

Fusobacterium nucleatum-Induced Pyopneumothorax: A Rare but Serious Clinical Entity

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Abstract: *Fusobacterium nucleatum* (*F. nucleatum*) is a Gram-negative, anaerobic bacterium predominantly found in the oral cavity, gastrointestinal tract, and urogenital system. It accounts for less than 1% of anaerobic bacterial infections in clinical settings and can lead to a spectrum of severe infections. This report details the case of a 55-year-old male who presented with a one-month history of productive cough, acute right-sided chest pain, dyspnea, and fever. Initial examinations showed elevated inflammatory markers and a right-sided pleural effusion on chest CT. Despite empirical therapy, the patient's condition worsened, culminating in a diagnosis of right-sided encapsulated hydropneumothorax. *F. nucleatum* was isolated from the pleural fluid culture. Treatment with meropenem and linezolid led to gradual clinical improvement, and the patient recovered without complications during follow-up. Although rare, *F. nucleatum* pleural infections can progress swiftly and are frequently misdiagnosed, posing significant diagnostic challenges. Given their potential severity, such as in cases of pyopneumothorax, immediate drainage and targeted antibiotic treatment are imperative. Clinicians should exercise heightened vigilance in diagnosing and managing this severe and often overlooked infection.

Keywords: *Fusobacterium nucleatum*, pyopneumothorax, pleural effusion, case report

Introduction

Fusobacterium nucleatum (*F. nucleatum*) is a Gram-negative, obligate anaerobic bacterium commonly found in both healthy and diseased sites of the oral cavity, as well as other body sites, including the lungs, gastrointestinal tract, genitourinary system, and female reproductive organs.^{1,2} Despite its capacity to cause severe infections, *F. nucleatum* remains relatively rare in clinical practice, accounting for less than 1% of all anaerobic bacterial infections,³ with estimated occurrences ranging from 0.6 to 3.5 cases per million population.⁴ It has been implicated in various organ infections, such as liver abscesses, lung abscesses, empyema, and brain abscesses.^{5,6} Additionally, it has been linked to the reactivation of colorectal adenocarcinoma and inflammatory bowel disease.^{7,8}

Infections caused by *F. nucleatum* often result in severe sequelae. However, traditional culture-based diagnostic methods exhibit limited sensitivity and specificity, complicating the isolation and cultivation of anaerobic bacteria in clinical settings. Consequently, the true prevalence of anaerobic bacterial infections is often underestimated, further complicating their diagnosis and management.⁹ The present case report describes a previously healthy patient who initially presented with dyspnea, fever, and cough, and subsequently deteriorated, developing a right-sided encapsulated

hydropneumothorax caused by *F. nucleatum*. This rare and severe clinical manifestation highlights the importance of heightened clinical awareness regarding the potential for *F. nucleatum* to cause life-threatening pleural infections, even in immunocompetent individuals. This report highlights the rarity of this complication and provides critical insights into the diagnostic challenges and treatment strategies for managing *F. nucleatum* infections.

Case Presentation

On December 16, 2023, a 55-year-old male presented to the Emergency Department of the First Hospital of Jilin University with a month-long intermittent cough, chest pain, and mild shortness of breath. His symptoms had temporarily improved with medication, but the day before admission, he developed sudden, severe right-sided chest pain, dyspnea, and a fever of 37.8°C. He denied any significant medical history, including oral disease, prior dental procedures, chronic gastrointestinal disorders, urinary tract infections, or reproductive system diseases. Written informed consent was obtained from the patient, and the study was approved by the ethics committee of the First Hospital of Jilin University, China.

