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Case presentation of *Campylobacter rectus* leading to pneumonia and literature review

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ABSTRACT

Pneumonia caused by *Campylobacter rectus* is very rare. Herein, we describe the treatment course and experiences of a patient with pneumonia caused by *Campylobacter rectus*. A 64-year-old woman with intermittent hemoptysis and part lung necrosis indicated by radiography was admitted to our hospital on March 15, 2021. After admission, a CT (Computer tomography)-guided percutaneous lung biopsy was identified as *Campylobacter rectus* positive by bacterial culture and metagenomic sequencing. The hemoptysis resolved, and the lesions in the right lower lung were gradually absorbed after treatment with anti-*Campylobacter rectus* drugs. In cases of pneumonia which unresolved by initial therapy and associated with more severe oral hygiene problems, the possibility of infection with oral pathogens (eg, *Campylobacter rectus*) should be considered. This case suggests that bacterial culture and metagenomic sequencing of the diseased tissue, particularly anaerobic culture, helps to clarify the etiological diagnosis.

1. Background

Campylobacter rectus in the pharynx oralis usually causes periodontal problems [1], and under certain conditions, it may also lead to an intracranial abscess, thrombo venous sinusitis, empyema, etc. [2], but it rarely causes pneumonia. A pneumonia patient with intermittent coughing, bloody sputum and necrotic lesions indicated by radiography was admitted to the hospital in March 2021. *Campylobacter rectus* was confirmed in the lung tissue by bacterial culture and Metagenomic next-generation sequencing. The hemoptysis resolved, and the lesions gradually reduced after antibiotic treatment.

2. Case report

A 64-year-old woman was admitted to the hospital on March 15, 2021 with “hemoptysis for one week”. One week ago, she developed hemoptysis with no obvious cause, mainly fresh blood, 3–5 times/day, a little yellow pus sputum, no fever, no hot flashes and night sweats, no dyspnea, no chest pain. The chest CT results showed severe inflammation in the right lower lobe (Fig. 1A). For further treatment, she was admitted to our hospital. The patient first visited the emergency department on January 6, 2021, complaining of a paroxysmal cough, dry cough without sputum after catching a cold. There was no fever, headache, stuffy nose, sore

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throat, nausea or vomiting, abdominal pain, diarrhea, or other symptoms. Routine blood tests revealed a white blood cell count of 8.8 $\times 10^9$/L, neutrophil count of 6.7 $\times 10^9$/L, red blood cell count of 4.44 $\times 10^{12}$/L, Hb of 138 g/L, platelet count of 146 $\times 10^9$/L, and hypersensitive C-reactive protein (hs-CRP) 57.6 mg/L. The chest CT indicated light inflammation in the upper lobe of the right lung and lower lobes of both lungs (Fig. 1B). The patient was given 0.5 g levofloxacin once a day in a continuous intravenous drip for one week, and the cough was relieved. Routine blood tests were normal, and hs-CRP had decreased significantly (4.9 mg/L) on January 11, 2021. However, her fever recurred the next day (2021.1.12), and her white blood cell count increased significantly to 13.6 $\times 10^9$/L.

