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CASE REPORT

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Lung abscess caused by the anaerobic pathogen *Tannerella forsythia*

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Abstract

Odontogenic infections can spread to the respiratory tract. Despite the known role of *Tannerella forsythia* as the primary pathogen in periodontitis, the association between *T. forsythia* infection and risk of pneumonia or lung abscess remains unknown. In this report, we present a case of lung abscess caused by *T. forsythia* infection. The pathogen was detected by metagenomic next-generation sequencing (mNGS) in the bronchoalveolar lavage fluid of the patient. The clinical characteristics and possible mechanisms of the infection are discussed. *T. forsythia* is a conditional pathogen that can cause lung abscess in the presence of helper bacteria and reduced host immune status. The course of treatment should be personalized and might be longer than 3 months.

KEYWORDS
lung abscess, metagenomic next-generation sequencing, pneumonia, *Tannerella forsythia*

INTRODUCTION

Early and accurate identification the microbial pathogens is crucial for the treatment of lung abscess. *Tannerella forsythia*, a gram-negative member of the *Cytophaga-Bacteroides* family, is frequently associated with periodontal infection. In this report we present a rare case of lung abscess caused by *T. forsythia* infection, along with the clinical characteristics. Our findings highlight very arduous of treatment and the importance of using new molecular methods, such as metagenomic next-generation sequencing (mNGS), for the detection of *T. forsythia* infection.

CASE REPORT

A 60-year-old male was diagnosed with coronavirus disease (COVID-19) 3 months ago. He had a fever for 5 days and then developed persistent cough with phlegm for approximately 1 month. Following treatment, the patient had occasional cough but did not report fever, haemoptysis, phlegm, chest tightness, night sweats, fatigue, muscle and joint pain, rash, or any other symptom. The patient visited the hospital for re-examination on the end of May, and the physical examination was unremarkable.

Chest computed tomography (CT): Chest CT revealed a patchy, dense shadow approximately 20 × 15 mm in size with uneven density and clear boundaries in the upper lobe of the left lung with a CT value of 1–17 HU. An obvious circular enhancement and patchy fuzzy shadows were visualized around the lesion. Thus, the CT was suggestive of an infectious lesion in the upper lobe of the left lung with abscess formation (Figure 1A,B).

Laboratory investigations: White blood cell count: 8.6×10^9/L, neutrophils: 62.6%, lymphocytes: 25.6%, monocytes: 10.2%↑, eosinophils: 1.3%, basophils: 0.3%, haemoglobin: 140 g/L, platelet count: 194×10^9/L; C-reactive protein: <0.50 mg/L; serum amyloid A (SAA): 9.71 mg/L; calcitonin:

XiaYi Miao and Wei Yang have contributed equally to the study.