Upon admission, the patient's vital signs were as follows: temperature 37.8°C, pulse rate 86 beats per minute, respiratory rate 22 breaths per minute, and blood pressure 112/70 mmHg. Peripheral oxygen saturation was 92%, with supplemental oxygen administered via nasal cannula at 3 L/min. Physical examination revealed coarse breath sounds bilaterally, with no evidence of oral mucosal ulceration. Laboratory investigations showed elevated white blood cell count (WBC), neutrophil percentage (NE%), C-reactive protein (CRP), and procalcitonin (PCT), along with a slight reduction in lymphocyte percentage (LY%). Detailed laboratory results are provided in Table 1. On admission, chest computed tomography (CT) revealed bronchitis, diffuse bilateral lung inflammation, right-sided pleural thickening, and a small pleural effusion on the right (Figure 1A and B).

On the first day of hospitalization, sputum and blood cultures were obtained, but no pathogenic organisms were detected. HIV serology was negative, and there was no clinical evidence of immunodeficiency. However, due to resource limitations, analysis of CD3 and CD4/CD8 lymphocyte subsets could not be performed. The patient commenced empirical anti-infective therapy with intravenous cefepime (2 g twice daily), supplemental oxygen via nasal cannula, and physical cooling and antipyretic agents. By the following day, his temperature normalized, yet symptoms such as dyspnea, cough, and white sputum persisted. Treatment was augmented with nebulized budesonide (1 mg twice daily) and oral acetylcysteine (0.6 g twice daily), as well as intravenous moxifloxacin hydrochloride (0.4 g once daily). By day 7, the patient exhibited notable clinical improvement.

On day 8, however, the patient experienced a resurgence of fever with a peak temperature of 38.5°C, accompanied by worsening dyspnea, cough, and yellow sputum. Despite oxygen supplementation at 5 L/min, his peripheral oxygen saturation remained at 91%. Retesting for respiratory pathogens—including Immunoglobulin M (IgM) for *parainfluenza virus*, *adenovirus*, *Legionella*, *influenza A* and *B* viruses, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *respiratory syncytial virus*—and COVID-19 nucleic acid testing returned negative results. A subsequent chest CT indicated exacerbated bilateral pneumonia and a right-sided encapsulated hydropneumothorax, raising high suspicion for a bronchopleural fistula (Figure 1C and D). Chest ultrasound confirmed a right-sided encapsulated effusion with a maximum depth of 7 cm. Based on these findings, the antibiotic regimen was revised to include intravenous meropenem (1 g twice daily) and linezolid (600 mg daily). By day 9, inflammatory markers increased compared to previous levels (Table 1), prompting an adjustment in the linezolid dosage to 600 mg twice daily.

Table 1 Serial Lab Testing During Hospitalization

	Reference Interval	Day 1	Day 7	Day 9	Day 14	Day 16	Day 19	Day 23
Leukocyte ($10^9/L$)	3.50–9.50	19.76	12.89	11.25	10.12	10.09	7.49	7.77
Neutrophils ($10^9/L$)	1.80–6.30	17.69	10.74	9.16	6.87	6.32	4.46	4.9
Lymphocytes ($10^9/L$)	1.10–3.20	0.92	0.75	1.17	2.05	2.49	2.06	1.86
Red blood cells ($10^{12}/L$)	4.30–5.80	4.25	3.51	3.7	3.99	3.57	3.63	3.45
C-reactive protein (mg/L)	0.00–5.00	67.41		185.55			38.29	
Procalcitonin (ng/mL)	0.00–0.50	1.040		0.67			<0.05	