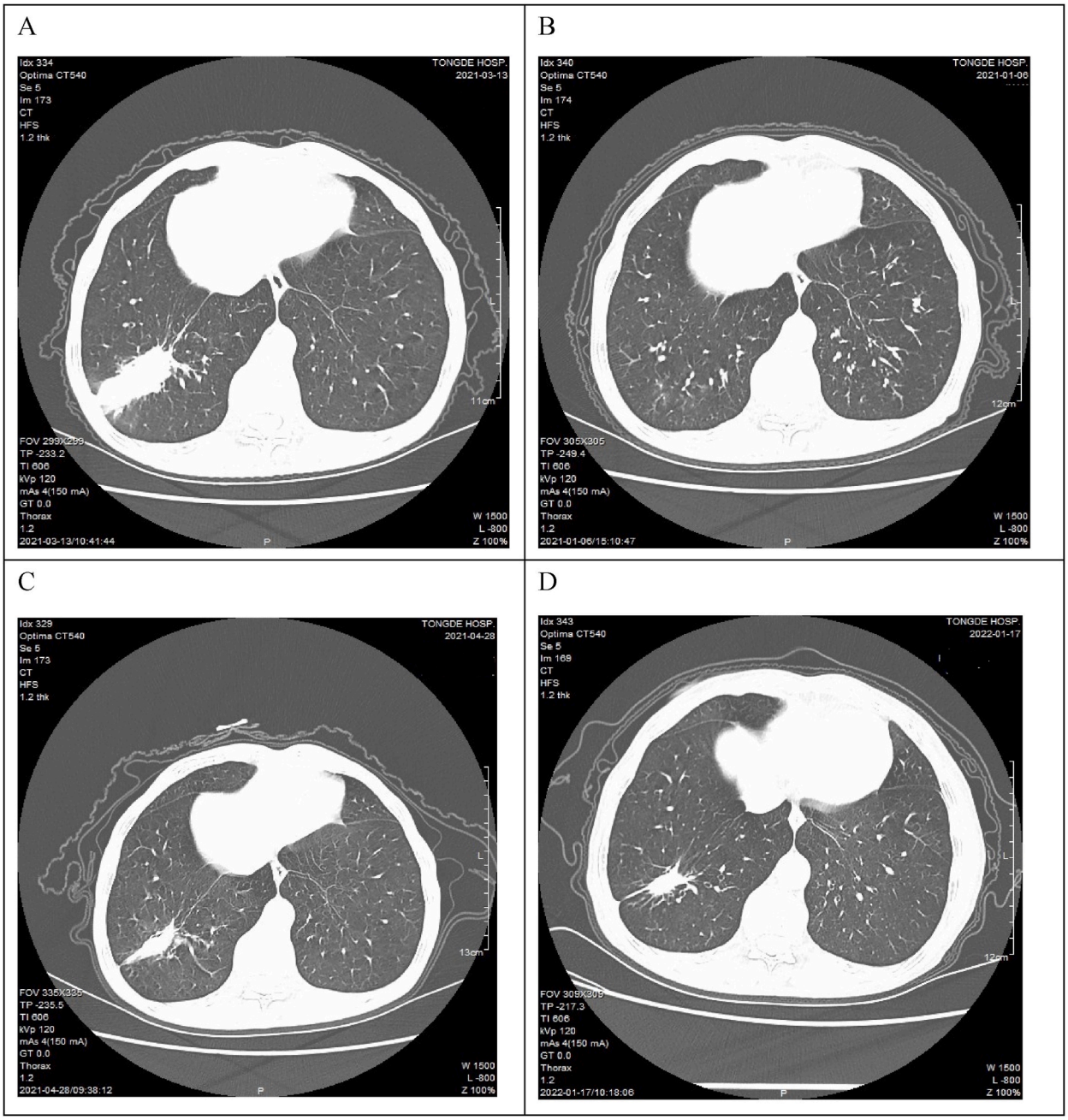

Fig. 1. Comparison of image findings pre-and post-treatment.
A. The chest CT on March 13, 2021, indicated that the inflammation in the right lower lobe increased significantly from January 6, 2021. B. The chest CT on January 6, 2021, showed a little exudate in the right lower lung lobe. C. After antibiotic treatment, the chest CT on April 28, 2021, showed that the inflammation in the right lower lung lobe was better absorbed than on March 13, 2021. D. The chest CT on January 17, 2022, one year after discharge, showed that the chronic inflammatory lesions in the right lower lung lobe were similar to those before. During this period, there was no cough, sputum, or hemoptysis.

The patient thought she had caught a cold and asked for Tylenol oral intake and to be discharged home. During this period, the patient had an intermittent, mainly dry cough, sometimes accompanied by bloody sputum with no fever, dyspnea, or headache. By reviewing the patient's past medical records, we found that the patient was relatively healthy and did not have serious medical diseases such as hypertension, diabetes mellitus, heart disease, kidney disease, etc. However, she visited our stomatology department on November 23, 2020, for "left upper posterior tooth pain" and was diagnosed as "elongation of the 28th tooth and caries of the 27th tooth". She was given "Clindamycin palmitate dispersible tablets 225mg tid po" for anti-infection treatment and recommended extraction of the 28th tooth, but the patient refused to extract the tooth.

