

[CASE REPORT]

Thoracic Empyema Caused by *Campylobacter rectus*

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Abstract:

Campylobacter rectus is a campylobacterium considered to be a primary periodontal pathogen. Thus, *C. rectus* has rarely been isolated from extraoral specimens, especially in the thoracic region. We herein report a case of thoracic empyema in which *Campylobacter* infection was suspected after Gram staining of the pleural effusion, and *C. rectus* was isolated using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. *Fusobacterium nucleatum* was also detected. Molecular identification was performed using polymerase chain reaction amplification and a sequencing analysis of the 16S rRNA gene. Estimation of the causative bacteria using Gram staining led to the proper culture and identification of the causative bacteria.

Key words: *Campylobacter rectus*, *C. rectus*, thoracic empyema, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry, 16S rRNA gene

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Introduction

Thoracic empyema, defined as the presence of bacteria or pus in the pleural cavity, is a potentially fatal infection with high morbidity and mortality and increasing incidence (1). The primary treatment for thoracic empyema is chest tube drainage and administration of appropriate antibiotics. If these treatments do not work, surgical procedures, such as thoroscopic debridement, intrathoracic lavage, and fenestration, are required (2). However, such procedures are highly invasive and may further reduce the patient's performance status, so accurately identifying the causative bacteria and selecting appropriate antibiotics are essential.

Gram staining, an important technique used to determine the causative organism of an infection, is easy to perform and the results are available immediately.

We herein report a case of thoracic empyema in which *Campylobacter rectus* and *Fusobacterium nucleatum* were isolated from pleural effusion. *C. rectus* is a campylobacterium considered to be a periodontal pathogen and has rarely been isolated from the thoracic region. In this case, Gram-negative, spiral rod-shaped bacteria were detected using Gram staining, and *Campylobacter*, which is an unlikely

causative agent of empyema, was presumed to be responsible. Furthermore, the culture conditions were optimized in order to identify the bacteria.

Case Report

A 71-year-old man was brought to our hospital by ambulance with complaints of chest pain and a high fever. He had a 20-day history of cough, left chest pain, and a fever. He had a smoking history of 30 cigarettes per day for 50 years. He had no remarkable medical history and was not taking any medication. He had only one tooth, and his oral hygiene was poor.

His vital signs were as follows: body temperature, 40.2 °C; blood pressure, 148/89 mmHg; heart rate, 110 bpm, and respiratory rate, 26 cycles/min with an oxygen saturation of 95% with 1 L/min oxygen. Hemogram results revealed a white blood cell count of 21,840 cells/mm³ (94.6% neutrophils, 2.0% lymphocytes, 3.3% monocytes, 0.0% eosinophils, and 0.1% basophils), and the serum C-reactive protein (CRP) level was 10.77 mg/dL. In addition, the blood glucose level was 275 mg/dL, and the hemoglobin A1c level was 9.1%, indicating uncontrolled diabetes. Chest X-ray showed pleural effusion in the left lung (Fig. 1a). Chest

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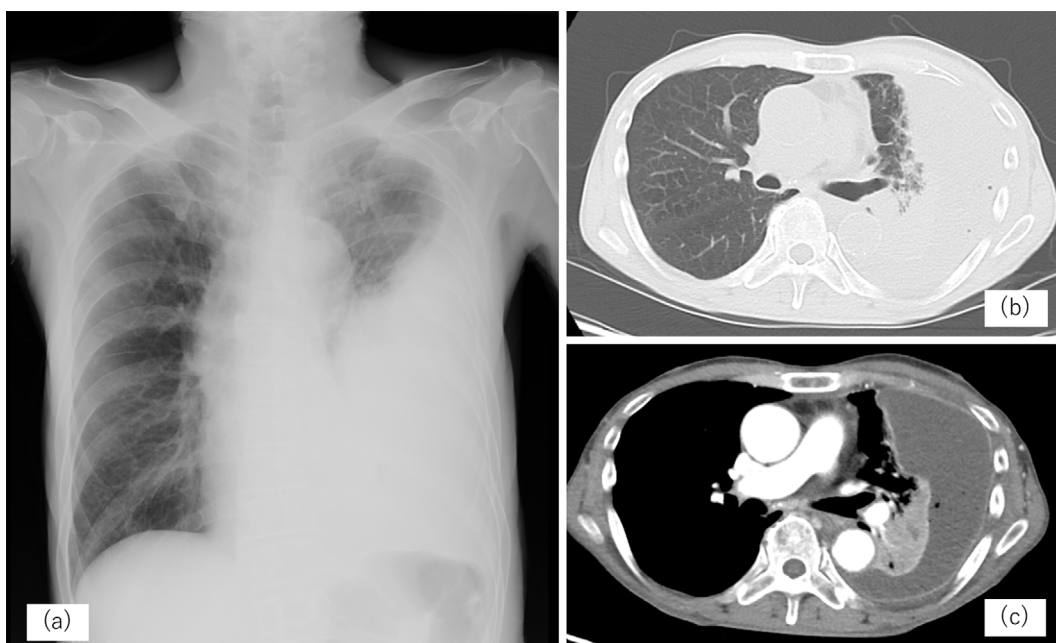


