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Case Report

Pneumonia, a pulmonary abscess, and an empyema caused by *Parvimonas micra*

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Abstract

Background: Pneumonia with an empyema caused by anaerobic bacteria is rare but can be life-threatening, especially in immunocompromised patients.

Case presentation: A 67-year-old man with diabetes and hypertension who presented with pneumonia and pleural effusion and was unresponsive to initial broad-spectrum antibiotics is presented. Next-generation sequencing identified *Parvimonas micra* and other pathogens. Therefore, targeted therapy with levornidazole was initiated. The patient's condition improved significantly after this treatment.

Conclusions: This case highlights the importance of considering anaerobic bacteria in immunocompromised patients and the utility of next-generation sequencing in identifying atypical pathogens.

Key words: Case report; *Parvimonas micra*; infection; NGS.

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Introduction

Parvimonas micra, initially known as *Peptostreptococcus micros* and *Micromonas micros*, is a gram-positive anaerobic coccus commonly detected in the skin, mouth, gastrointestinal tract, and female genital tract [1]. *P. micra* is known to cause gingival infections. *P. micra* is the only species in the *Parvimonas* genus and often contributes to mixed anaerobic infections, such as intra-abdominal abscesses, and has been reported in infections of the vertebral spine, heart valves, and pulmonary system [2].

Pneumonia with pulmonary infections due to *P. micra* have been reported [2,3]. Moreover, *P. micra* co-infections with other pathogens, including SARS-CoV-2, *Streptococcus constellatus*, and influenza have been associated in patients with pneumonia and empyema [2,4]. However, pneumonia combined with an empyema caused by *P. micra* alone is exceptionally rare. This case report describes a unique case of pneumonia with a pulmonary abscess and an empyema caused by *P. micra*. Given the organism's anaerobic nature and involvement in severe infections, this report aims to contribute to our evolving understanding of *P. micra* infections.

Case report

A 67-year-old man with a 4-day history of cough and pectoralgia presented to our hospital on 30 March 2021. During the 4 days prior to admission, his symptoms included a cough and occasional chest pain that primarily involved his back. He did not experience expectoration or radiating pain. He had a fever with a temperature of 38.5 ℃. The patient had a medical history of well-controlled hypertension and diabetes managed with oral medications. The vital signs were as follows at the time of admission: temperature, 36.5 ℃; pulse, 91/min; respiration, 30 /min; and blood pressure, 157/73 mmHg. He was conscious, alert, and oriented with mild tachypnea. No superficial lymphadenopathy was noted. The respiratory sounds were clear bilaterally without rales. The heart rhythm was normal with no heart murmurs. The abdomen was flat and soft with no masses in the hepatosplenic regions and no edema involving the lower extremities.

The patient was first admitted to the emergency department of the hospital on 29 March 2021. The blood tests were significant for a white blood cell (WBC) count of 12.07 × 10^9/L (93.2% neutrophils and 3.5% lymphocytes) and a procalcitonin (PCT) level of 5.95 ng/ml. After admission, he occasionally

experienced chest pain, chest tightness, and shortness of breath. A chest CT on 30 March revealed scattered pneumonia in both lungs with the formation of pulmonary abscesses and pleural effusions in the left lung and interlobar fissure of the right lung (Figure 1A-D). An analysis of the pleural fluid was as follows: nucleated cell count, 24,150 × 10^6/L; neutral multinucleated cells, 74%; and Rivalta test, positive (++). He was diagnosed with pneumonia and pulmonary abscesses and was treated with medications, as below.

The patient was initially treated with piperacillin tazobactam, levofloxacin, and linezolid for experimental anti-inflammatory therapy. However, the respiratory rate rapidly increased and he had worsening chest tightness with shortness of breath and poor oxygenation, which necessitated non-invasive mechanical ventilation. A follow-up CT on 4 April showed a significant increase in the pleural effusion in the left thoracic cavity (Figure 2A-D). A thoracentesis was performed and biochemical tests of the pleural fluid showed adenosine deaminase (ADA) and lactate dehydrogenase (LDH) levels of 51 U/L and 33,07I U/L, respectively.

The patient had a history of diabetes and pulmonary tuberculosis. The thoracic drainage was consistent with an exudate. The ADA and LDH levels increased significantly and the patient's condition deteriorated rapidly. Because tuberculosis could not be completely ruled out, empirical anti-tuberculosis therapy was initiated on 6 April with isoniazid (0.3 g), rifampicin (0.45 g), ethambutol (0.75 g), and pyrazinamide (1.5 g).