Physical examination after admission: body temperature, 37.1 °C; respiratory rate, 16 cycles/min; pulse rate, 102 cycles/min; blood pressure, 139/96 mmHg, thin in body and fair in spirit. Poor oral hygiene, swollen and thickened gingival margins, materia alba III degree, more pigmentation on the tooth surface, mainly the lower front teeth, and no swelling of cervical and submental lymph nodes. Scattered moist rales were heard in the right lower lung, soft abdomen, no tenderness, no edema in the lower limbs, and no skin rash, ecchymosis, or petechiae on the whole body. Laboratory test results revealed a white blood cell count of 6.2×10^9/L (62% neutrophils, 24.2% lymphocytes), hemoglobin was 106 g/L, platelet count was 234×10^9/L, D-dimer was 0.22 mg/L, procalcitonin was 0.06 μg/L, hs-CRP was 2.95 mg/L, and total IgE was 51.77 IU/mL (Table 1). There were no significant abnormalities in tumor markers, and the tests for HIV and syphilis were negative. We also took sputum cultures and sputum tests for *Mycobacterium tuberculosis*, and no positive results were found. The patient was initially diagnosed with community-acquired pneumonia and treated with a piperacillin-tazobactam injection of 4.5g q8h combined with levofloxacin injection of 0.5g qd intravenous anti-infection treatment. At the same time of anti-infective treatment, considering that the patient's main complaint was "hemoptysis", and the blood inflammation index was not high, we also suspected the possibility of "pulmonary embolism" and gave CTA examination of pulmonary, but the results did not show any evidence of thrombosis. To exclude other non-infectious diseases such as tumor, we asked radiologists to consult and concluded that the risk of CT-guided lung biopsy in this area was relatively low and that it could be performed. A CT-guided lung biopsy was performed on March 23, 2021, and the puncture was simultaneously subjected to pathological examination, bacterial smear, bacterial and fungal culture, and pathogenic microorganism metagenomic detection. After the operation, the patient's general condition was good and her vital signs were stable, and She had no further symptoms such as hemoptysis or shortness of breath. The pathological results showed that the lung tissue had fibrous hyperplasia, foamy tissue cell aggregation, infiltration of lymphocytes, plasma cells, neutrophils, and focal alveolar epithelial atypical hyperplasia (Fig. 2). The lung tissue was positive for gram-negative bacilli according to the bacterial smear and *Campylobacter rectus* and *Streptococcus microdigestiae* by tissue culture. And we inoculated the specimens with Colombian blood plate and cultured them anaerobically with GEN anaerobic gas bag and identified them as *Campylobacter rectus* and micro digested streptococci by MALDI Time-of-Flight Mass Spectrometry. At the same time, we also send part of the lung puncture biopsy tissue to Nanjing BGI (The Beijing Genomics Institute) Medical Laboratory for Next Generation Sequencing (NGS) testing by professionals who perform nucleic acid extraction, library construction, sequencing, bioinformatics analysis, and generation of test reports for second-generation sequencing and bioinformatics analysis. Metagenome results showed that the sequence number of *Campylobacter rectus* was six (Table 2), consistent with the bacterial culture results. These results supported a diagnosis of pneumonia caused by *Campylobacter rectus*.

It was a challenge for us when we found *Campylobacter rectus*, a rare pathogen, so we reviewed the relevant literature and decided to use piperacillin-tazobactam 4.5g q8h combined with levofloxacin 0.5g qd intravenously during the hospitalization (2021.3.15–2021.3.31). After the above treatment, the patient's hemoptysis gradually improved, and she was free of hemoptysis five days before discharge. On March 31, 2021, the patient requested to be discharged after feeling improvement in her symptoms, and we decided to give oral antibiotic sequential treatment. Since there was no standardized antibiotic treatment plan, we decided to give amoxicillin capsules 0.25 g bid Po combined with amoxicillin clavulanate potassium tablets 0.375 g bid Po and moxifloxacin tablets 0.4 g qd Po for 14 days.

The reason for choosing amoxicillin in combination with amoxicillin clavulanate potassium is that the effective dose of amoxicillin for the treatment of *Campylobacter rectus* infection mentioned in the literature is 1–1.5 g/d [3], and the use of penicillin containing β-lactamase inhibitors such as amoxicillin clavulanate potassium is recommended whenever possible. Unfortunately, the ratio of amoxicillin clavulanate tablets in our hospital was low in "amoxicillin", so we had to combine what appeared to be the same type of antibiotic (amoxicillin + amoxicillin clavulanate potassium). The patient asked to be discharged on March 31, 2021.

After discharge, she was followed up and she had no further hemoptysis, and chest CT showed chronic inflammation on June 16, 2021, like the findings on April 28, 2021 (Fig. 1 C). Six months later, she had a repeat chest CT on January 17, 2022, which showed similar chronic inflammation in the lower lobe of the right lung (Fig. 1 D). To date, her symptoms of hemoptysis did not recur.

Table 1
Comparison of the laboratory results pre-and post-treatment.

