

This article is licensed under the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC) (<http://www.karger.com/Services/OpenAccessLicense>). Usage and distribution for commercial purposes requires written permission.

Single Case

Clostridium difficile Causing Empyema

Abdalla Mohamed^a Vanessa Sostre^a Hiren Patel^b Prem Patel^a
Luis C. Ortiz^a Walid J. Baddoura^b

^aDepartment of Medicine, St. Joseph's University Hospital Paterson, Paterson, NJ, USA;

^bDivision of Gastroenterology and Hepatology, St. Joseph's University Hospital Paterson, Paterson, NJ, USA

Keywords

Clostridium difficile · Empyema · Achalasia

Abstract

Extraintestinal *Clostridium difficile* infection (CDI) is extremely uncommon. High mortality and poor outcomes have been observed among individuals with this rare medical condition. Empyema is one of the extraintestinal manifestations of CDI. Possible mechanisms to develop this parapneumonic effusion are aspiration and contamination of the chest tube. We present a 42-year-old Hispanic male with *C. difficile* empyema without any prior history of CDI.

© 2018 The Author(s)
Published by S. Karger AG, Basel

Introduction

Clostridium difficile was discovered in the stool in 1935 by Hall and O'Toole [1], but it was not until approximately 43 years later when in 1978 George et al. [2] and Bartlett et al. [3] discovered that *C. difficile* was the organism responsible for most of the cases of antibiotic-associated diarrhea. *C. difficile* was estimated to cause almost half a million infections in the

United States in 2011. Approximately 29,000 died within 30 days of the initial diagnosis [4]. *C. difficile* is a spore-forming, Gram-positive anaerobic bacillus that produces two exotoxins: toxin A and toxin B. It is a common cause of antibiotic-associated diarrhea. It accounts for 15–25% of all episodes of antibiotic-associated diarrhea [4]. Risk factors associated with transmission are antibiotic exposure, gastrointestinal surgery/manipulation, a long length of stay in healthcare settings, a serious underlying illness, immunocompromising conditions, and advanced age [4]. Extraintestinal manifestations of CDI especially empyema are rare. Smith and King [5] were one of the first to describe extracolonic CDI. They reported on 2 cases of empyema caused by CDI. Methods of inoculation are usually that of aspiration, although some had described external contamination through chest tubes [5–8]. To our knowledge, only 6 previous cases of CDI causing empyema were described, ours being the seventh.

Case Report

A 42-year-old Hispanic male presented to our hospital with worsening shortness of breath of 3 weeks' duration, cough with green color sputum, subjective fevers, decreased PO intake, and as per the patient a 40-pound weight loss. His weight documented on previous admission was approximately 175 pounds, and upon the current admission the patient weight approximately 158 pounds amounting to a weight loss of 9.71% in approximately 2 months. Four months prior to this presentation, the patient was admitted to our hospital with similar complaints and he was diagnosed with *Klebsiella pneumoniae* with parapneumonic effusion. The patient was given antibiotics and thoracentesis was done. Pleural fluid analysis is shown in Table 1. His past medical history including liver cirrhosis secondary to NAFLD, hypothyroidism, and morbid obesity for which he had undergone Roux-en-Y gastric bypass 7 years prior to the current presentation. He also developed achalasia, 6 years after gastric bypass surgery for which he got Botox injection with symptomatic improvement. His initial labs were essentially benign, physical exam was normal except for diminished lung sounds in the right lower and right middle lobes. Computed tomography of the chest was done which was consistent with a thick-walled fluid collection at the right lower chest cavity containing fluid and air, suspicious for empyema (Fig. 1, 2). The patient was admitted to the general medical floors and started on meropenem and linezolid. A 14-Fr pigtail catheter was inserted in pleural cavity with removal of approximately 200 cm³ of thick purulent pleural fluid. The fluid was sent for evaluation including cytology which was suggestive of empyema (Table 1). Due to decreased drainage of the pleural fluid through the catheter which was likely secondary to loculations and worsening of patient's respiratory status, surgery was consulted for video-assisted thoracoscopic surgery (VATS). The patient underwent VATS which showed extensive empyema with numerous adhesions and a thickened pleural peel. The patient underwent extensive lysis of adhesions, and right lower lobe wedge resection, and insertion of two 32-Fr chest tubes for continued drainage. During the VATS procedure, the pleural fluid was sent for analysis including anaerobic and aerobic Gram culture and stain which was positive for *C. difficile*. Intravenous metronidazole was started. The patient had no history of CDI, and blood cultures were negative for *C. difficile* but were positive for *K. pneumoniae*. A stool *C. difficile* toxin assay was sent which returned negative for toxin, antigen, and PCR testing. The chest tubes were removed and the patient recovered well.

Discussion

Extra-intestinal manifestations of CDI are rare. In 2013, Mattila et al. [9] conducted a retrospective study of extraintestinal CDIs during a 10-year period. Extraintestinal CDI was found in 31 patients who comprised 0.17% of all CDIs [9]. Two patients had bacteremic infections, 4 had abdominal infections without any prior surgery, 7 had abdominal infections after surgery, 4 had perianal abscesses, 13 had wound infections, and 1 had *C. difficile* in a urinary catheter [9]. García-Lechuz et al. [10] reported 17 cases of extracolonic *C. difficile* from a single institution over a 10-year period. Peritonitis, intra-abdominal abscess, or abdominal wound infection were identified in 13 of the 17 cases. Additionally, brain abscess, chronic osteomyelitis, and pyelonephritis were each reported [10].

