Infection and Drug Resistance

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CASE REPORT

Metagenomic Next-Generation Sequencing Reveals *Porphyromonas gingivalis* in Geriatric Severe Pneumonia Complicated by Empyema: Case Report

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Background: Severe pneumonia with empyema in elderly patients presents diagnostic and therapeutic challenges. Traditional culture methods often fail to identify the causative pathogen, leading to delays in targeted treatment. Metagenomic next-generation sequencing (mNGS) has emerged as a powerful tool for detecting rare and fastidious pathogens.

Case Presentation: We report a 77-year-old male with a history of chronic smoking and alcohol consumption who presented with a two-month history of cough, sputum production, and progressive dyspnea. His condition rapidly deteriorated with high fever and respiratory failure. Initial antibiotic therapy was ineffective, and multiple cultures of blood, sputum, and pleural fluid were negative. However, mNGS of blood and pleural fluid identified *Porphyromonas gingivalis*, a well-known periodontal pathogen rarely associated with pulmonary infections. The patient's treatment was adjusted to include targeted anaerobic coverage (imipenem plus vancomycin) alongside chest tube drainage, leading to significant clinical improvement.

Conclusion: This case highlights the clinical utility of mNGS in diagnosing culture-negative pulmonary infections. *Porphyromonas gingivalis* should be considered a potential pathogen in patients with severe pneumonia and empyema, particularly in those with poor oral hygiene or periodontal disease.

Keywords: *Porphyromonas gingivalis*, metagenomic next-generation sequencing, severe pneumonia, empyema, case report

Introduction

Severe pneumonia and empyema in elderly patients pose significant diagnostic and therapeutic challenges.[1] Traditional microbial cultures have limitations, particularly for anaerobic or fastidious bacteria.[2] In such cases, metagenomic next-generation sequencing (mNGS) offers a precise diagnostic alternative.[3,4] *Porphyromonas gingivalis*, a major pathogen in periodontal disease, has been extensively studied in this context. However, recent research indicates that *P. gingivalis* is not limited to oral health issues and may be associated with various systemic diseases.[5] For instance, its outer membrane vesicles (OMVs) are thought to play a significant role in periodontitis development and may influence disease progression by modulating host cell apoptosis and inflammatory responses.[6] Furthermore, *P. gingivalis* can disrupt the balance of other microbial communities, leading to systemic health problems. Studies suggest that it may affect lung health through toxic factors it produces, although its specific mechanisms as a pulmonary infection pathogen remain unclear.[7] This case demonstrates the role of mNGS in detecting *P. gingivalis* as the primary pathogen in an elderly patient with pneumonia and empyema, leading to targeted therapy and clinical improvement.

Received: 29 May 2025
Accepted: 5 September 2025
Published: 9 September 2025

Case Presentation

A 77-year-old male, living alone, was admitted with complaints of progressive cough and dyspnea for two months, worsening in the past two days with high fever and altered mental status. The patient had no documented history of chronic cardiometabolic conditions such as hypertension or diabetes mellitus. Notably, he reported significant long-term behavioral risk factors, including a 30-year history of heavy tobacco use (20 cigarettes/day) and chronic alcohol consumption (approximately 500 mL/day). Over the past year prior to admission, he developed progressive constitutional symptoms characterized by unintentional weight loss of 5 kg accompanied by sustained appetite reduction, with no identifiable dietary or lifestyle modifications to account for these changes.

On admission, the patient presented with hemodynamic instability manifested by fever (39.2°C), tachycardia (HR 120 bpm), and tachypnea (RR 43 breaths/min), accompanied by hypoxemia (SpO_2 90% on 5 L/min supplemental oxygen) despite normotension (BP 111/73 mmHg). Physical examination revealed cachectic nutritional status and asymmetrical pulmonary findings: diminished breath sounds over the left lung field contrasted with bilateral diffuse crackles upon auscultation, suggesting possible consolidation with concurrent diffuse inflammatory involvement.

Initial laboratory investigations revealed marked systemic inflammation, including leukocytosis (WBC 25.63×10^9/L) with neutrophilic predominance (95%), accompanied by elevated acute-phase reactants (CRP 201 mg/L; procalcitonin 5.1 ng/mL). The patient also exhibited moderate respiratory acidosis ($PaCO_2$ 26.1 mmHg) with a decreased oxygenation index (202 mmHg), hypoalbuminemia (23.5 g/L), and mildly elevated liver enzymes (AST 70 U/L). Coagulation studies showed an increased D-dimer level (1500 μg/L), raising suspicion for concurrent thromboembolic events.

