diagnosed with lung abscess according to their medical history and imaging examination results; 2) the diagnosis of lung abscess caused by *Streptococcus constellatus* infection was confirmed by traditional culture or mNGS; and 3) HIV-negative patients. The exclusion criterium was when patients had a malignant tumor.

The bronchoalveolar lavage fluid (BALF) and puncture drainage fluid were sent for traditional pathogen detection (including smear, culture, and PCR) and mNGS after undergoing bronchoscopy with bronchoalveolar lavage (BAL) or a CT-guided percutaneous lung puncture and a catheter drainage. Patients' demographic characteristics, comorbidities, blood gas analysis (tested by using the electrode potential difference method), blood routine (tested by using flow cytometry), Albumin (tested by using the bromocresol green method), procalcitonin (PCT, tested by using radioimmunological assay), C-reactive protein (CRP, tested by using immunoturbidimetry), fasting blood-glucose (FBG, tested by using the hexokinase method), glycosylated hemoglobin A1c (A1c, tested by using a high performance liquid chromatography), smear, culture, mNGS results, and chest CT findings were collected from an electronic medical record management system. Smear and culture tests were used to detect the bacteria, fungi, and acid-fast bacilli. The type of samples submitted for smear included sputum, BALF, or fluid drained during a CT-guided percutaneous lung puncture drainage; the type of samples submitted for culture test included blood, sputum, BALF, or drainage fluid. The type of samples submitted for PCR assay also included sputum, BALF, and drainage fluid. PCR assay was used for the detection of influenza A and B viruses, cytomegalovirus, mycoplasma, chlamydia, and novel coronavirus. And GeneXpert-TB PCR assay was used for the detection of *Mycobacterium tuberculosis*. BALF or drainage fluid samples were also sent for exfoliative cytology, cell sorting, and counting. Serum samples were sent for (1,3)-beta-D-glucan test and galactomannan test.

The study was approved by the ethics committee of our hospital and written informed consent was obtained from the participants.

Bronchoscopy with BAL

After local anesthesia was induced via injection of 2% lidocaine, a fiberoptic bronchoscope (Olympus) was inserted transnasally. Lidocaine local anesthesia can be given through the biopsy channel if necessary. After careful examination of the entire bronchial tree, BAL

was performed in the most affected lung lobe on the chest CT. 20 mL of saline (37°C) was instilled and then withdrawn. This procedure was repeated until a total of 100 mL of saline was instilled. BAL was considered technically acceptable if the recovery is > 40%. BALF samples were routinely sent for smear, culture, mNGS, PCR, exfoliative cytology, cell sorting, and counting.

CT-guided percutaneous lung puncture and catheter drainage

For patients who showed an area of liquefactive necrosis on an enhanced chest CT and exhibited obvious clinical symptoms, percutaneous lung puncture and catheter drainage were performed by using a disposable thoracic and abdominal puncture and drainage package (Abel) under CT guidance. After CT localization, local anesthesia was induced via injection of 2% lidocaine. Subsequently, the puncture needle in the puncture and drainage package was used to guide the placement of the thoracic drainage tube. Drainage fluid was sent for smear, culture, mNGS, PCR, exfoliative cytology, cell sorting, and counting. After the procedures were completed, a CT re-examination was performed to determine the presence or absence of a pneumothorax and the catheter location. Then patients were returned to the ward.

Sputum smear examination

Sputum smears were examined with Gram and Wright's acid-fast staining techniques.