Date	White blood cell count (10^9/L)	Neutrophil count (10^9/L)	Hemoglobin (g/L)	Platelet count (10^9/L)	Hs-CRP (mg/L)
2021.3.08	7.8	5.8	121	252	2.6
2021.3.15	6.2	3.8	106	234	2.95
2021.3.23	8.3	6.0	115	255	0.63
2021.3.30	2.6	1.4	110	133	8.06

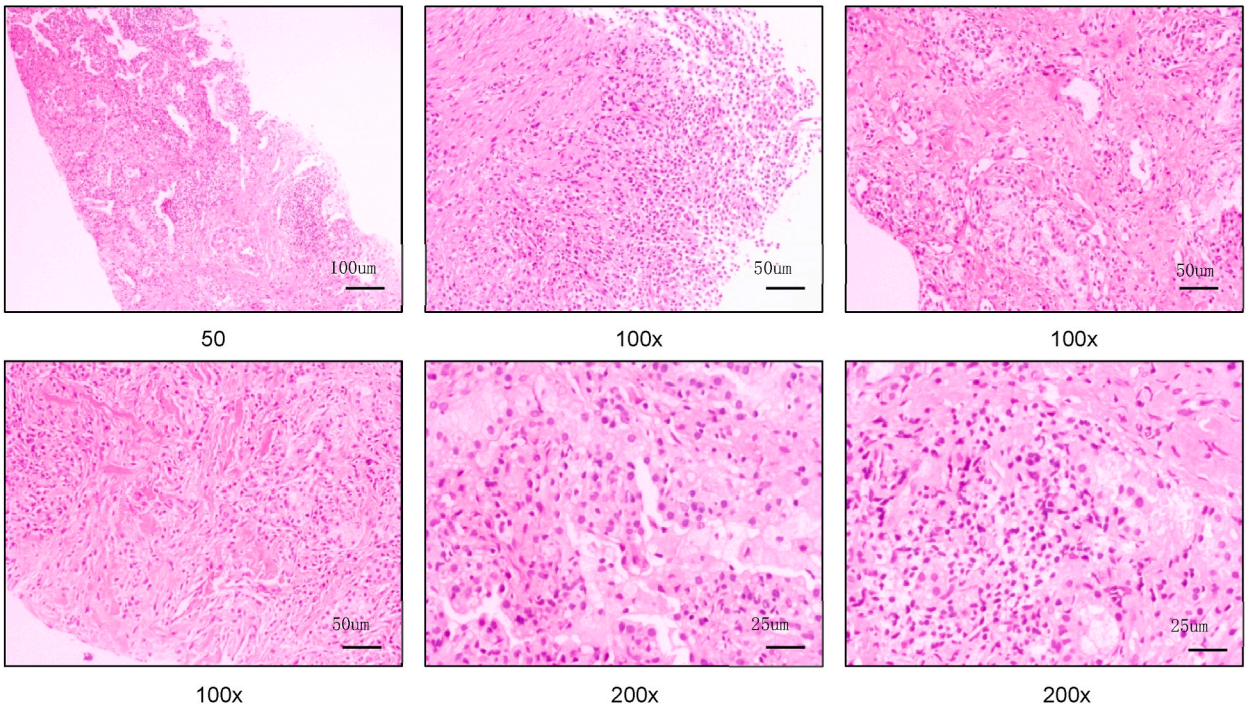

Fig. 2. Pathological section.
The figure shows the inflammatory changes in the lung tissue with interstitial fibrosis.

Table 2
PMseq-DNA high-throughput genetic detection of pathogenic microorganisms in respiratory system infections.

Type	Genus			Species		
	English name	Latin name	Number of sequences	English name	Latin name	Number of sequences
G-	Campylobacter	*Campylobacter*	10	Campylobacter rectus	*Campylobacter rectus*	6
Fungus	Not found	Not found	0	Not found	Not found	0
DNA virus	Not found	Not found	0	Not found	Not found	0
Parasite	Not found	Not found	0	Not found	Not found	0
Mycobacterium tuberculosis	Not found	Not found	0	Not found	Not found	0
Mycoplasma/Chlamydia/ Rickettsia	Not found	Not found	0	Not found	Not found	0

Footnote: G-: Gram-negative bacteria.