Thoracic computed tomography (CT) demonstrated left-sided pulmonary consolidation with ipsilateral multiloculated pleural effusion, right lung parenchymal infiltrates, and mediastinal lymphadenopathy (Figure 1). Electrocardiography revealed sinus tachycardia (heart rate 123 bpm) with QTc prolongation. Diagnostic thoracentesis yielded exudative pleural fluid showing neutrophilic pleocytosis (85%), markedly elevated lactate dehydrogenase (3640 U/L), and critically low glucose levels (0.05 mmol/L).

Standard microbial cultures of blood and pleural specimens remained negative for bacterial, fungal, and viral pathogens. On October 9, 2024, metagenomic next-generation sequencing (mNGS) was performed, rapidly identifying Porphyromonas gingivalis genomic sequences in both pleural fluid and paired blood samples within 48 hours of sample submission, establishing the microbiological diagnosis (Table 1). This enabled a targeted adjustment of antibiotic therapy on October 10, 2024, leading to significant clinical improvement by October 13, 2024 (Figure 2).

Empirical antimicrobial therapy with meropenem (1g q8h) and vancomycin (1g q12h) was initiated but yielded no clinical response. Following mNGS identification of Porphyromonas gingivalis, antimicrobial therapy was adjusted to imipenem/cilastatin (500mg q6h) combined with vancomycin (1g q12h) to optimize anaerobic coverage.

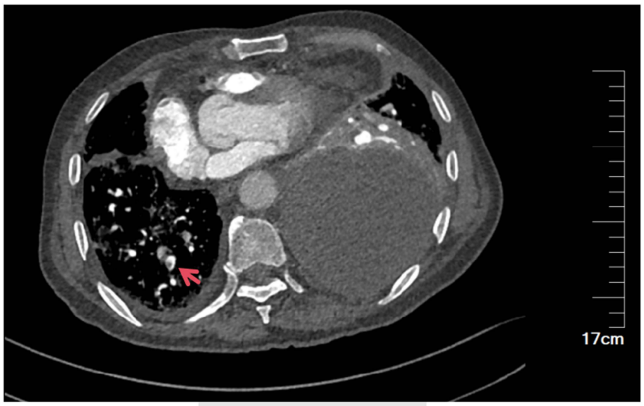

Figure 1 The enhanced CT of the patient's chest showed pulmonary embolism. Chest enhanced computed tomography (CT) suggests pulmonary embolism. The red arrow identifies a filling defect in the outer basal segment of the right lower lungobe, which is a typicaradiological finding of pulmonary embolism.

Table 1 Metagenomic List of Suspected Infectious Agents

Source	Genus	Sequence Reads	Species	Sequence Reads
Blood	Porphyromonas	59	*Porphyromonas gingivalis*	51
Hydrothorax	Porphyromonas	13	*Porphyromonas gingivalis*	11

The patient underwent ultrasound-guided chest tube drainage initially, but due to persistent loculated effusion and fibrinopurulent septations, video-assisted thoracoscopic surgery with pleural decortication was ultimately required. At 4-week follow-up, inflammatory markers normalized (CRP <5 mg/L, procalcitonin 0.1 ng/mL), with radiologic resolution of empyema and restoration of functional capacity (Figure 3).

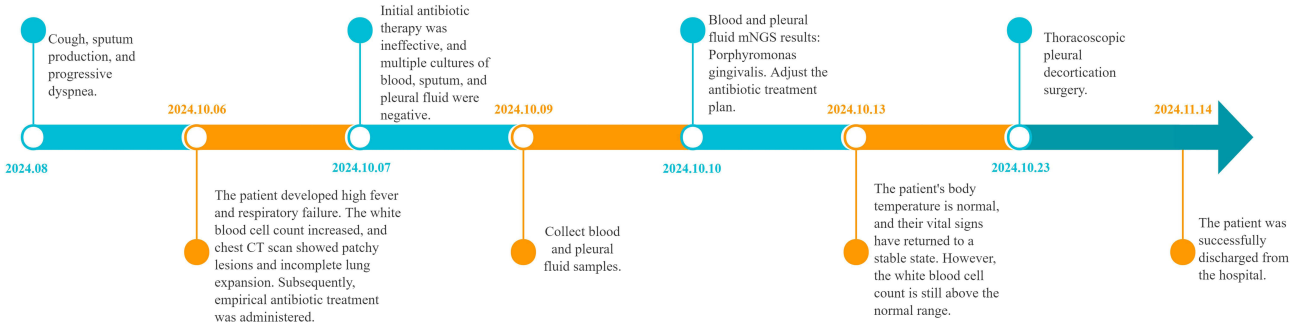

Figure 2 Timeline of Patient Management and Diagnostic Process.