Culture, identification, and drug sensitivity test of pathogens

Culture and identification of pathogens were performed according to the National guide to Clinical Laboratory Procedures of China. Samples were inoculated onto blood agar (Sigma company, USA) and chocolate agar plates (Sigma company, USA) for bacterial culture under aerobic and microaerophilic conditions (5% CO_2) at 37°C for up to 1 week, which were inoculated onto Candida chromogenic agar (BD company, USA) and Sabouraud dextrose agar (BD company, USA) plates for fungal and mycobacterial culture under aerobic and microaerophilic conditions (5% CO_2) at 37°C for up to 1 week. The growth of pathogen on the plate and the morphology of the colony were observed every day. Then the colony was subcultured after 24 hours. Whether the sample was culture-positive or culture-negative, all samples were sent to the First Affiliated Hospital of the Chongqing Medical University and tested for *Mycobacterium tuberculosis* by using GeneXpert-TB PCR assay. Culture-positive samples were identified by using MALDI-TOF-MS mass spectrometer (Bruker company, Germany) and biotyper system (Bruker company, Germany). Pure culture colonies were smeared on the sample detection plate of the MALDI-TOF-MS mass spectrometer by using sterile inoculation loop (Sigma-Aldrich, USA), then the sample detection plate was put into the MALDI-TOF-MS mass spectrometer for detection. The quality control strain *Escherichia coli* ATCC 8739 was used as the calibration target of each group. Spectral peaks of peptides and proteins were collected by MALDI-TOF-MS mass spectrometer, and then finger patterns were formed according to their mass. Bacteria can be identified by their unique protein composition, which can be applied to the identification and differentiation of different kinds of bacterial strain. The spectrum of relative molecular therapy 2 - 20kDa was collected with the maximum frequency (20 - 200Hz) in linear positive mode, and all the collected spectra were analyzed with the Biotyper system. When the score of Bruker biotyper system was equal or greater than 1.7, the results were considered highly credible.

Antimicrobial susceptibility testing, including ampicillin, penicillin G, cefotaxime, ceftriaxone, cefepime, meropenem, chloramphenicol, linezolid, levofloxacin, vancomycin, tetracycline, and clindamycin, was performed by using the disk diffusion method (Oxoid company). The inhibition zone diameter breakpoints for disk diffusion and susceptibility results were interpreted according to the criteria published by the Clinical and Laboratory Standards Institute (2020) [14].

mNGS

DNA was extracted from BALF or drainage fluid by using the TIANamp DNA kit (DP316, Tiangen Biotech Co., Ltd., Beijing, China) according to the manufacturer's instruction. The DNA library was constructed by enzyme-based DNA fragmentation, end-repair, adaptor ligation, and PCR amplification. The Agilent 2100 Bioanalyzer (Agilent, USA) was used for quality control of the DNA library. Then the qualified library was sequenced by using the illumin Nextseq 550 sequencing platform. The resulting data were analyzed by Burrows-Wheeler Aligner software, followed by alignment with four Microbial Genome Databases consisting of bacteria, fungi, viruses, and parasites. The classification reference databases were downloaded and optimized from public database such as NCBI (https://www.ncbi.nlm.nih.gov/), EMBL-EBI (https://www.ebi.ac.uk/), or Genbank (https://www.ncbi.nlm.nih.gov/genbank/).

The drug resistance genes were obtained through an alignment with the CARD databases (https://card.mcmaster.ca/). mNGS test was performed by Vision Medicals Co., Ltd., Guangzhou, China.

Pathogenic diagnostic criteria

Lung abscess is a suppurative inflammation of the lung tissue that results in necrosis of the lung parenchyma due to various bacterial infections. Lung abscess is manifested as cavity formation with an air-fluid level or as a low-density shadow in the center of the lesion on a chest CT.

The criteria for pathogens identified by traditional detection methods included: 1) positive sputum (BALF or drainage fluid) culture results; 2) positive GeneXpert-TB PCR results in sputum samples (BALF or drainage fluid); and 3) positive sputum (BALF or drainage fluid)

smear results for fungi and *Mycobacterium tuberculosis complex*.

The criteria for positive mNGS results included: 1) > 30% relative abundance of bacteria or fungi at the genus level; 2) at least three sequence reads from a single viral, bacterial, or fungal species; and 3) at least one sequence read matching the *Mycobacterium tuberculosis* complex. If more than one pathogen was detected, the pathogen with the greatest relative abundance yielding the highest number of sequence reads was considered to be associated with lung abscess in that patient.