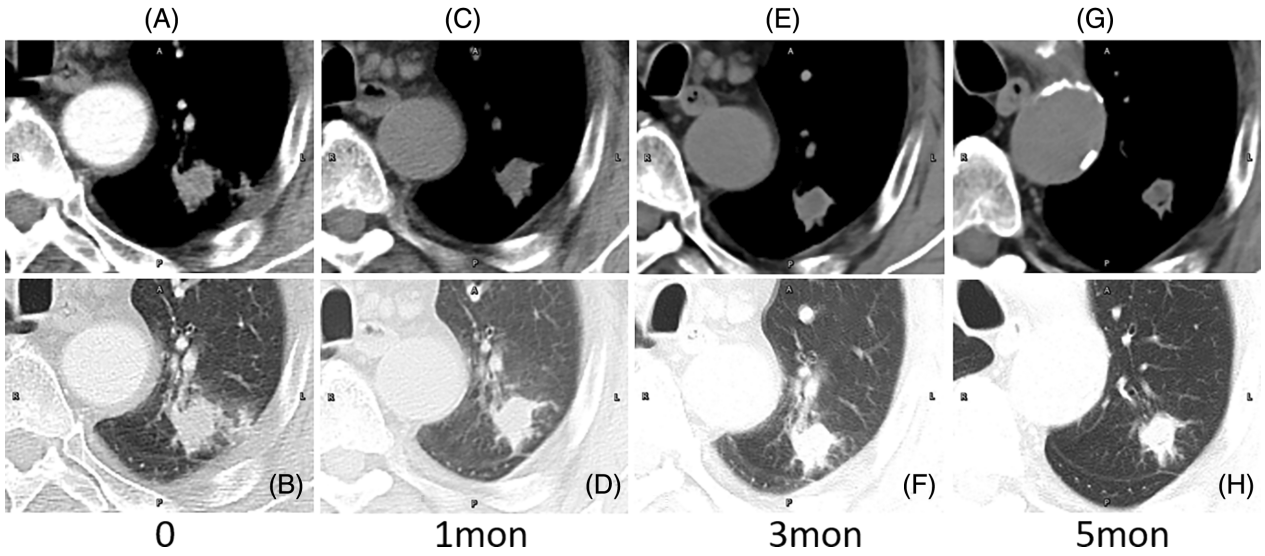

FIGURE 1 Computed tomography (CT) chest showing abscess within the posterolateral left lower lobe with surrounding consolidation performed on the end of May (A, B), and follow-up CTs performed showing reduction of the abscess (C–H).

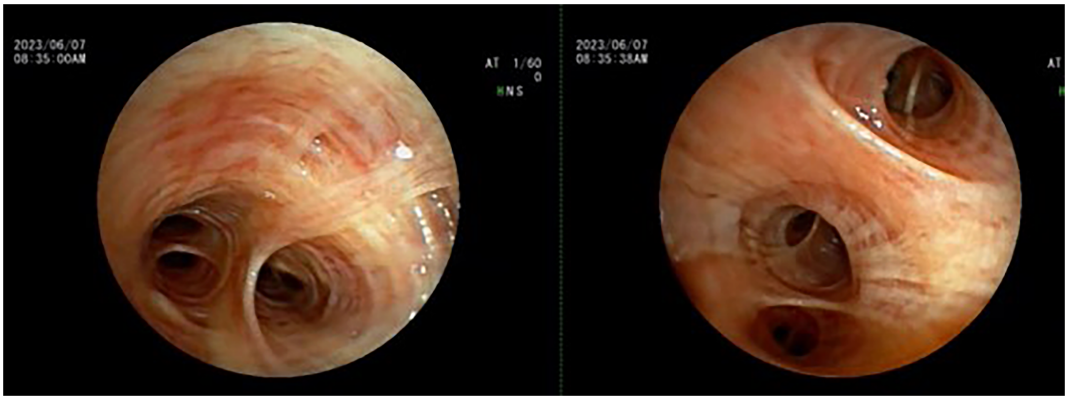

FIGURE 2 Electronic bronchoscopy of left bronchus. Ursu RG, Iancu LS, Porumb-Andrese E, Damian C, Cobzaru RG, Nichitean G.

0.02 ng/mL; erythrocyte sedimentation rate: 8; total protein: 75 g/L, albumin: 42 g/L. Serum pathogen tests were negative for immunoglobulin M antibodies against nine respiratory infection pathogens, including *Legionella pneumoniae*, *Mycoplasma pneumoniae*, Rickettsia, *Chlamydia pneumoniae*, adenovirus, respiratory syncytial virus, influenza A, influenza B, and parainfluenza viruses. Aspergillus galactomannan: <0.1000 ng/mL, G-lipopolysaccharide: <5.00 pg/mL, 1–3-β-D glucan: <10.00 pg/mL; interferon-γ release assay for *Mycobacterium tuberculosis* and anti-human immune defective virus antibody were negative. Immune function: peripheral blood FACS was normal. Immunoglobulin A: 3.38 g/L, immunoglobulin M: 0.95 g/L, immunoglobulin G: 16.5 g/L↑, complement C3:1.05 g/L, complement C4: 0.26 g/L, anti-haemolytic streptococcus O: 37.5 IU/mL, rheumatoid factor: 16.5 IU/mL↑, complement C1q: 158.6 mg/L↓.The full set of autoantibodies tested negative. All tumour-related antigen values were negative. Sputum examination: Routine bacterial culture of sputum showed normal bacterial growth. Tests for aerobic bacteria and anti-acid bacillus cultures of sputum were negative. No fungal growth or spore mycelia were detected.