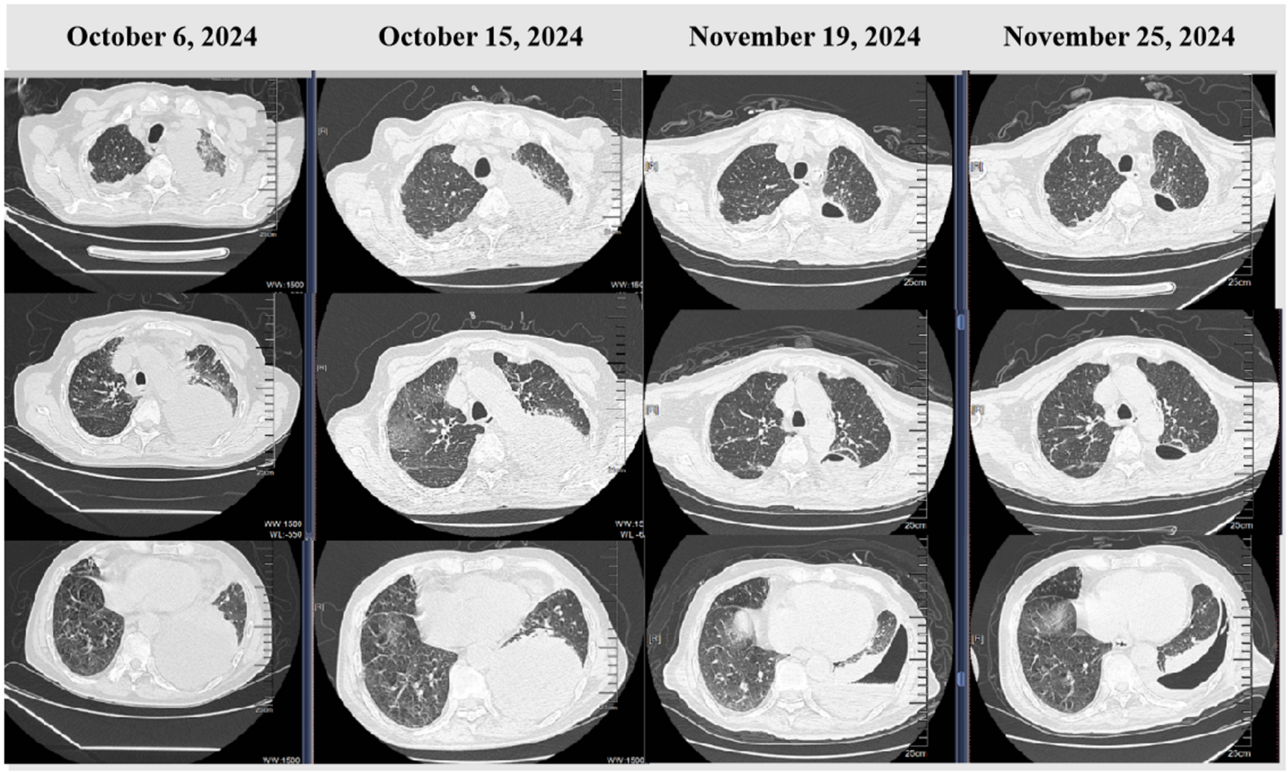

Figure 3 Chest imaging of the patient at different times.

https://doi.org/10.2147/IDR.S543666

A timeline illustrating the patient's clinical course from symptom onset on August, 2024, to discharge on November 14, 2024, is presented in Figure 2, highlighting the critical role of metagenomic next-generation sequencing (mNGS) in identifying Porphyromonas gingivalis and guiding effective treatment.