RESULTS

Clinical characteristics of patients and their underlying diseases

A total of 52 patients were diagnosed with lung abscess, of which 33 patients completed the traditional detection (including culture, smear, and PCR) and mNGS. The sample type included sputum (n = 33), BALF (n = 24), and drainage fluid (n = 14). Lung abscess was finally confirmed to be caused by pure *Streptococcus constellatus* infection in 9 patients, *Streptococcus constellatus* combined with *Mycobacterium tuberculosis* in 1 patient, *Streptococcus constellatus* combined with *Tropheryma whipplei* in 1 patient, *Pseudomonas aeruginosa* combined with *Aspergillus fumigatus* in 1 patient, *Klebsiella pneumoniae* combined with *Mycobacterium tuberculosis* in 1 patient, adenocarcinoma combined with *Pseudomonas aeruginosa* in 1 patient, *Pseudomonas aeruginosa* in 5 patients, *Staphylococcus aureus* in 4 patients, *Klebsiella pneumoniae* in 7 patients, and *Escherichia coli* in 3 patients.

Among these 9 patients with pure *Streptococcus constellatus* infection, 8 were male and 1 was female with an age range of 34 - 73 years. Seven out of the 9 patients had underlying diseases, including type 2 diabetes (n = 3), diabetic nephropathy (n = 1), chronic lung disease (n = 4, including 1 case of bronchial asthma and 3 cases of chronic obstructive pulmonary disease), coronary heart disease (n = 2), hypertension (n = 1), and kidney stones (n = 1). Two patients reported long-term staying up all night to play video games. Among the 9 patients, the duration from disease onset to admission ranged from 1 to 10 days, and was < 1 week in 7 out of these 9 patients. All these 9 patients had varying degrees of symptoms such as cough, sputum production, fever, chest pain, and/or dyspnea. Physical examination upon admission showed that all 9 patients exhibited tachypnea, with reduced breath sounds on the affected side. Obvious moist rales were heard in the lung on the affected side in 3 patients.

All patients underwent blood culture and an abdominal ultrasound examination at the time of admission; bloodborne infections and infections within other tissues such as the liver and abdominal cavity caused by *Streptococcus constellatus* were excluded. Four patients with lung abscess developed pyothorax during the treatment. The detailed clinical data of these 9 patients are shown in Table 1.

Laboratory test results

Routine laboratory tests were performed on all patients at the time of admission, including blood gas analysis, blood routine, liver and kidney function, blood lipid profile, and fasting blood glucose. Laboratory test results showed that 8 patients had an elevated white blood cell count and 8 patients had hypoproteinemia (albumin level < 35 g/L) at admission. Blood gas analysis revealed an oxygenation index of all patients < 300 mmHg. In 3 patients who had underlying disease of type 2 diabetes, the glycosylated hemoglobin A1c level was > 6.1%. Laboratory test results of these 9 patients are detailed in Table 2.

Treatment and prognosis of patients

All patients underwent a chest CT on the day of admission. According to the pneumonia severity index score, 3 patients were admitted to the respiratory intermediate care unit and 6 patients were admitted to the general hospital ward. The treatment included empiric antimicrobial therapy with ceftizoxime (n = 2), piperacillin sodium and sulbactam sodium (n = 3), moxifloxacin (n = 2), levofloxacin (n = 1), meropenem (n = 2), and ornidazole (n = 3); nasal cannula oxygen therapy (n = 3), face mask oxygen administration (n = 1), and noninvasive ventilator-assisted ventilation therapy (n = 5). From the 2nd until 6th day of admission, BALF or drainage fluid was sent for traditional culture and mNGS test. BALF culture and mNGS did not detect any pathogenic bacteria in 3 patients, they continued to receive empirical antimicrobial therapy for 2 days, but their symptoms did not improve. The chest CT re-examination showed the expansion of the liquefactive necrosis area. After obtaining the consent of the patients and their family members, a CT-guided percutaneous lung puncture and catheter drainage was performed, and the drainage fluid was then sent for traditional culture and mNGS test. Drainage fluid cultures yielded negative results in these patients, while mNGS test detected the presence of *Streptococcus constellatus*. According to the test results, the antibacterial drug was adjusted to piperacillin sodium and sulbactam sodium. Subsequently, patients' symptoms improved.

Out of the 9 patients, 4 patients experienced a worsening of the dyspnea within 6 days prior to the hospitalization. The chest CT re-examination displayed new-onset pleural effusion in 2 patients (including 1 case of small pleural effusion and 1 case of moderate pleural effusion) and an increase in the amount of pleural effusion in 2 patients as compared to those observed on the first day of admission. A closed thoracic drainage tube was placed in 3 patients, followed by submitting the fluid drained from the pleural effusion for laboratory testing. These patients were diagnosed as having pyothorax.