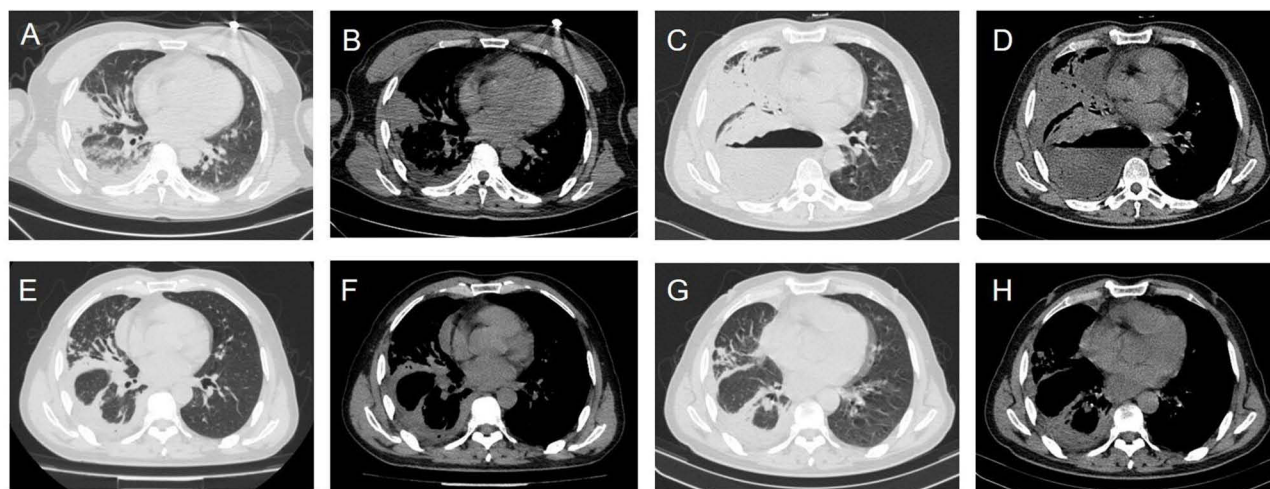


Figure 1 Chest CT imaging of a 55-year-old male with pyopneumothorax caused by *Fusobacterium nucleatum*: 1) Day 1: Pneumonia with right pleural thickening and pleural effusion (A and B); 2) Day 8: Worsening pneumonia with enlargement of right-sided encapsulated fluid pneumothorax (C and D); 3) Day 16: Improvement of right-sided liquid pneumothorax with reduced inflammation (E and F); 4) Day 24: Resolution following appropriate antibiotic treatment (G and H).

On day 11, a chest drainage tube was inserted, and approximately 500 mL of grey-green, foul-smelling pus was drained. Pleural fluid analysis showed: protein 15.64 g/L, red blood cell count $114,600 \times 10^6/L$, WBC $187,345 \times 10^6/L$, polymorphonuclear cells 76%, mononuclear cells 24%, glucose 0.59 mmol/L, lactate dehydrogenase 18,986 U/L, adenosine deaminase 191 U/L, carcinoembryonic antigen (CEA) 2.82 ng/mL, and a positive T-SPOT.TB result. However, smear, IgG, nucleic acid amplification, and Xpert tests for tuberculosis were all negative. On day 12, *F. nucleatum* was isolated from the pleural fluid culture, confirmed by VITEK MS (bioMérieux, Marcy l’Etoile, France; Figure 2). Due to the unavailability of drug susceptibility testing, we consulted with the pharmacy department and conducted a literature review. Based on current evidence, the combination of meropenem and linezolid offers sufficient coverage against this organism. Subsequently, the patient’s temperature returned to normal and remained stable (Figure 3). Notably, during the disease, the patient exhibited no abdominal pain, diarrhea, or symptoms of urinary tract infection, and routine urinalysis results were unremarkable.

Chest CT scans repeated on days 16 and 24 (Figure 1E–H) demonstrated gradual improvement in the patient’s condition. Notably, the size of the right-sided liquid pneumothorax diminished over time. Concurrently, the drainage fluid volume decreased progressively to 20 mL/day, transitioning from a grey-green, purulent appearance to a yellow, turbid one. Additionally, there was a significant decrease in WBC count, PCT, and CRP levels. As the patient’s condition improved, the antibiotic regimen was switched to ceftriaxone (2 g, once daily). By day 30, the drainage volume had decreased to less than 3 mL/day, and the fluid had become pale yellow and clear. The patient was asymptomatic by this point, exhibiting no fever, cough, or dyspnea, which facilitated the removal of the chest drainage tube and his eventual discharge. Two months following discharge, during a follow-up visit, no complications were reported (Figure 4).