Electronic bronchoscopy revealed that the left bronchial tissue was unobstructed, the protuberance was sharp, and the bronchial mucosa was congested with oedema and a small amount of white purulent secretion (Figure 2). A bacterial or fungal culture of the bronchoalveolar lavage fluid (BALF), a routine aerobic bacterial culture, was negative. Metagenomic next-generation sequencing (mNGS) of the BALF revealed the presence of *T. forsythia* (Figure 3).

Consultation of the stomatology department led to the diagnosis of severe periodontitis.

The patient was diagnosed with a *T. forsythia* pulmonary abscess and was prescribed cefoperazone sodium, sulbactam sodium, and metronidazole for 7 days, followed by 3 months metronidazole treatment. The patient refused to receive any drug later. A CT performed after 1 month showed partial absorption of the left lung abscess and the patchy fuzzy shadows around the lesion (Figure 1C,D).

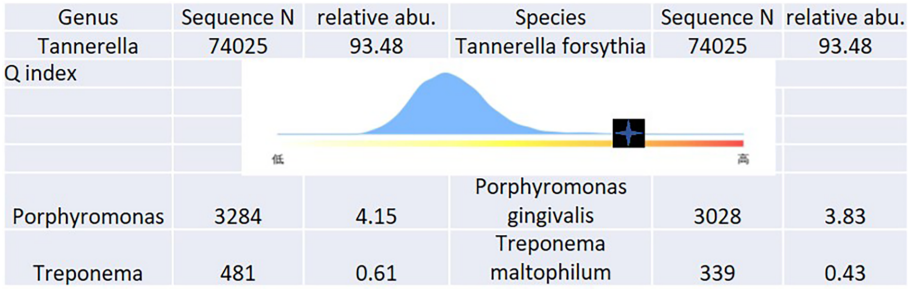

FIGURE 3 Quantitative metagenomics of bronchoalveolar lavage fluid.

Follow-up has been carried out by CT at 3 and 5 months with reduced shadow (Figure 1E–H) and the patient experienced no symptom during this period. The patient was diagnosed with abscess absorption 3 months later.

DISCUSSION

T. forsythia is an anaerobic gram-negative pathogenic bacteria belonging to the *Cytophaga-Bacteroides* family, and was initially identified in the subgingival periodontal pocket.[1] The characteristics and virulence of *T. forsythia* have been studied and reviewed previously.[2,3] Most clinical reports have focused on the role of *T. forsythia* in periodontitis.[4,5] However, reports on its role in infection of the lower respiratory tract and other tissues is limited. This bacteria was determined as the pathogen for these reasons: (1) The patient had suffered from severe periodontitis; (2) Though only one BALF sample detected the bacteria by mNGS, the mNGS detection report usually can be considered reliable because of its high specificity; (3) The patient had no fever, cough, expectoration, that is, the symptoms that would be induced by infection of common pathogens for abscess such as staphylococcus aureus and anaerobic bacteria; (4) The therapy was effective. To the best of our knowledge, this is the first report on pneumonia and lung abscess caused by *T. forsythia*.