Table 1. The detailed clinical data of the 9 patients.

	Gender	Age (year)	Body mass index (kg/m^2)	Underlying diseases or causes	Chief complaint	Physical examination
Case 1	**male**	**63**	**21.6**	**Type 2 diabetes, diabetic nephropathy**	**Cough and shortness of breath after activity for 5 days**	**T: 36.8°C, P: 98 bpm, R: 24 rpm, BP: 122/68 mmHg, decreased respiratory sounds of the right lung**
Case 2	**male**	**56**	**20.4**	**Chronic obstructive pulmonary disease**	**Repeated cough, phlegm, and wheezing for 40+ years, dyspnea for 2 days**	**T: 37.3°C, P: 108 bpm, R: 24 rpm, BP: 102/57mmHg, distinct moist crackles in the right lung**
Case 3	**male**	**35**	**24.8**	**Long-term staying up all night to play video games**	**Cough for 1 week, fever, and dyspnea for 3 days**	**T: 38.3°C, P: 114 bpm, R: 24 rpm, BP: 134/88mmHg, decreased respiratory sounds of the left lung**
Case 4	**female**	**67**	**19.2**	**Bronchial asthma, kidney stones**	**Repeated cough, phlegm, and wheezing for 6 years, aggravated for 5 days**	**T: 36.3°C, P: 102 bpm, R: 22 rpm, BP:124/70mmHg, wheezing sound in both lungs, obvious moist rales in the right lung**
Case 5	**male**	**70**	**18.4**	**Coronary heart disease, type 2 diabetes**	**Dizziness, weakness for 10 days, chest pain, and dyspnea for 4 days**	**T: 36.8°C, P: 92 bpm, R: 21 rpm BP: 114/70mmHg, slightly decreased respiratory sounds of the right lung**
Case 6	**male**	**72**	**21.7**	**Chronic obstructive pulmonary disease**	**Recurrent cough, phlegm, and wheezing for 6 years, aggravated for 1 week**	**T: 36.8°C, P: 112 bpm, R: 24 rpm, BP: 124/76mmHg, obvious moist rales and wheezing in the right lung**
Case 7	**male**	**73**	**22.3**	**Chronic obstructive pulmonary disease**	**Repeated cough, phlegm, and wheezing for 6 years, aggravated for 5 days**	**T: 37.8°C, P: 104 bpm, R: 22 rpm, BP: 122/64mmHg, decreased respiratory sounds in both lungs, notably in the left lung**
Case 8	**male**	**73**	**18.4**	**Coronary heart disease, type 2 diabetes**	**Cough, shortness of breath after activity for 9 days, and dyspnea for 1 day**	**T: 37.8°C, P: 104 bpm, R: 22 rpm, BP: 122/64mmHg, decreased respiratory sound in the right lung**
Case 9	**male**	**34**	**25.3**	**Hypertension, long-term staying up all night to play video games**	**Headache, fatigue for 3 days, and chest pain for 1 day**	**T: 39.8°C, P: 118 bpm, R: 25 rpm, BP: 124/76mmHg, decreased breathing sound in the right lung**

All patients were discharged from the hospital after active antimicrobial therapy or puncture and drainage. The average length of the hospital stay was 19 days (range: 15 - 23 days). During the 3-month follow-up period, 5 patients visited our hospital for a re-examination, none of them suffered from recurrence and aggravation of the infection or death; 3 patients were followed up via telephone interview and did not report infection recurrence; one patient was lost to follow-up (Table 3).

Pathogenic bacteria and antimicrobial susceptibility test results

In one patient, the diagnosis of *Streptococcus constellatus* was confirmed by drainage fluid culture and the mNGS results also revealed a *Streptococcus constellatus* infection. In 8 patients, traditional cultures were negative, while the results of mNGS in BALF (n = 3) and drainage fluid samples (n = 5) showed a *Streptococcus constellatus* infection.

Antimicrobial susceptibility test results in the above-mentioned patient with culture-confirmed pathogen

Table 2. The laboratory test results of the 9 patients.