Discussion

F. nucleatum is a rare, anaerobic Gram-negative bacterium predominantly found in the oral cavity, gastrointestinal tract, and urogenital system. *F. nucleatum* has been reported to be closely associated with several conditions and diseases. Recent studies suggested a potential role for *F. nucleatum* in developing various cancers,^{10,11} including laryngeal, esophageal, gastric, and colorectal cancers.^{12,13} By modulating the expression of surface receptors on respiratory epithelial cells, *F. nucleatum* can upregulate mucus secretion, facilitating the adhesion and invasion of respiratory pathogens, such as *Streptococcus pneumoniae*, thereby increasing susceptibility to infections like pneumonia. Additionally, *F. nucleatum* is capable of inducing apoptosis in alveolar epithelial cells and modulating host immune responses by releasing pro-inflammatory cytokines, both of which can exacerbate the progression of lung diseases and contribute to the maintenance or worsening of conditions like chronic obstructive pulmonary disease.^{14–17} Although its

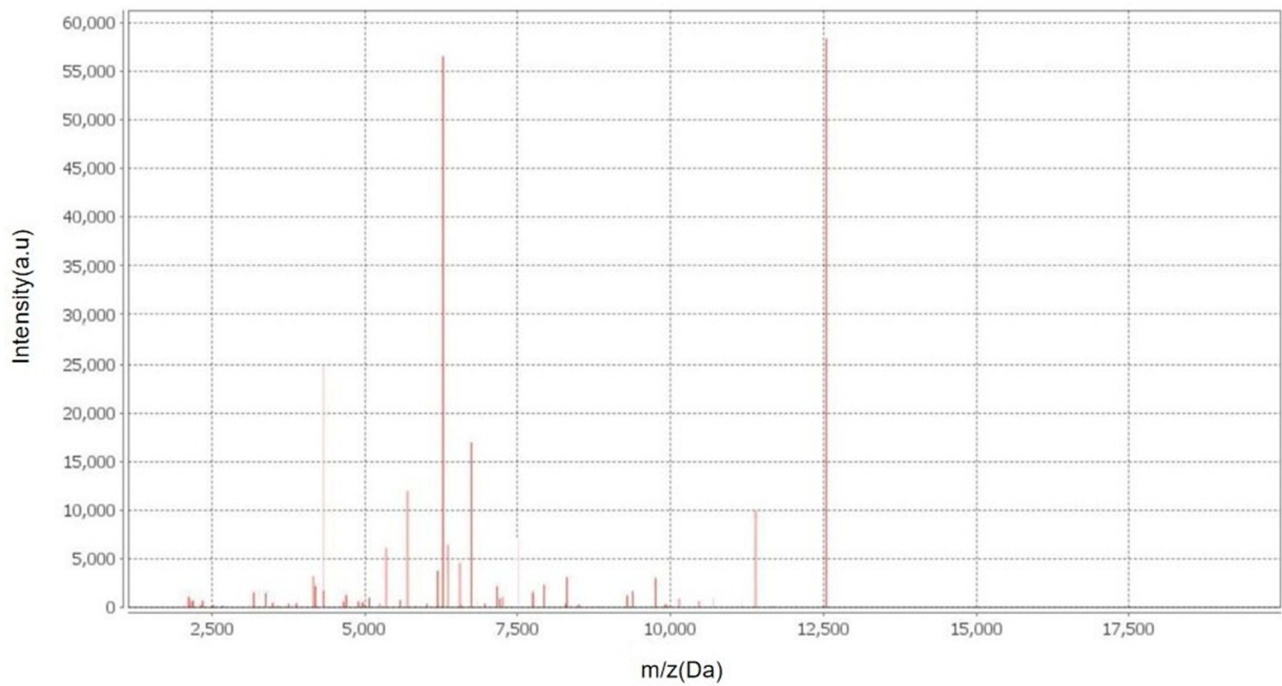


Figure 2 Identification of *Fusobacterium nucleatum* using VITEK Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry. The spectrum is consistent with *Fusobacterium nucleatum*, with a confidence level of 99.9%.