Subsequent bacteriologic and pathologic examinations of the pleural effusion, sputum, and throat swabs were conducted. The throat swab cultures on 8 April grew *Klebsiella pneumoniae* and *Candida albicans*, while the remaining throat swab cultures had no growth. The pleural fluid culture for *Mycobacterium tuberculosis* (Xpert MTB) was also negative. Therefore, the antibiotic regimen was changed to meropenem, amikacin, and caspofungin. The minimum inhibitory concentration of the antibiotics was as follows: meropenem, 8 mg/L; amikacin, 4 mg/L; and caspofungin. Total DNA from pleural fluid samples collected on 10 April was extracted using the HostZERO Microbial DNA Kit (Zymo Research, USA) and subjected to next-generation sequencing (NGS), as previously described [5]. The NGS results were significant for anaerobic bacteria, including *P. micra*, prompting the addition of levornidazole to the antibiotic regimen (Figure 3A-B). Levofloxacin (minimum inhibitory concentration, 4 mg/L) was used instead of

Figure 1. Scattered inflammation on 30 March 2021. Both lungs showed abscess formation, and pleural effusions on the left and interlobar fissure on the right. Cavity with fluid level in the upper lobe of the right lung (A); arcuate hypodense shadow in the left thoracic cavity (B); oval hypodense shadow in the right horizontal fissure with additional hypodense areas in the left thoracic cavity and lower lobe of the left lung (C); hypodense area in the lesion of the left lower lung (D).

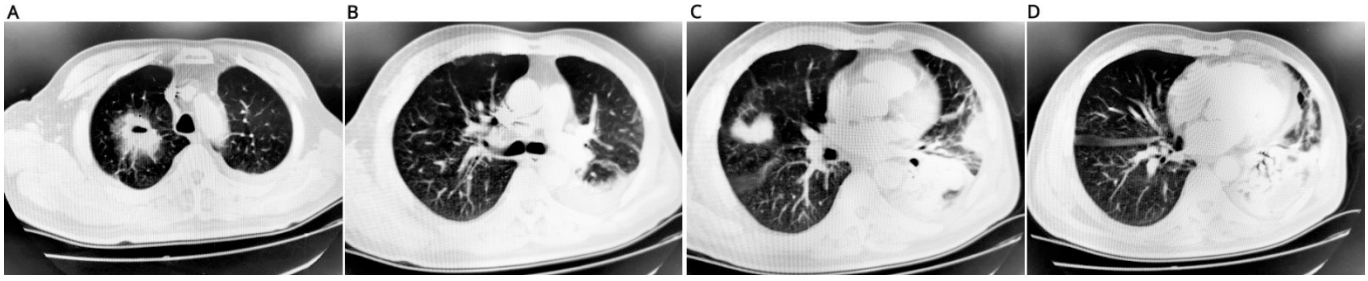


Figure 2. Evolution of scattered inflammation in the patient on 10 April 2021. Cavity and fluid levels in the right upper lung lesion that were slightly absorbed compared to 30 March 2021; left pleural effusion (A); left pleural effusion (B); ovoid hypodense shadow in the right horizontal fissure; hypodense shadow in the left thoracic cavity; lamellar hypodense area in the left lower lung (C); hypodense area in the left lower lung lesion and left pleural effusion (D).