In the present case report, the patient presented with the following clinical characteristics: (1) Infection in the lung tissue may be occult as there were few symptoms and signs. (2) None of the laboratory tests, particularly the ones for inflammatory markers, were positive. (3) Chest CT revealed a single distal lung abscess with exudative satellite lesions. (4) Pathogen was detected by next-generation sequencing assay (NGS) in BALF, but not in routine culture. (5) The patients also presented with severe periodontitis. (6) The patient had COVID-19 pneumonia 3 months prior to current evaluation. (7) The treatment is very arduous as the shadow was still there after 3 months treatment though the abscess was reduced and complete absorption of the patchy fuzzy shadows around the lesion occurred in 5 months.

The following findings were noted on chest CT (Figure 1): (1) Upper lung affected. (2) Involvement of the peripheral lung tissue. (3) Lesions showed signs of liquefaction necrosis. (4) The lesion had no cavity in first time but cavity occurred after 5 months, which is quite different from the abscess caused by staphylococcus aureus or other gram-pyogenic bacteria.

The anti-anaerobic gram-negative bacterial treatment regimen was effective, but the course of treatment had to be maintained for a relatively long period because although the size of abscess was reduced after 3 months, but it had not disappeared. Still, the surrounding infiltration was left over. Although the outcome in the absence of treatment remains unknown, the presence of exudative lesions around the abscess suggests that the infection could have spread to more lung tissues. The final diagnosis was confirmed by the curative effect visualized on CT.

The differential diagnosis should include lung cancer, tuberculosis, and fungal infection. However, there were no clinical symptoms, signs, or laboratory data to support any of these in the present case. A bronchoscopic biopsy or percutaneous lung puncture may also be considered.

Except mNGS, none of the important laboratory tests, including BALF culture and inflammatory marker assay data supported pneumonia and lung abscess. Routine pathogen examinations are often ineffective in such situations. The application of NGS, including mNGS, in clinical microbiological testing provides an unbiased approach for the detection of pathogens. Negative data for the inflammatory markers indicated that the lung abscess caused by *T. forsythia* infection had not led to systemic inflammation.

Periodontal infection may be an important risk factor for lower respiratory tract infections caused by the spread of pathogens. There is considerable evidence in support of the oral origin of pathogens in samples of pulmonary abscesses and pyothorax in patients.[6] Three gram-negative species, collectively known as the red complex (*Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*), are strongly associated with periodontitis.[7] As a common causative pathogen of periodontitis, *T. forsythia* may be a frequent cause of pneumonia, especially aspiration pneumonia. In fact, several reports have documented the presence of *T. forsythia* in the respiratory tract. Porto et al. assessed the colonization of periodontal pathogens in endotracheal tubes (ET) in the ICU by PCR.[8] Dentate patients showed no correlation between oral and ET bacterial levels, whereas edentulous patients showed positive correlations between oral

and ET levels of *T. forsythia*. However, among dentates, there was no correlation between the clinical parameters and ET bacterial levels. A strong association has also been reported between periodontitis and chronic obstructive pulmonary disease (COPD).[9] A previous study used a metagenomic approach based on bacterial 16S rDNA sequences to compare the distribution of species present in the dental plaque and lungs of AE-COPD patients.[10] In the samples from 53 patients, *T. forsythia* was found to simultaneously colonize the paired sample in one patient. Another study evaluated the levels of periodontal pathogenic bacteria in subglottic samples from intubated and mechanically ventilated patients, and the effect of oral decontamination with chlorhexidine (CHX) on the subglottic levels of these microorganisms.[11] Three hours after orotracheal intubation, the subglottic contents were collected. The control and CHX groups showed no difference in subglottic detection rates and *T. forsythia* abundance. Moreover, the data indicated that periodontal health had no impact on the subglottic levels of *T. forsythia*. These studies indicate the potentially pathogenic role of *T. forsythia* in lower respiratory tract infections.