3. Discussion and conclusions

Campylobacter rectus was first described in 1981 as *Wolinella recta* [4], a small, unbranched, straight, nonsporulating, anaerobic, gram-negative rod with rapid darting motility using a single, polar flagellum. Some strains can grow in the presence of 5% O_2 but not in air enriched with 10% CO_2. Based on phylogenetic studies, the organism was transferred to the genus Campylobacter in 1991 [5]. Rectus is a member of the human oral flora and has been found in areas such as the periodontal sulcus, tongue, cheek mucosa, and saliva. It is associated with human periodontal disease, being present in higher numbers in diseased than in healthy subgingival sites [6,7]. *Campylobacter rectus* is usually involved in initial periodontitis, chronic periodontitis lesions, and root canal infections [6]. To date, five other Campylobacter species (*C. concisus, C. curvus, C. gracilis, C. showae,* and *C. sputorum*) have been isolated from the human oral cavity. Besides infection of the oral cavity, *Campylobacter rectus* can cause infections in other parts of the body, but this is rare, with only ten cases reported to date (Table 3). It has been reported that the prevalence of periodontal pathogens, including *Campylobacter rectus*, is higher in the subgingival biofilms of patients with coronary artery disease than in non-cardiac subjects. Furthermore, *Campylobacter rectus* and other periodontal pathogens were significantly associated with the subgingival and atherosclerotic plaques in cardiac patients [8]. *Campylobacter rectus* IgG has also been detected at a higher level in acute stroke patients, so it is speculated the *Campylobacter rectus* participate in the disease course of acute stroke [9]. Oral microorganisms have also been shown to be involved in the pathogenesis of CSVD (cerebral small vessel disease) [10].

Table 3
Summary of reported extraoral infections due to *Campylobacter rectus*.

Case	Author (year)	Age/Sex	Diagnosis	Underlying diseases and risky factors	Associated organisms	Treatment	Treatment course	Outcome
1	Spiegel (1984) [11]	62/M	Left chest wall abscess	Poor oral hygiene, alcoholism	*Actinomyces viscosus*	Drainage, antibiotics	Penicillin intravenous drip for 38 days, then penicillin orally for 6 months	Recovery
2	Han (2005) [12]	32/ female	Breast abscess	Large-cell lymphoma anemia, neutropenia, nipple piercing	Non-group A beta-hemolytic streptococcus	Percutaneous, drainage, antibiotics	Vancomycin, clindamycin, and aztreonam possibly for 4 weeks	Recovery
3	Lam (2011) [13]	56/M	Right thoracic empyema	Oral hygiene was poor, gingivitis and multiple, dental caries, hyperglycemia	*Streptococcus constellatus, Fusobacterium nucleatum*	Drainage, antibiotics	After intravenous injection of amoxicillin clavulanate for 29 days, it was taken orally for 1 month	Recovery
4	Ogata (2017) [14]	75/M	Thoracic empyema	Periodontitis with massive dental plaque	NA	Drainage, antibiotics	Sulbactam-ampicillin, garenoxacin, levofloxacin (detailed treatment course not mentioned)	Recovery
5	Noel (2018) [15]	69/M	Thoracic empyema	Poor dental hygiene, alcoholism, chronic renal failure, chronic obstructive pulmonary disease	*Actinomyces meyeri*	Drainage, antibiotics	Amoxicillin clavulanate and amikacin (detailed treatment course not mentioned)	Death
6	Chen (2016) [16]	10-month/ girl	Pneumonia with empyema	The patient is healthy; however, her mother had poor dentition	NA	Drainage, antibiotics, mechanical ventilation	Piperacillin tazobactam and ampicillin-sulbactam for 12 days, then oral amoxicillin clavulanate potassium for 16 days	Recovery
7	Jawad (2018) [17]	29/M	Cavitating pneumonia with Lemierre's syndrome	Glucose-6-phosphate dehydrogenase (G6PD) deficiency	NA	Antibiotics, anticoagulation, and supportive care	Amoxicillin and clavulanate potassium intravenously orally for 6 weeks, rivaroxaban anticoagulation for 3 months	Recovery
8	Gray (2019) [18]	65/M	Pneumonia with empyema	Cerebrovascular disease and chronic excessive alcohol consumption, poor dentition	*Filifactor alocis*	Drainage, antibiotics	Amoxicillin clavulanate for 28 days	Recovery
9	Harada (2019) [19]	51/M	Empyema with bronchopleural fistula	Temporal lobe epilepsy, schizophrenia and multiple dental caries	*Fusobacteriumnucleatum, Campylobacter rectus*	Drainage, antibiotics	Ampicillin/sulbactam and clindamycin for 6 weeks	Recovery
10	Zhu (2021) [20]	73/M	Lung abscess	Chronic Obstructive Pulmonary Disease (COPD)	*Campylobacter rectus, Parvimonasmicra*	Antibiotics	Tazobactam/piperacillin and etimicin for 1 month and oral levofloxacin for 4 months	Recovery
11	Matsumoto (2021) [21]	71/M	Thoracic Empyema	Poor oral hygiene with only one tooth and uncontrolled diabetes	*Campylobacter, Fusobacterium nucleatum*	Drainage, antibiotics	Sulbactam-ampicillin for 24 days	Recovery
12	Figueiredo (2022) [22]	37/ female	Pleural empyema	Sclerosing panencephalitis, poor oral hygiene, and dental plaque	*Campylobacter rectus*	Drainage, antibiotics	17 days of piperacillin + tazobactam, four days of clindamycin, 21 days of meropenem, and 24 hours of amoxicillin and clavulanic acid treatment	Recovery