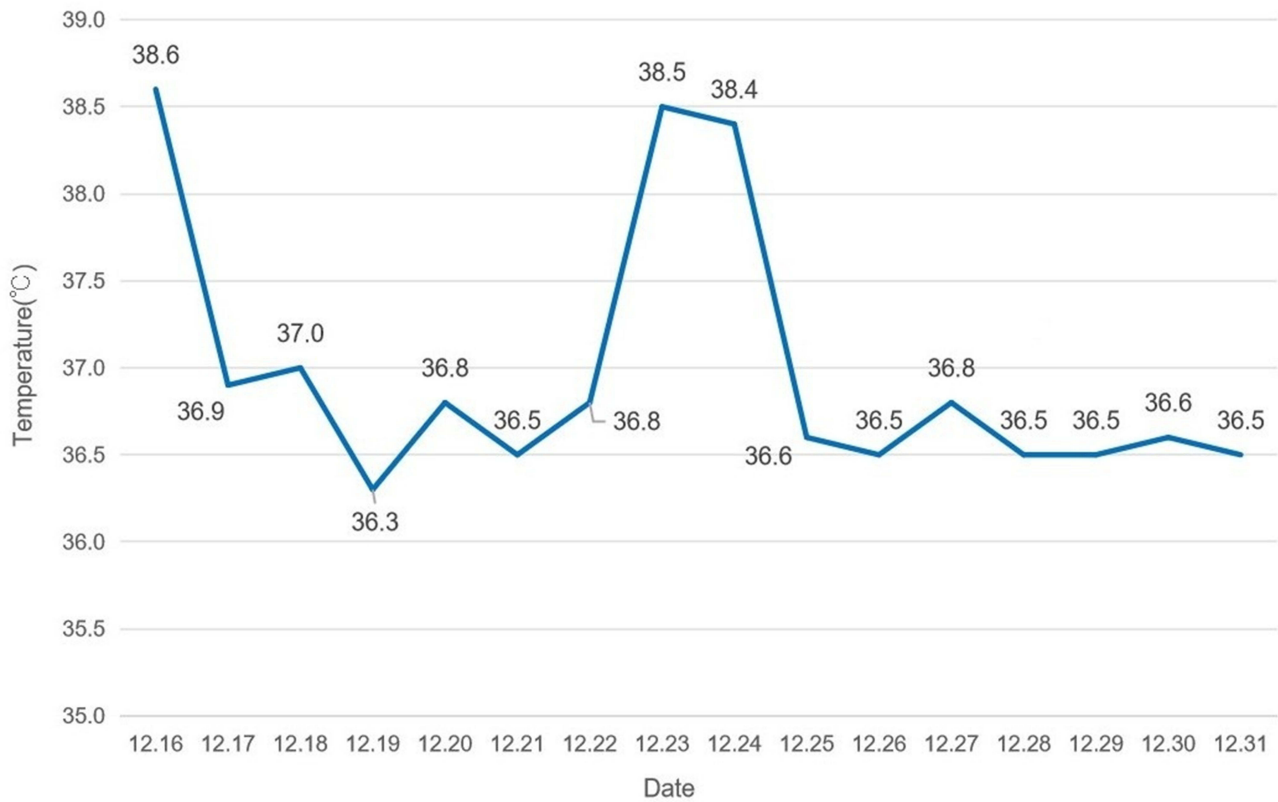


Figure 3 Trend of body temperature during hospitalization.