	PH	OI (mmHg)	WBC (x 10^9/L)	PCT (ng/mL)	CRP (mg/L)	Albumin (g/L)	FBG (mmol/L)	A1c (%)
Case 1	7.43	249.3	10.89	0.07	12.39	32.0	8.2	9.3
Case2	7.42	209.5	11.57	0.05	44.93	34.82	4.9	
Case 3	7.51	204.8	14.69	4.56	168.04	31.3	7.5	
Case 4	7.48	241.5	15.11	0.46	115.72	33.19	6.8	
Case 5	7.39	244.2	12.58	0.34	194.44	34.32	6.7	7.9
Case 6	7.46	247.1	5.83	0.03	61.95	34.71	5.9	
Case 7	7.55	193.1	11.61	0.56	187.49	31.32	7.2	
Case 8	7.41	203.0	23.29	1.5	183.57	22.57	9.1	10.2
Case 9	7.48	210.8	15.2	0.12	> 200	38.06	8.1	

PH, potential of hydrogen, was tested by using the electrode potential difference method, the PH normal reference range is 7.35 - 7.45; OI, oxygenation index, is equal to the ratio of the oxygen partial pressure to oxygen concentration, oxygen partial pressure was tested by using the electrode potential difference method, the OI normal reference range is equal or greater than 300 mmHg; WBC, white blood count, was tested by using electrical impedance and flow cytometry, the WBC normal reference range is from 4 x 10^9 to 10 x 10^9/L; PCT, procalcitonin, was tested by using radioimmunological assay, the PCT normal reference range is less than 0.5ng/mL; CRP, C-reactive protein, was tested by using immunoturbidimetry, the CRP normal reference range is from 5 to 10ng/mL; Albumin, was tested by using the bromocresol green method, the Albumin normal reference range is from 40 to 50 g/L; FBG, fasting blood-glucose, was tested by using the orthotolidine method, the FBG normal reference range is from 3.9 to 6.0 mmol/L; A1c, glycosylated hemoglobin A1c, was tested by using high performance liquid chromatography, the A1c normal reference range is from 5.0 to 6.8%.

diagnosis showed that *Streptococcus constellatus* was susceptible to ampicillin, penicillin G, cefotaxime, ceftriaxone, cefepime, meropenem, chloramphenicol, linezolid, levofloxacin, and vancomycin, and resistant to tetracycline and clindamycin. Relevant antibiotic resistance genes, including ermB, mefE, pbp2b, pbp2x, and so on, obtained through alignment with the CARD databases (https://card.mcmaster.ca/), were not detected by mNGS in the 8 patients with negative culture and positive mNGS results.

Imaging findings

On admission, all of the 9 patients underwent a chest CT. The results showed solid exudation shadows in the right lung in 6 patients, cavity with air-fluid level in 4 patients, lesions with interlobar fissural involvement in 1 patient, and lesions adjacent to the pleura (the distance between the lesion boundary and pleura was < 1 mm) in 3 patients. Chest CT also revealed solid exudation shadows in the left lung in 2 patients, with cavity containing an air-fluid level being observed in 2 patients and lesions adjacent to the pleura being observed in 1 patient. Among these 9 patients, 5 patients had a small amount of pleural effusion, 1 had lesions involving the interlobar fissure, and 4 had lesions adjacent to the pleura.