Campylobacter rectus infection can occur when certain fundamental diseases exist, such as uncontrolled diabetes, neutropenia after chemotherapy, and chronic kidney disease [12]. However, poor oral hygiene is the most important risk factor [15] since most other infections in the body are directly associated with poor oral hygiene [23]. A long chronic periodontal latent infection may also lead to infection in other body parts [13], indicating infection spread via the blood. However, our patient was probably infected through the respiratory pathway, and their unsanitary oral secretion may directly lead to pneumonia. In addition, the disease site was in the lower lung, and the single lesion supported incorrect inhalation leading to infection. Furthermore, other pathogen microorganisms such as actinomycetes or streptococcus, common colonizing oral bacteria, participate in the infection process with *Campylobacter rectus*, further proving that the oral flora is associated with infections in other parts of the body.

Treatment options for *Campylobacter rectus* infections vary depending on the site and degree of the infection. For example, common inflammation may be treated with antibiotics, but if an abscess forms or there is a deep tissue infection, this may need surgical drainage combined with long-term antibiotic treatment. At present, there is no definitive anti-infectious treatment plan, but generally, β-lactam antibiotics and clindamycin have good sensitivity. Antibiotic resistance in *Campylobacter rectus* is rare, and it is highly sensitive to most anti-anaerobic drugs such as amoxicillin/clavulanate, cefoxitin, carbapenems, clindamycin, and metronidazole. It has been reported that *Campylobacter rectus* is sensitive to chloramphenicol, levofloxacin, or moxifloxacin [19], but no studies have been conducted to evaluate whether *Campylobacter rectus* produces β-amidase. Considering that *Campylobacter rectus* infection is often combined with other anaerobic microorganisms in the oral cavity, and these anaerobic bacteria often produce highly pathogenic β-lactamases, the combination of β-lactamase inhibitors is a good choice for serious infections.

Campylobacter rectus is generally considered a pathogenic microorganism causing periodontitis and can cause lower respiratory tract infection. Intraoral organisms, such as streptococci and anaerobes, are major causes of pleural infection, especially in community-acquired cases [24,25]. However, isolation of *Campylobacter rectus* from relevant specimens of lower respiratory tract infection has rarely been reported [13]. In the case we reported, the patient did not have a valid pathogenic basis after routine sputum culture examination, but we could have obtained more information with the help of bronchoscopic pathogenic culture of alveolar lavage fluid. We opted for CT-guided lung aspiration biopsy to facilitate simultaneous acquisition of pathogenic and pathological evidence, although this is not routinely performed in pneumonia. Finally, her pathology was suggestive of inflammatory lesions, and Campylobacter rectus was found by NGS. For cases of pneumonia that are not resolved by initial treatment and are accompanied by more serious oral hygiene problems or underlying diseases, the possibility of oral-derived pathogenic microorganism infection should be considered, such as Campylobacter rectus. Since *Campylobacter rectus* is difficult to culture and characterize, it needs a specific anaerobic environment for optimal isolation. *Campylobacter rectus* only grows on anaerobic blood agar and is motile, oxidase-positive, urease-negative, and catalase-variable; therefore, we speculate that systemic *Campylobacter rectus* infection may be underestimated. In clinical practice, Bacterial culture and metagenomic sequencing of the diseased tissue, especially anaerobic culture, can help clarify the etiological diagnosis.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patients for publication of this case report.

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e20014.

Abbreviations

CT	Computer Tomography
G-	Gram-negative bacteria

DNA	Deoxyribonucleic Acid
CSVD	Cerebral Small Vessel Disease
G6PD	Glucose-6-phosphate Dehydrogenase
COPD	Chronic Obstructive Pulmonary Disease

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