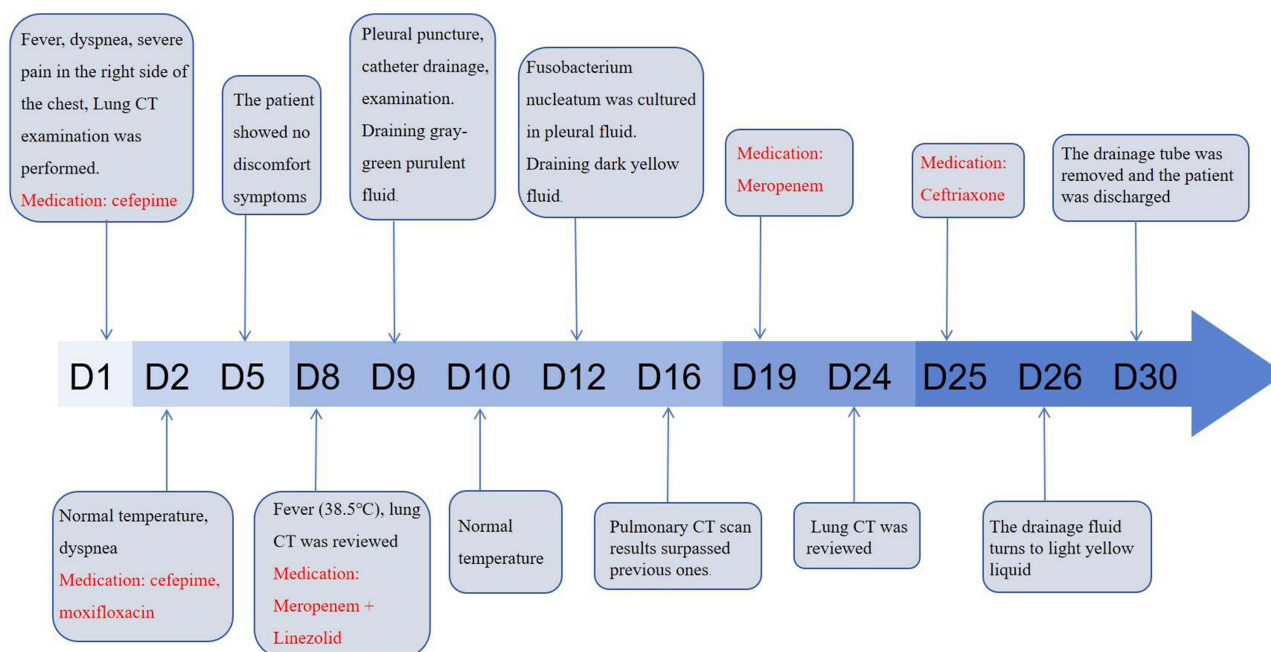


Figure 4 Timeline of disease progression and treatment from admission to discharge.

infection is relatively infrequent in clinical practice, accounting for less than 1% of all anaerobic infections, *F. nucleatum* can lead to severe, life-threatening conditions. These include endocarditis, lung infections, Lemierre's syndrome, and recurrent tonsillitis.^{18,19} In our case, we report the first known instance of a pyopneumothorax caused by *F. nucleatum*, emphasizing the bacterium's ability to cause severe pleural infections.

Pyopneumothorax is a rare but severe complication that can arise from various causes, including the direct spread of pleuropneumonia, rupture of a lung abscess, mediastinal infection, aspiration, trauma, pneumocystosis, and the development of bronchopleural or pleural fistulas.^{20–22} In this case, we suspect that the pyopneumothorax resulted from the direct extension of pneumonia and the formation of a bronchopleural fistula. While common risk factors for *F. nucleatum* infection include poor oral hygiene, advanced age, long-term steroid use, and the presence of other infections,^{23,24} this patient did not present with these typical predisposing conditions. This highlights the importance of vigilance for such infections, even in the absence of conventional risk factors.