T. forsythia is a common periodontal pathogen. However, its causative role in pneumonia and lung abscesses remains unknown. This may be attributed to the limitations of the detection technologies used, and to its unique growth characteristics. *T. forsythia* is a nutritionally fastidious bacteria. It grows slowly on blood agar plates when co-streaked with *Fusobacterium nucleatum* as a helper bacterium. Wyss C. showed that the bacteria depends on an exogenous supply of the cell wall sugar N-acetylmuramic acid (MurNAc) for peptidoglycan synthesis, which is essential for the growth and proliferation of the organism.[12] Further studies have confirmed that *T. forsythia* depends on exogenous MurNAc and muropeptide fragments, which are likely made available to the bacterium by cohabiting bacteria, such as oral streptococci and Actinomyces spp., in the oral cavity via specific surface molecule interactions.[13] This may be the main reason for rare infections of the lower respiratory tract by *T. forsythia*. *T. forsythia* pneumonia requires helpers to supply MurNAc and muropeptide fragments. In the case presented in this report, another periodontal pathogen, *porphyromonas*, may have been the source of these molecules.

In addition to its unique growth characteristics and virulence,[14,15] strong evidence suggests that being a periodontal pathogen, *T. forsythia* requires to be present in sufficient numbers and requires a susceptible host.[16,17] Thus, the host immune status is critical for *T. forsythia* to cause pneumonia or lung abscesses. The patient in the present case report had COVID-19, and later developed *T. forsythia* pneumonia and lung abscess. COVID-19 has been shown to seriously damage the host immune system.[18] However, the underlying mechanisms remain unknown.

Local pulmonary infections are routinely diagnosed using sputum culture, bronchoscopy, CT, or ultrasound-guided percutaneous lung biopsy to identify the pathogen. In recent years, mNGS has been applied in clinical practice for the detection of pathogen in a variety of clinical specimens, such as blood and BALF. mNGS offers significant advantages in the diagnosis of mixed infections and infections caused by difficult-to-culture bacteria.[19] Lung abscesses often develop because of the aspiration of oropharyngeal secretions, and the common causative pathogens include obligate and facultative anaerobic bacteria. The detection of obligate anaerobes requires anaerobic culture conditions and an appropriate culture duration. Compared with conventional methods, molecular diagnostic methods offer several advantages in the identification of pathogens in lung abscesses. Using a new method that incorporates quantitative PCR and next-generation sequencing, Katsuda et al.[6] presented direct genetic evidence that some of the bacteria in pulmonary abscesses and pyothorax are derived from the oral flora. Su et al.[20] evaluated the value of mNGS in lung tissue specimens obtained by CT-guided biopsy and found that the sensitivity of mNGS was 53.9% versus 42.1% for conventional examinations, whereas the specificity was 56.7% versus 96.7%. Mukae et al.[21] investigated the pathogens in lung abscesses using 59 BALF samples and found 94.9% positivity by PCR analysis versus 66.1% by conventional culture. In this report, we used BALF sample for mNGS. Although we did not perform conventional culture to confirm *T. forsythia* infection, the positive response to metronidazole treatment supported the diagnosis of the pathogen.

AUTHOR CONTRIBUTIONS

Sample collection: XY. M. and W. Y. *Case follow-up*: SQ. W. and JH. T. *Manuscript writing*: XY. M. *Supervision*: XM. L. and T. C.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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REFERENCES

1. Tanner AC, Izard J. Tannerella forsythia, a periodontal pathogen entering the genomic era. Periodontol 2000. 2000;2006(42):88–113.