DISCUSSION

Streptococcus constellatus was described by Guthof in 1956 after being isolated from periodontal abscess [15]. It is a Gram-positive cocci, which is difficult to grow in an aerobic condition and grows well in 5% CO_2 or anaerobic conditions, thus leading to low rates of clinical isolation [16]. *Streptococcus constellatus* belongs to the *Streptococcus milleri* group, along with *Streptococcus intermedius* and *Streptococcus anginosus*. They are commensal bacteria of the oral cavity, throat, gastrointestinal tract, and genitourinary tract, their pathogenicity is weak; they are considered opportunistic pathogens [17,18]. *Streptococcus constellatus* causes purulent infections in various tissues and organs of the body, when the body's resistance decreases [17-21]. In this study, among 9 patients with *Streptococcus constellatus* infection, 8 had underlying diseases, and 3 were young patients who stayed up all night playing video games for a long time; the immunity is low in such patients. Zhang et al. found that *Streptococcus constellatus* was mainly isolated from pus, blood, and sputum, with pus being the most frequent sample type, accounting for nearly 15.7% of the isolates [22]. Lin et al. found that among 47 *Streptococcus constellatus* strains, 62.7% were isolated from ascites [23]. The results of the present study showed that *Streptococcus constellatus* isolated from lung abscess drainage fluid accounted for 66.7% of the isolates, and only 33.3% were isolated from BALF. In particular, mNGS did not detect any pathogenic bacteria in the BALF samples of 3 patients but identified *Streptococcus constellatus* in the drainage fluid samples of these patients. Su et al. reported that for pathogen detection of lower respiratory tract infections and lung abscess, mNGS was superior to traditional detection methods in detecting potential pathogens and mixed infections [24]. In this study, among 9 patients with *Strepto-*

Table 3. Treatment and prognosis of the 9 patients.

	Imaging findings	Treatment ward	Respiratory support method	Antibiotic therapy	Invasive operation	Sample type and test method for a definitive diagnosis	Complicated with empyema	Course of treatment (days)	Prognosis
Case 1	Cavity with air-fluid level and lesions adjacent to the pleura in the right lung	General ward	Nasal cannula oxygen therapy	Cefzoxime and ornidazole for 4 days, piperacillin sulbactam sodium for 13 days	CT-guided percutaneous lung puncture and catheter drainage	Drainage fluid, mNGS	Yes, thoracic drainage tube	17	Improved
Case 2	Solid exudation shadow, cavity with air-fluid level, lesions with interlobar fissural involvement, and a small amount of pleural effusion in the right lung	RICU	Noninvasive ventilator-assisted ventilation therapy	Meropenem and Levofloxacin for 7 days, piperacillin sulbactam sodium for 16 days	CT-guided percutaneous lung puncture and catheter drainage	Drainage fluid, mNGS	Yes, thoracic drainage tube	23	Improved
Case 3	Solid exudation shadow, cavity with air-fluid level, lesions adjacent to the pleura, and a small amount of pleural effusion in the left lung	general ward (refused admission to RICU)	Noninvasive ventilator-assisted ventilation therapy	Moxifloxacin and Meropenem for 4 days, Piperacillin sulbactam sodium for 17 days	Bronchoscopy with bronchoalveolar lavage, CT-guided percutaneous lung puncture and catheter drainage	Drainage fluid, mNGS		21	Improved
Case 4	Solid exudation shadow with a low-density shadow in the right lung	General ward	Face mask oxygen administration	Piperacillin and sulbactam sodium and ornidazole for 15 days	Bronchoscopy with bronchoalveolar lavage	BALF, mNGS		15	Improved
Case 5	Solid exudation shadow, cavity with air-fluid level, lesions adjacent to the pleura, and a small amount of pleural effusion in the right lung	General ward	Nasal cannula oxygen therapy	Cefazoxime and ornidazole for 3 days, piperacillin sulbactam sodium and Ornidazole for 15 days	CT-guided percutaneous lung puncture and catheter drainage	Drainage fluid, traditional cultures, and mNGS	Yes, thoracic drainage tube	18	Improved
Case 6	Solid exudation shadow with a low-density shadow in the right lung	General ward	Nasal cannula oxygen therapy	Piperacillin and sulbactam sodium and ornidazole for 16 days	Bronchoscopy with bronchoalveolar lavage	BALF, mNGS		16	Improved
Case 7	Solid exudation shadow, and cavity with air-fluid level in the left lung	RICU	Noninvasive ventilator-assisted ventilation therapy	Meropenem and moxifloxacin for 5 days, piperacillin sulbactam sodium for 18 days	Bronchoscopy with bronchoalveolar lavage, CT-guided percutaneous lung puncture and catheter drainage	Drainage fluid, mNGS		23	Improved

Table 3. Treatment and prognosis of the 9 patients (continued).