Figure 1. (a) Chest X-ray showing pleural effusion in the left thoracic cavity and collapse of the left lung. (b) Chest computed tomography showing pleural effusion in the left thoracic cavity (pulmonary window). (c) Contrast-enhanced computed tomography (mediastinal window).

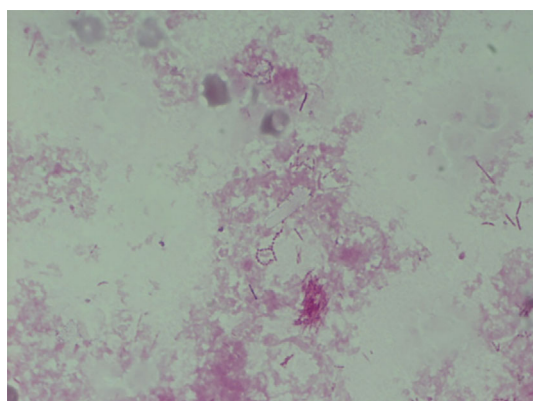


Figure 2. Gram staining of the pleural effusion revealed Gram-negative, spiral, rod-shaped bacteria and phagocytosis.

computed tomography (CT) showed left pleural effusion and air bubbles in the left thoracic cavity, mild thickening of the pleura, and high contrast enhancement (Fig. 1b, c). CT findings of air bubbles in the thoracic cavity suggested an anaerobic infection.

Based on these findings, the patient was diagnosed with thoracic empyema, and chest drainage was performed with a 20-Fr double-lumen thoracic tube. The pleural fluid was yellow in color, cloudy, and polymorphonuclear leukocyte-dominant (91%). The level of pleural lactate dehydrogenase was 1,724 IU/L, and the levels of protein in the pleural fluid and serum were 4.9 g/dL and 6.2 g/dL, respectively. The level of pleural glucose was 2.0 mg/dL.

The purulent pleural effusion obtained via chest drainage was subjected to Gram staining and a culture test. Gram staining of the pleural effusion revealed Gram-negative, spi-

ral rod-shaped bacteria and phagocytosis, suggesting *Campylobacter* infection (Fig. 2). Empirical antibiotic therapy was started with intravenous sulbactam-ampicillin (SBT/ABPC) 12 g/day. From the third day after drain insertion, intrathoracic administration of 120,000 units of urokinase was performed for 3 days. Intensive insulin therapy was started because of uncontrolled diabetes found on admission. Subsequently, the fever and subjective symptoms improved. A follow-up blood test showed that the white blood cell count and serum CRP level had returned to the normal range.

The purulent pleural effusion was centrifuged, and the sediment was inoculated into Brucella agar with hemin and vitamin K1 (Brucella HK agar). Brucella HK agar was incubated at 35 °C under anaerobic conditions. After 48 hours of incubation, matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) was performed to identify the isolate of the causative bacteria, which was confirmed to be *C. rectus*. Regarding the culture conditions, because this bacterium requires hydrogen, anaerobic culture and hydrogen-generating agent were added. Under these culture conditions, good growth of *C. rectus* was obtained.