2. Miralda I, Uriarte SM. Periodontal pathogens' strategies disarm neutrophils to promote dysregulated inflammation. Mol Oral Microbiol. 2021;36(2):103–20.
3. Bloch S, Tomek MB, Friedrich V, Messner P, Schäffer C. Nonulosonic acids contribute to the pathogenicity of the oral bacterium *Tannerella forsythia*. Interface Focus. 2019;9(2):20180064.
4. Pinto KP, Barbosa AFA, Silva E, Santos APP, Sassone LM. What is the microbial profile in persistent endodontic infections? A scoping review. J Endod. 2023;49(7):786–98.
5. Ursu RG, Iancu LS, Porumb-Andrese E, Damian C, Cobzaru RG, Nichitean G, et al. Host mRNA analysis of periodontal disease patients positive for Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans and Tannerella forsythia. Int J Mol Sci. 2022;23(17):9915.
6. Katsuda R, Inubushi J, Tobata H, Eguchi T, Terada K, Kagami R, et al. Genetic homology between bacteria isolated from pulmonary abscesses or pyothorax and bacteria from the Oral cavity. Microbiol Spectr. 2022;10(1):e0097421.
7. Jenkinson HF, Lamont RJ. Oral microbial communities in sickness and in health. Trends Microbiol. 2005;13(12):589–95.
8. Porto AN, Cortelli SC, Borges AH, Matos FZ, Aquino DR, Miranda TB, et al. Oral and endotracheal tubes colonization by periodontal bacteria: a case-control ICU study. Eur J Clin Microbiol Infect Dis. 2016;35(3):343–51.
9. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P, et al. Global initiative for chronic obstructive lung disease 2023 report: GOLD executive summary. Respirology. 2023;28(4):316–38.
10. Tan L, Wang H, Li C, Pan Y. 16S rDNA-based metagenomic analysis of dental plaque and lung bacteria in patients with severe acute exacerbations of chronic obstructive pulmonary disease. J Periodontal Res. 2014;49(6):760–9.
11. Morillo CMR, Saraiva L, Romito GA, Pannuti CM, Oliveira HP, Peres M, et al. Periodontopathogenic bacteria in subglottic samples from patients undergoing elective intubation for general anesthesia: a pilot study. J Periodontol. 2021;92(8):e94–e102.
12. Wyss C. Dependence of proliferation of Bacteroides forsythus on exogenous N-acetylmuramic acid. Infect Immun. 1989;57(6):1757–9.
13. Hottmann I, Borisova M, Schäffer C, Mayer C. Peptidoglycan salvage enables the periodontal pathogen Tannerella forsythia to survive within the Oral microbial community. Microb Physiol. 2021;31(2):123–34.
14. Sharma A. Virulence mechanisms of Tannerella forsythia. Periodontol 2000 2000. 2010;54(1):106–16.
15. Sharma A. Persistence of Tannerella forsythia and fusobacterium nucleatum in dental plaque: a strategic alliance. Curr Oral Health Rep. 2020;7(1):22–8.
16. Consensus report. Periodontal diseases: pathogenesis and microbial factors. Ann Periodontol. 1996;1(1):926–32.
17. Silva N, Abusleme L, Bravo D, Dutzan N, Garcia-Sesnich J, Vernal R, et al. Host response mechanisms in periodontal diseases. J Appl Oral Sci. 2015;23(3):329–55.
18. Torki E, Gharezade A, Doroudchi M, Sheikhi S, Mansury D, Sullman MJM, et al. The kinetics of inhibitory immune checkpoints during and post-COVID-19: the knowns and unknowns. Clin Exp Med. 2023;23:3299–319.
19. Yatera K, Noguchi S, Mukae H. Perspective on the clone library method for infectious diseases. Respir Investig. 2021;59(6):741–7.
20. Su SS, Chen XB, Zhou LP, Lin PC, Chen JJ, Chen CS, et al. Diagnostic performance of the metagenomic next-generation sequencing in lung biopsy tissues in patients suspected of having a local pulmonary infection. BMC Pulm Med. 2022;22(1):112.
21. Mukae H, Noguchi S, Naito K, Kawanami T, Yamasaki K, Fukuda K, et al. The importance of obligate anaerobes and the *Streptococcus anginosus* Group in Pulmonary Abscess: a clone library analysis using bronchoalveolar lavage fluid. Respiration. 2016;92(2):80–9.

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