Discussion

The advent of metagenomic next-generation sequencing (mNGS) has revolutionized pathogen detection in complex infections where traditional culture-based methods frequently fail. Compared with conventional cultures, mNGS demonstrates superior sensitivity (88.5% vs 69.2% in osteoarticular infections; 94.49% detection rate in culture-negative pulmonary infections),[8,9] particularly in antibiotic-pretreated patients. This culture-independent approach not only expands the detectable pathogen spectrum but also enables precise therapeutic adjustments. Clinical studies report that mNGS-guided interventions modified treatment strategies in 27.4% of cases through antibiotic escalation, de-escalation, or targeted regimens.[10] A notable example includes the identification of Porphyromonas gingivalis (*P. gingivalis*) in a culture-negative pulmonary infection, which directly informed pathogen-specific therapy.[11]

Emerging evidence positions *P. gingivalis*, a keystone periodontal pathogen, as a systemic threat beyond oral cavities. Its virulence arsenal—including gingipain proteases that degrade epithelial tight junction proteins (JAM1, CXADR)—facilitates hematogenous dissemination and barrier disruption.[12,13] In elderly populations with immunosenescence and impaired swallowing reflexes, *P. gingivalis* aspiration or systemic spread may trigger severe pulmonary complications such as pyopneumothorax and bronchopleural fistula.[14] The bacterium further exacerbates respiratory defenses by dysregulating airway mucin secretion via MUC5AC modulation.[15] Alarmingly, traditional culture methods systematically underestimate *P. gingivalis* due to its anaerobic requirements, a diagnostic void effectively bridged by mNGS.[16,17]

This paradigm shift underscores periodontal disease as a modifiable risk factor for pulmonary infections. A seminal case involving a 49-year-old male with periodontitis-associated pyopneumothorax highlights the clinical imperative: mNGS detected *P. gingivalis* in bronchoalveolar lavage fluid, enabling targeted carbapenem/metronidazole therapy after culture failure.[11] Such findings advocate for integrating oral health management into pulmonary infection prevention strategies, particularly in geriatric care.

The successful identification of Porphyromonas gingivalis using metagenomic next-generation sequencing (mNGS) in this case underscores its critical role as a powerful diagnostic tool for complex infectious diseases, particularly when conventional methods fail. Beyond severe pneumonia, mNGS offers broad applicability in detecting pathogens across various infectious conditions, enhancing diagnostic precision and enabling targeted therapies. This case highlights the potential of mNGS to strengthen laboratory capacity by providing rapid and comprehensive pathogen identification, which is essential for improving clinical outcomes in challenging cases, such as geriatric infections with atypical presentations. However, the limited availability of mNGS in many healthcare settings underscores the need for expanded access and infrastructure development to fully realize its clinical and research potential.

Therapeutic optimization requires dual considerations: anaerobic coverage and rising antimicrobial resistance. Carbapenems (eg, meropenem) and nitroimidazoles (eg, metronidazole) remain first-line options, with amoxicillin/metronidazole combinations and moxifloxacin showing efficacy in severe cases.[10] However, escalating clindamycin and amoxicillin resistance necessitates routine susceptibility testing to combat antimicrobial misuse. For complicated empyema or bronchopleural fistulas, early thoracic drainage coupled with surgical interventions (eg, thoracoscopic debridement) significantly improves outcomes.[11,18]

This case provides critical validation of mNGS in resolving diagnostically challenging pulmonary infections refractory to conventional methodologies. Our findings collectively emphasize two clinical imperatives: *P. gingivalis* warrants particular consideration in culture-negative pneumonia/empyema among patients with periodontal comorbidities, and the oral-lung pathogenic axis demands heightened vigilance given the potential for commensal oral flora to instigate fulminant systemic infections. To address current technological constraints—including cost barriers, bioinformatic interpretative challenges, and standardization gaps—a three-pronged strategic development is proposed: accelerated sequencing workflows, machine learning-enhanced diagnostic specificity, and evidence-based deployment frameworks. Such advancements will be pivotal in democratizing mNGS applications while maintaining antimicrobial stewardship in resource-variable clinical environments.

Data Sharing Statement

The original contributions of this study are all incorporated into the article. Should there be any further questions, please feel free to contact the corresponding author.

Ethics Approval and Consent to Participate

The publication of case details requires institutional approval. This case report was approved by the Institutional Review Board of Aerospace Center Hospital (Approval No. 20200522-CHDRP-02). Informed consent for publication of the case details was obtained from the patient.

Consent for Publication

Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article.

Acknowledgments

Thanks to DIAN Diagnostics for the technical support in detection technical support.

Author Contributions

Na Guo and Guannan Ma are co-first authors who contributed equally to this work. 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.

Funding

This study was supported by the scientific research fund of aerospace center hospital (No. YN202523).

Disclosure

The authors declare that there is no conflict of interest.

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