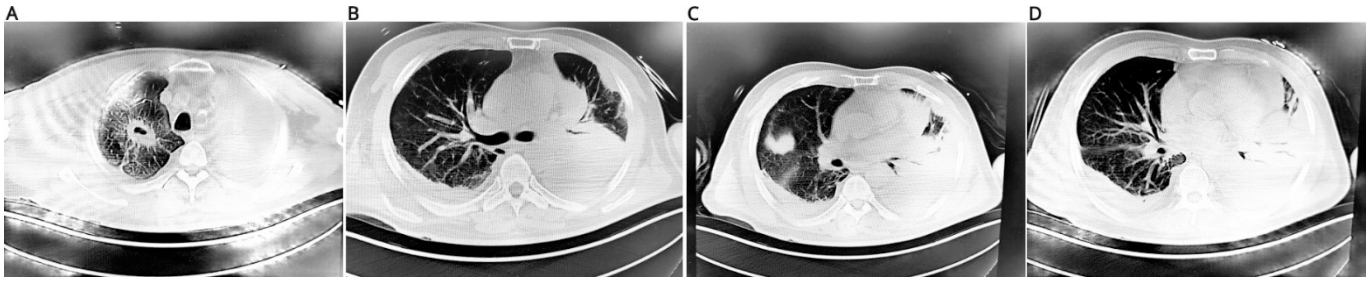
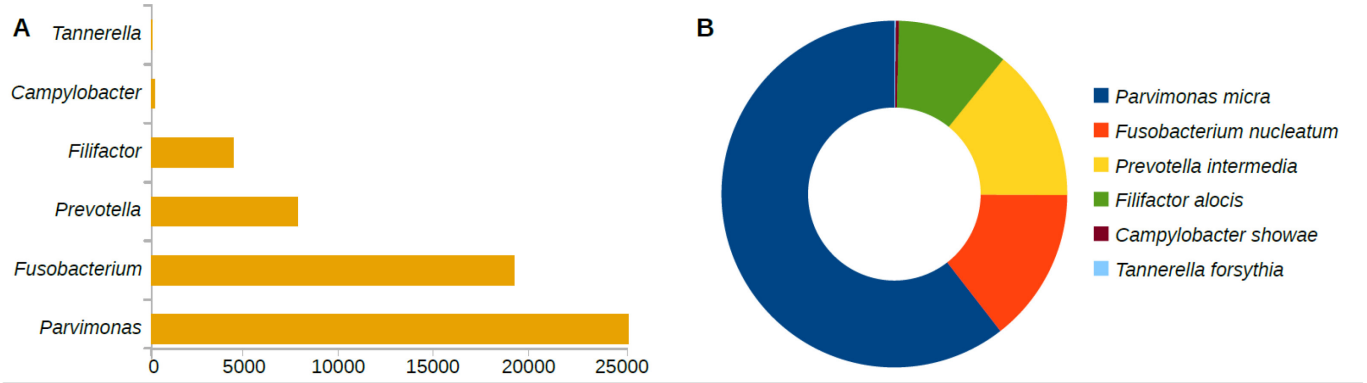


Figure 3. Results of next-generation sequencing on pleural fluid. Read abundance of major bacterial genera (A), and dominant bacterial species (B).



amikacin based on the antimicrobial susceptibility and pharmacokinetics of *K. pneumoniae*. The patient continued to receive meropenem but caspofungin was discontinued due to the detection of *K. pneumoniae*. Because clinical evidence of tuberculosis was lacking, the antibiotic regimen was revised to include rifampicin and isoniazid.

A chest CT image on 21 April after discontinuing the anti-tuberculosis antibiotics showed an increased pleural effusion compared to previous CT scans, which was suspicious for tuberculosis. A sputum culture for *Mycobacterium tuberculosis* and a chest X-ray to confirm tuberculosis were recommended but the patient and his family members declined. Therefore, tuberculosis could not be completely ruled out based on the medical history, so ethambutol and pyrazinamide were restarted on 21 April. The pleural effusion decreased but was encapsulated, which required intermittent thoracocentesis. The respiratory status improved with reduced chest pain and decreased coughing. Inflammatory markers, including the WBC count, neutrophil to lymphocyte ratio, and PCT level, normalized. A follow-up CT on 10 May showed further absorption of the pleural effusion, so consolidated anti-inflammatory therapy was continued (Figure 4A-D). By 17 May the chest CT showed marked improvement in the pleural effusion and the oxygenation level improved significantly (terminal oxygen saturation of

Figure 4. Reduction of scattered inflammation in the patient lungs on 10 May 2021. Absorption of lesions in the upper lobe of the right lung (A); patchy solid shadow in the right lung and pleural effusion on the left side (B); ovoid low-density shadow in the right horizontal fissure area and low-density shadow in the left thoracic cavity (C); low-density area in part of the lesion in the left lower lung (D).