In addition, we performed molecular identification using polymerase chain reaction amplification and a sequencing analysis of the 16S rRNA gene using DNA extracted from the isolated organism. The sequence of the 16S rRNA gene confirmed the organism to be *C. rectus*. Antimicrobial susceptibility testing was performed by the microbroth dilution method for determining the minimal inhibitory concentration. The minimal inhibitory concentration was measured using a Dry Plate Eiken (Eiken Chemical, Tokyo, Japan). Antibiotic susceptibility of *C. rectus* was identified for penicillin

Table 1. Result of Antimicrobial Susceptibility Tests.

Antibiotics	<i>C.rectus</i>	<i>Fusobacterium nucleatum</i>	
PCG	≤0.03	≤0.03	S
ABPC	≤0.03	0.06	S
CMZ	≤1	≤1	S
CAZ	≤1	4	
CFPM	≤1	2	
FMOX	≤1	≤1	
IPM	≤0.25	≤0.25	S
MEPM	≤0.25	0.5	S
CLDM	≤0.12	≤0.12	S
LVFX	>2	2	
MINO	≤0.25	≤0.25	
C/S	≤8	≤8	
CP	≤0.5	4	S
CZX	≤2	≤2	

PCG: penicillin G, ABPC: ampicillin, CMZ: cefmetazole, CAZ: ceftazidime, CFPM: cefepime, FMOX: flomoxef, IPM: imipenem, MEPM: meropenem, CLDM: clindamycin, LVFX: levofloxacin, MINO: minocycline, C/S: cycloserine, CP: chloramphenicol, CZX: ceftizoxime, S: susceptible.

compounds, cephem compounds, clindamycin, and carbapenem compounds. *F. nucleatum* was also cultured from the pleural effusion. Because the agent was also susceptible to SBT/ABPC, the treatment course was retained (Table 1).

Chest CT performed 14 days after medical treatment confirmed the abscess cavity to have shrunk (Fig. 3), and the chest drainage tube was removed on the 15th day. The intravenous administration of antibiotics (SBT/ABPC) was continued until the 24th day without any consecutive oral antibiotics, and the patient was discharged on the 25th day. The condition has not recurred since then.

Appropriate written informed consent was obtained for the publication of this case report and accompanying images.

Discussion

Targeted therapy is the most desirable treatment for infectious diseases. It is thus important to identify the causative bacteria via a rapid testing method and Gram staining. It is also vital to collect and culture appropriate samples for bacterial identification and antibiotic susceptibility testing. In our case, Gram staining of pleural effusion revealed spiral bacteria, and *Campylobacter* was suspected as the causative agent. In addition, *C. rectus* was presumed to be the causative bacterium by MALDI-TOF-MS performed at an early stage.

C. rectus is a small, unbranched, straight, nonsporulating, anaerobic, Gram-negative rod (3). It is part of the human oral flora and is found in areas such as the gingival sulcus, tongue, cheek mucosa, and saliva (4). *C. rectus* has been implicated as a periodontal pathogen and is found more frequently in diseased sites than in healthy subgingival sites (5). In recent years, extraoral infections caused by *C.*

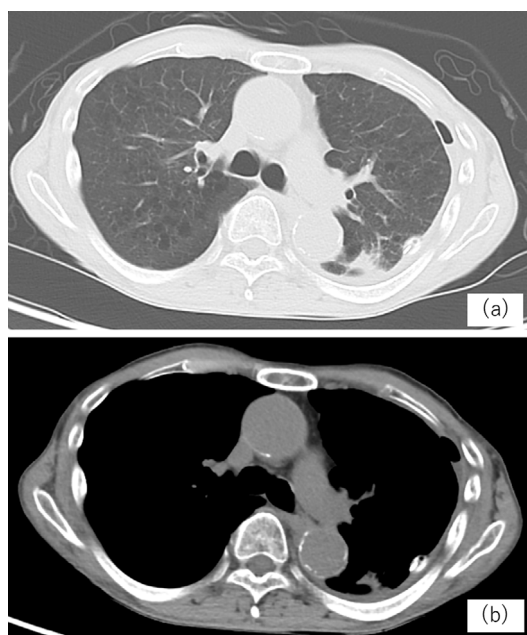


Figure 3. Chest computed tomography showing the shrunken abscess cavity. (a) Pulmonary window. (b) Mediastinal window.

rectus have been reported. Among them, empyema was reported in five cases, including our own, which is considered to be relatively rare (Table 2) (6-9). Of these five cases, three have been reported as mixed infections with anaerobic bacteria, such as *Fusobacterium*. This suggests that, similar to empyema, *C. rectus* is caused pneumonia and empyema via the trachea from the oral cavity. All cases were treated via chest tube drainage and antibiotics. The antibiotics used in the successfully managed cases included amoxicillin-clavulanic acid, SBT/ABPC, meropenem, garenoxacin, and levofloxacin.