Diagnosing *F. nucleatum* infections presents notable challenges, particularly when differential diagnoses such as tuberculosis manifest similar symptoms. In the case discussed, elevated pleural adenosine deaminase levels and a positive T-SPOT.TB test initially suggested tuberculosis. Pyopneumothorax, although rare, is a serious complication of pulmonary tuberculosis, typically resulting from the rupture of *Mycobacterium tuberculosis* lesions into the pleural cavity. This rupture can trigger a delayed hypersensitivity reaction, increasing capillary permeability and accumulating pleural fluid.¹ However, subsequent diagnostic efforts, including a negative pleural fluid Xpert test and the isolation of *F. nucleatum* from anaerobic culture, facilitated a definitive diagnosis of empyema due to *F. nucleatum*. Despite the initial concerns, anti-tuberculosis therapy was deemed unnecessary following negative tuberculosis tests, though the patient was advised to undergo follow-up assessments to monitor for any potential latent tuberculosis. In this case, due to the patient's financial constraints, further molecular testing was not available, which represents a limitation of this report. Modern molecular diagnostic techniques have been increasingly utilized for the detection of *Fusobacterium nucleatum*. For instance, Gomes et al compared two methods for detecting *F. nucleatum* in pulp infections and found that nested PCR identified a higher prevalence than culture-based approaches.²⁵ Additionally, Huang et al were the first to report the use of loop-mediated isothermal amplification to detect two target genes, *nusG* and *fadA*, in *F. nucleatum*.²⁶ This method allows for rapid, sensitive, and efficient identification of the organism and its virulence factors, offering promising diagnostic utility in clinical settings.

F. nucleatum's resistance to β -lactamases and fluoroquinolones complicates treatment. It exhibits weak sensitivity to erythromycin and penicillin²⁷ yet remains highly susceptible to carbapenem antibiotics, such as meropenem and imipenem, as well as metronidazole, clindamycin, and amoxicillin/clavulanate.²⁸ The recommended duration of antibiotic therapy typically ranges from 3 to 5 weeks, with a minimum period of 2 weeks.²⁹ In cases where bacteria are sequestered within abscesses or thrombi, an extended course of antibiotics for up to 8 weeks may be necessary.³⁰ In this patient, after 16 days of treatment with meropenem and linezolid, clinical improvement and a reduction in inflammatory markers were observed, confirming the effectiveness of this therapeutic regimen.

In addition, the management of *F. nucleatum* pyopneumothorax emphasizes the importance of a multidisciplinary approach. In this case, collaboration among specialists from microbiology, pharmacy, respiratory medicine, thoracic surgery, intensive care, and emergency medicine was critical to ensure optimal patient care. The treatment of pyopneumothorax typically requires both surgical and medical interventions. Our strategy involved a combination of chest tube drainage and targeted antibiotic therapy, which significantly reduced fluid volume and resolved the infection. The therapeutic strategy employed four essential components: (i) early chest tube insertion and regular drainage, facilitating fluid removal; (ii) supplemental oxygen and nutritional support, bolstering the patient's immunity; (iii) pathogen isolation, aiding in the selection of appropriate antibiotics; and (iv) continuous monitoring and timely antibiotic adjustment. For 30 days, the patient's clinical condition improved steadily, evidenced by a marked decrease in drainage volume and normalization of inflammatory markers. Two months following treatment, follow-up imaging confirmed the complete resolution of the infection, with no recurrence or other complications. It is important to acknowledge that this case report is constrained by the rarity of *F. nucleatum* infections and the absence of drug susceptibility testing for the isolated pathogen, which limits its generalizability.

Conclusion

Recent epidemiological studies on *F. nucleatum* infections are scarce, though reports of these infections are increasing. This case report highlights the rare but severe complication of pyopneumothorax caused by *F. nucleatum*, highlighting its potential to precipitate life-threatening infections. Despite the bacterium's low incidence in clinical settings, this case highlights the need for increased clinical vigilance and early diagnostic efforts in the face of atypical presentations of pleural infections. The successful management of this patient was achieved through a multidisciplinary approach that included appropriate antibiotic therapy, surgical drainage, and meticulous monitoring. Timely interventions, such as pathogen identification and targeted therapy, enhance patient outcomes, particularly in anaerobic infections with uncommon manifestations.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of The First Hospital of Jilin University. All procedures involving human participants were conducted per the ethical standards of the institutional and/or national research committee, as well as the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical principles (ethical number: 2025-190).

Consent for Publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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