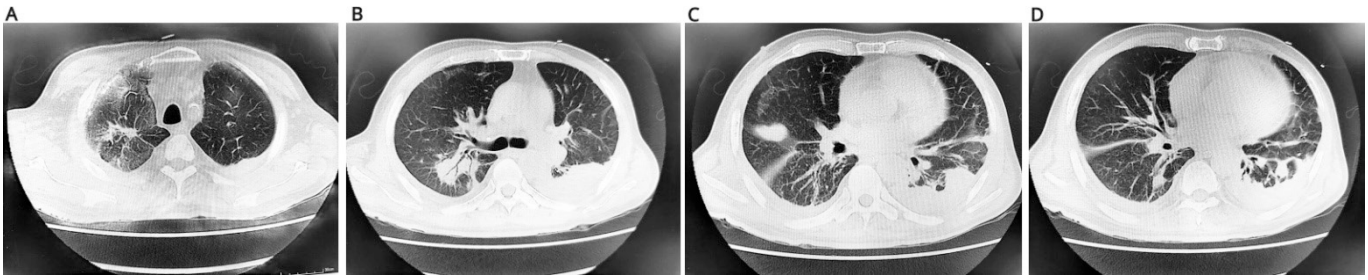


Figure 5. Scattered inflammation on 17 May 2021. Increased resorption of the lesion in the upper lobe of the right lung (A); hypodense shadow seen in the left thoracic cavity (B); disappearance of the ovoid hypodense shadow seen in the right horizontal fissure area and hypodense shadow seen in the left thoracic cavity (C); resorption of the lesion in the left lower lung (D).

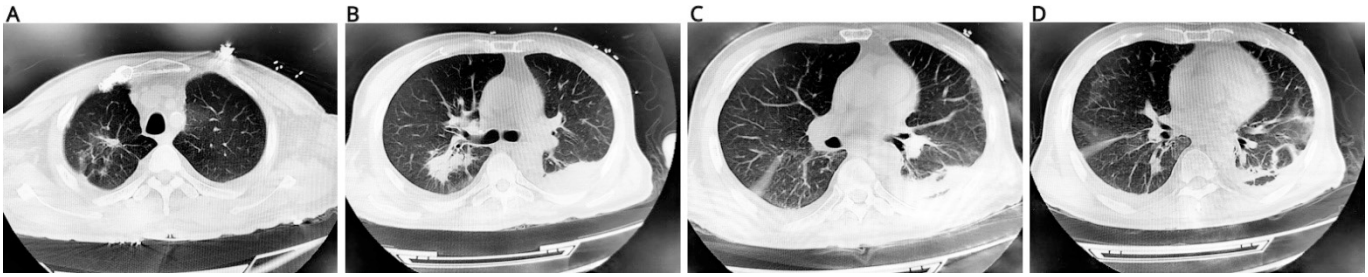


Table 1. Lung abscess and/or pleural empyema caused by *Parvimonas micra*.