C. rectus is a difficult organism to culture and identify (10). In our patient, it was identified by 16S rRNA gene sequencing. *C. rectus* requires an anaerobic atmosphere for optimal isolation, and the composition of gases necessary for its cultivation varies. Recent reviews on the genus *Campylobacter* report that *C. rectus* requires an atmosphere of 6% H₂ and 10% CO₂, with the remaining being N₂ (11).

As preliminary identification of *C. rectus* was performed by MALDI-TOF-MS, we were able to properly culture the bacteria using the abovementioned conditions. Identifying the causative organism by MALDI-TOF-MS was useful for suitable subsequent culture. The adoption of MALDI-TOF-MS going forward may increase the detection of bacteria that were previously difficult to identify. Although *C. rectus* could not be identified via routine biochemical bacterial identification methods usually used in the laboratory, it was identified using 16S rRNA sequencing. In previous reports, *C. rectus* was identified by similar methods. When a bacterial species is indicated, selecting the appropriate culture method and identifying the bacterial species using 16S rRNA sequencing is necessary.

Table 2. Summary of Thoracic Empyema by *Campylobacter rectus*.

Case	Age/Sex	Comorbidity	Oral condition	Concomitant isolate	Treatment	Antibiotics	Outcome	Reference
1	56/M	Not described	Poor	<i>Fusobacterium nucleatum</i>	Drainage, antibiotics	AMPC/CVA	Cured	6
2	75/M	Diabetes mellitus	Poor	None	Drainage, antibiotics	ABPC/SBT, GRNX, LVFX	Cured	7
3	65/M	Cerebrovascular disease and alcoholism	Poor	<i>Filifactor alocis</i>	Drainage, antibiotics	MEPM	Cured	8
4	69/M	Not described	Poor	Not described	Not described	Not described	Fatal	9
5	71/M	Diabetes mellitus	Poor	<i>Fusobacterium nucleatum</i>	Drainage, antibiotics	ABPC/SBT	Cured	Present case

M: male, AMPC/CVA: amoxicillin-clavulanate, GRNX: garenoxacin (oral, 400mg/day), LVFX: levofloxacin (oral, 500mg/day)

Regarding treatment, treatment with ABPC/SBT was continued based on previous case reports (6, 7) and data on the antimicrobial susceptibility of *C. rectus* in *in vitro* studies (12). *In vivo* treatment data for *C. rectus* are insufficient, and the accumulation of further data on this point is awaited.

Considering the abovementioned infection route, *C. rectus* is a bacterium that exists in the oral cavity. In previous case reports on empyema, most of the cases occurred in patients with poor oral hygiene; hence, it is highly possible that aspiration resulted in pneumonia and spread to the thoracic cavity, similar to the usual route. The detection of *F. nucleatum* in the pleural effusion also supports this hypothesis.

In conclusion, we encountered a case of thoracic empyema caused by *C. rectus* and *F. nucleatum*. *Campylobacter*, which is not normally found in the pleural effusion and is usually not considered as the causative agent of empyema, was suspected by Gram staining of the pleural effusion, and *C. rectus* was detected using MALDI-TOF-MS. In addition, we optimized the culture conditions and detected *C. rectus* using polymerase chain reaction amplification and a sequencing analysis of the 16S rRNA gene. With the increased use of MALDI-TOF-MS, it is expected that many pathogens rarely considered to be causative agents will be identified in the future. However, similar to the approach with normal culture tests, it is necessary to determine whether or not the bacteria detected using MALDI-TOF-MS are indeed the true causative agents of the disease by referring to the clinical findings, patient background, infected organs, and Gram staining.

The authors state that they have no Conflict of Interest (COI).

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