	Imaging findings	Treatment ward	Respiratory support method	Antibiotic therapy	Invasive operation	Sample type and test method for a definitive diagnosis	Complicated with empyema	Course of treatment (days)	Prognosis
Case 8	Solid exudation shadow, and cavity with air-fluid level in the right lung	RICU	Noninvasive ventilator-assisted ventilation therapy	Meropenem for 4 days, piperacillin sulbactam sodium for 15 days	Bronchoscopy with bronchoalveolar lavage, CT-guided percutaneous lung puncture and catheter drainage	Drainage fluid, mNGS		23	Improved
Case 9	Solid exudation shadow with a low-density shadow and lesions adjacent to the pleura in the right lung	General ward (refused admission to RICU)	Noninvasive ventilator-assisted ventilation therapy	Piperacillin sulbactam sodium and moxifloxacin for 17 days	Bronchoscopy with bronchoalveolar lavage	BALF, mNGS		17	Lost to follow-up

coccus constellatus infection, only 1 (11.1%) patient was identified as positive by traditional methods, while 8 (88.9%) were identified as positive by mNGS.

Wu et al. analyzed the antimicrobial susceptibility rates of *Streptococcus constellatus* isolates and found that *Streptococcus constellatus* had a susceptibility of 100% to vancomycin, linezolid, quinolones, and penicillins, 70% to cephalosporins, 13.8% to erythromycin, and 12.5% to clindamycin [25]. Zhang et al. reported that *Streptococcus constellatus* had susceptibility rates of 85% to glycopeptides and quinolones, 70% to cephalosporins and penicillins, 32% to erythromycin, and 28% to clindamycin [26]. Two previous studies from China [23,26] also obtained the same results, showing that *Streptococcus constellatus* was highly susceptible to vancomycin, linezolid, quinolone, cephalosporin, and penicillin, and was relatively less susceptible to erythromycin and clindamycin. An international study conducted by Ram et al. analyzed the antimicrobial susceptibility of 33 *Streptococcus constellatus* strains isolated from patients with severe chronic periodontitis and found that clindamycin was the most effective antibiotic against *Streptococcus constellatus* [27]. This finding is completely contrary to the results of this study and the above-mentioned previous studies from China. The reason for this may be due to the fact that the study of Ram et al. mainly focused on patients with severe chronic periodontitis [27]. Mohanty et al. reported a case of a patient with liver abscess due to *Streptococcus constellatus* and found that *Streptococcus constellatus* isolates were susceptible to cefotaxime, ceftriaxone, vancomycin, levofloxacin, clindamycin, and linezolid [28]. In the present study, we found that *Streptococcus constellatus* had high susceptibility to vancomycin, linezolid, quinolone, cephalosporin, and penicillin and showed high resistance rates to erythromycin and clindamycin. The differences in the antimicrobial susceptibility test results among the above-mentioned studies may be related to the difference in the list of antibiotics and antibiotic choices across the different countries.

It has been reported in the literature, that the imaging manifestations of pyothorax or lung abscess caused by *Streptococcus constellatus* infection are mostly unilateral pleural effusion or pulmonary infiltrates, partially encapsulated pleural effusion, lung tissue compression, and atelectasis [26,29]. In this study, all nine patients showed unilateral pulmonary infiltrates.

CONCLUSION

In conclusion, lung abscess caused by *Streptococcus constellatus* infection is easy to be missed clinically when only using traditional detection methods. For patients with lung abscess with low immunity, acute onset, severe condition, or rapid disease progression, *Streptococcus constellatus* infection needs to be suspected. Culture and mNGS testing of BALF or drainage fluid should be performed as early as possible to assist in confirming the diagnosis. Penicillin is the drug of

choice in treating such infection. If patients' condition worsen during treatment, especially for those who have lesions involving the interlobar fissure or pleura, compressive atelectasis caused by pleural fluid formation or an increase in the amount of pleural effusion need to be highly suspected, and puncture and drainage should be performed earlier to reduce lung compression.

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Ethics Approval Statement:
The study was approved by the ethics committee of our hospital, and written informed consent was obtained from the participants.

Data Availability Statement:
Data are available upon direct request. Chest CT images of the patient can be obtained by email.

Declaration of Interest:
The authors declare no conflicts of interest. The funder had no role in the design of the study, in the collection, analyses, or interpretation of the data, in the writing of the manuscript, nor in the decision to publish the results.

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