Author	Gender/age	Oncologic history of immunosuppression	Previous dental procedure or pulmonary disease	Clinical presentation	BAL/pleural fluid characteristics	Blood laboratory test results	Treatment and outcomes
Duan et al. [2]	Male/late 60s	No, but had poor oral hygiene	No	Complaint of wheezing with cough and sputum expectoration. The severity gradually increased and increasing pain developed in the left hypochondrium.	CT showed a left pleural effusion with pulmonary atelectasis. Drainage of yellow, turbid, and purulent pleural effusion	Blood and sputum cultures were negative for pathogens, but the pleural effusion culture was positive for *S. constellatus* and was also shown to contain *P. micra* that was confirmed by mNGS.	The patient's condition worsened after admission. A thoracentesis was performed. The pleural effusion sample was analyzed for pathogens by mNGS and revealed the presence of *P. micra* (4516 reads) and *S. contellatus* (30 reads). The patient's symptoms improved after treatment with cefoperazone/sulbactam and moxifloxacin. The patient recovered fully.
Yu et al. [12]	Female/35	No	She underwent a caesarean section and brain surgery before admission to the ICU.	She developed severe pneumonia and hypoxemia in the ICU.	*P. micra* was shown to be the causative pathogen by NGS.	No pathogen was identified based on multiple sputum and blood cultures. IgM for *Chlamydia* and *Mycoplasma* were negative, which ruled out common hospital-acquired pneumonia caused by *Streptococcus pneumoniae*, *Klebsiella pneumoniae,* or *Staphylococcus aureus*. *P. micra* was determined to be the causative pathogen by NGS.	She was treated with ornidazole for *P. micra* and sulfamethoxazole for *Stenotrophomonas maltophilia*. Unfortunately, due to the massive cerebral hemorrhage, brain death was diagnosed.
Iijima et al. [13]	Male/70	No, but he has hypertension, atrial fibrillation, untreated dental caries, and periodontitis.	No	Exacerbation of dyspnea and anorexia	Chest X-ray imaging revealed a leftward deviation of the mediastinum, pleural effusion, and collapse of the right lung.	Intrathoracic urokinase was administered postoperatively due to persistent high inflammatory marker levels and a multilocular pleural effusion.	A thoracotomy was performed and chest drainage, debridement, and parietal and visceral decortication were then performed. The patient recovered.
Gumbs et al. [4]	Male/50	No	History of cigarette smoking (17.5 pack-year), polysubstance use disorder (cocaine and heroin), and hyperlipidemia.	Chest pain, productive cough, and hypoxia	A right hydropneumothorax/loculated pleural effusion was noted on chest x-ray.	The following findings were significant: SpO_2 >95%; the WBC count was elevated; the neutrophil % was elevated; the lactate level was within the normal range; pro-inflammatory markers were elevated (procalcitonin, ferritin, C-reactive protein, LDH, and D-dimer; and an elevated pro-BNP level.	Bedside drainage; The patient underwent right postero-lateral open thoracotomy, total lung decortication, wedge resection, pneumonolysis, and mechanical pleurodesis; bedside drainage was performed. The antimicrobial dose was adjusted. The patient recovered.
Feng et al. [14]	Male/74	No	Microbiome analysis revealed dysbiosis of the oral flora that was possibly related to poor oral hygiene and a 20-year history of cigarette smoking. The patient wore dentures for an extended period of time.	A complaint of dry cough, fever, and intermittent chest pain and shortness of breath after activity	CT images showed an increasing number of nodules and exudative inflammatory lesions with a newly emerged pleural effusion.	The leukocyte level was normal but the erythrocyte sedimentation rate was elevated (61 mm/h). The laboratory tests, such as galactomannan antigen (GM), b-D-glucan fungal antigen (G test), and tests for cryptococcal pod antigen, were negative. The patient was positive for *Mycoplasma* antibody (IgM).	The patient was treated with moxifloxacin for 3 months. mNGS confirmed that *Parvimonas* not only in the oral cavity but also in the BALF. Moxifloxacin treatment was continued. The patient recovered.
Lai et al. [3]	(4 cases) 3 males and 1 female/ 8-13 years of age	No	All four patients had different basic medical histories (1 case of Down's syndrome, 2 cases of cerebral palsy, and 1 case of hypophrenia). The patients required long-term bed rest, and had severe malnutrition and poor oral hygiene.	All four patients had fevers, cough, shortness of breath, and hemoptysis; one patient had respiratory failure	Pleural effusion	Plot of the lung damaged tissue and pathologic sections in one case. Extensive leukocyte infiltration was noted in the pathologic sections.	NGS showed oral obligate anaerobes represented by *Parvimonas micra* and *Porphyromonas gingivalis*. Piperacillin tazobactam and metronidazole were administered for anti-infection treatment. All four children recovered.
Fukushima et al. [15]	Female/57	No	No	She was admitted in shock.	CT and MRI revealed a multilocular lung abscess in the right upper lobe.	Blood culture revealed *Parvimonas micra*.	The patient was treated with ceftriaxone, vancomycin, and azithromycin but high fevers with circulatory failure persisted. She underwent a right upper lobectomy on the 10th day following admission to eliminate the infectious focus. The patient was discharged with a prescription of amoxicillin clavulanic acid for 10 weeks of antibiotic therapy.
Zhu et al. [16]	9 cases/ all males, 33-69 years of age	No but all patients had different underlying diseases.	No but all patients had a long history of smoking.	All patients had chest pain, fevers, cough, and hypoxemia symptoms; 90% had expectoration.	Chest CT indicated different degrees of lobar pneumonia and pleural effusions in all patients.	The laboratory tests revealed that all patients had elevated white blood cell and neutrophil counts, and C-reactive protein (CRP) levels.	mNGS confirmed *Parvimonas micra* infections. All patients had drainage tubes placed and underwent fibrinolysis therapy. Three of the patients received surgical treatment. Carbapenem and nitroimidazole were administered to all patients. All patients were discharged in stable condition.

approximately 97%; Figure 5A-D). The patient was discharged from the hospital and gradually recovered with no recurrences.

Discussion and Conclusions

We have presented a rare case involving a 67-year-old patient with pneumonia and an empyema caused by *P. micra.* The patient had a history of diabetes and poor oral hygiene. Despite initial treatment with broad-spectrum antibiotics, the patient's condition worsened, requiring a thoracentesis and targeted antimicrobial therapy. The case highlights the importance of considering anaerobic bacterial infections in immunocompromised patients, and as previously reported, the utility of NGS for accurate pathogen identification [3].

P. micra is part of the normal flora and other mucosal surfaces [6]. While *P. micra* is not typically a dominant bacterium in an aerobic environment, *P. micra* has been implicated in abdominal, intracranial, pulmonary, and bloodstream infections [3,7–10]. However, cases of pneumonia with empyema caused by *P. micra* are rare due to the oxygenated environment in the lung, which is not suitable for anaerobe growth. This rarity is compounded by the difficulty in culturing *P. micra* using conventional methods due to the specific growth requirements [11]. Based on a literature review (Table 1), all patients with *P. micra*-associated pneumonia can be accurately diagnosed using NGS [2-4,12-16].

Diabetes and poor oral hygiene likely contributed to the infection in the patient presented herein, as well as male patients with a history of cigarette smoking, as shown in Table 1 [2-4,12-16]. Diabetes can impair immune function, making individuals more susceptible to infections. In our case, poor oral hygiene may have facilitated the aspiration of *P. micra*, leading to pneumonia and empyema. Similar cases have been reported that immunocompromised patients, including patients with diabetes, are partially susceptible to *P. micra*, which often originates from the oral cavity [17].

Previous studies have documented *P. micra* infections in several body sites, but pulmonary infections are scarce. The anaerobic nature of *P. micra* makes culturing difficult and often requires advanced diagnostic techniques, such as molecular detection methods, including a polymerase chain reaction (PCR) and NGS. In the present case, NGS had a crucial role in identifying *P. micra* and guiding appropriate antimicrobial therapy. The timely identification and treatment of the pathogen were critical to the patient's recovery.

Despite initial treatment with broad-spectrum antibiotics, the patient's condition deteriorated, highlighting the limitations of empirical therapy for unusual pathogens. As shown in Table 1, treatment should be individualized to facilitate optimal treatment [2-4,12-16]. The shift to targeted therapy based on the chest CT and NGS findings, including the use of levornidazole for *P. micra,* and the reconsideration of ethambutol and pyrazinamide proved effective. This finding emphasizes the need for clinicians to consider anaerobic bacteria in similar clinical scenarios and the value of NGS in identifying elusive pathogens. In addition to NGS, other detection methods, including MALDI-TOF MS and 16S PCR, have previously been used to screen *P. micra* and other pathogens [6,18].

The presence of other bacteria, including *K. pneumoniae* and *C. albicans*, increased the diversity of pathogenic bacteria. *K. pneumoniae* is commonly identified in hospital-acquired pneumonia, particularly in elderly patients with multiple co-morbidities [19]. However, the persistence of *K. pneumoniae* despite potent antibacterial therapy suggests that *K. pneumoniae* might have been a colonizing organism rather than the primary pathogen. This finding showed the importance of comprehensive diagnostic evaluations to discriminate between colonization and infection. Some rare instances of pleural empyema caused by *P. micra,* including one patient with COVID-19 pneumonia and another patient with an *S. constellatus* co-infection*,* were previously recorded [2,4]. Both cases were confirmed by advanced diagnostic methods and successfully treated with tailored antimicrobial therapy [2,4]. These cases underscore the importance of considering atypical pathogens in severe pneumonia and the efficacy of NGS in identifying elusive bacterial infections [20-22].

The high ADA and LDH levels in the pleural fluid initially suggested the possibility of tuberculosis, resulting in the administration of anti-tuberculosis therapy. However, the absence of *M. tuberculosis* in cultures and the eventual clinical response to antibiotics targeting *P. micra* indicated that tuberculosis was not the primary clinical issue.

This case report had some limitations. First, the NGS of the hydrothorax specimen was not repeated after adding levornidazole to the treatment. Therefore, *P. micra* clearance was not confirmed. Second, the patient was treated with clopidogrel bisulfate and rifampicin without genetic testing to assess potential drug interactions with metabolic complications.

In conclusion, this case highlights the importance of considering anaerobic bacteria, such as *P. micra,* in

patients with pneumonia and empyema, especially patients with risk factors, such as diabetes and poor oral hygiene. Advanced diagnostic methods, such as NGS, are invaluable in identifying atypical pathogens and guiding effective treatment. Continuous monitoring and adjustment of the treatment strategy based on clinical improvement are essential for managing complex infections.

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Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of the institution. The patient in this case report has provided written informed consent for the study and publication of related data.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors contributions

Yuxiang Li: Manuscript preparation; Xia Wang: Data analysis; Lidi Zhang: Literature research; Yanxia Huang: Manuscript review; Yong'an Liu: Study design and manuscript editing.

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Conflict of interests

No conflict of interests is declared.

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