Smith and King [5] were among the first to describe extracolonic CDI (Table 2). They described 2 cases of empyema caused by CDI; the first case was a 65-year-old man who had suffered from chronic pleuritis where CDI was isolated on two separate occasions. The second case was a 58-year-old male with a pneumothorax and subsequent pleural effusion. In both cases, the infections were likely secondary to aspiration [5]. Simpson et al. [6] also reported one case of CDI in empyema. In that case, the proposed method of infection was a chest tube into a pre-existing empyema. Unfortunately, no stool samples were sent for culture. The only other mechanism through which the pleural fluid could be contaminated is hematogenous spread. However, in a review by Feldman et al. [11], no cases of *C. difficile* bacteremia resulted in pneumonia or empyema.

It is important to report that most cases of extraintestinal CDI were polymicrobial in nature, Spagnuolo and Payne [12] showed that *Clostridium perfringens* is more likely to infect the pleural cavity as a pure culture with no other microbial infection. Marina et al. [13] reported on anaerobic pleuropulmonary infections and found that of 116 organisms isolated, only two were *C. difficile* and only one of these was a pure culture.

The precise mechanism of *C. difficile* empyema in our patient is unclear. Possible risk factors were prolonged hospital stay and broad-spectrum antibiotics. Given his history of achalasia, it is possible he could have aspirated resulting in pulmonary infection. In addition, he had undergone a prior thoracentesis which could have caused contamination of pleural space. Interestingly, he had never been infected with *C. difficile* on the current or prior admission. His stool toxin assay was negative and blood cultures sent on two separate occasions remained negative.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Funding Sources

The authors have no funding sources to declare.

Author Contributions

Abdalla Mohamed: Primary author. Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; rafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Vanessa Sostre: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Drafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Hiren Patel: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Drafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Prem Patel: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Drafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Carlos Ortiz: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Drafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Walid J. Baddoura: Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Drafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

- 1 Hall IC, O'Toole E. Intestinal flora in nwe-born infants. *Am J Dis Child*. 1935;49(2):390.
- 2 George WL, Sutter VL, Goldstein EJ, Ludwig SL, Finegold SM. Aetiology of antimicrobial-agent-associated colitis. *Lancet*. 1978 Apr;1(8068):802–3. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/85818>

- 3 Bartlett JG, Moon N, Chang TW, Taylor N, Onderdonk AB. Role of *Clostridium difficile* in antibiotic-associated pseudomembranous colitis. *Gastroenterology*. 1978 Nov;75(5):778–82. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/700321>
- 4 Tosh PK, McDonald LC. Infection control in the multidrug-resistant era: tending the human microbiome. *Clin Infect Dis*. 2012 Mar;54(5):707–13.
- 5 Smith LD, King EO. Occurrence of *Clostridium difficile* in infections of man. *J Bacteriol*. 1962 Jul;84:65–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/13914327>
- 6 Simpson AJ, Das SS, Tabaqchali S. Nosocomial empyema caused by *Clostridium difficile*. *J Clin Pathol*. 1996 Feb;49(2):172–3. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8655688>
- 7 Hudson DA, Gibb AP, Gill MJ. Empyema caused by *Clostridium difficile*. *Can J Infect Dis*. 1999 Mar;10(2):170–1. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22346383>
- 8 Ali Imtiaz M, Pandya M. PANDYA M. A Rare Case of Pleural Empyema Secondary to *Clostridium difficile*. *Chest*. 2015;148(4):98A.
- 9 Mattila E, Arkkila P, Mattila PS, Tarkka E, Tissari P, Anttila VJ. Extraintestinal *Clostridium difficile* infections. *Clin Infect Dis*. 2013 Sep;57(6):e148–53.
- 10 García-Lechuz JM, Hernangómez S, Juan RS, Peláez T, Alcalá L, Bouza E. Extra-intestinal infections caused by *Clostridium difficile*. *Clin Microbiol Infect*. 2001 Aug;7(8):453–7. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/11591212>
- 11 Feldman RJ, Kallich M, Weinstein MP. Bacteremia due to *Clostridium difficile*: case report and review of extraintestinal *C. difficile* infections. *Clin Infect Dis*. 1995 Jun;20(6):1560–2. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/7548512>
- 12 Spagnuolo PJ, Payne VD. Clostridial pleuropulmonary infection. *Chest*. 1980 Oct;78(4):622–5. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/6251997>
- 13 Marina M, Strong CA, Civen R, Molitoris E, Finegold SM. Bacteriology of anaerobic pleuropulmonary infections: preliminary report. *Clin Infect Dis*. 1993 Jun;16 Suppl 4:S256–62. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/8324128>
- 14 Diarrhea in my lung? A rare case of *Clostridium difficile* empyema – SHM Abstracts [cited 2018 Jun 13]. Available from: <https://www.shmabstracts.com/abstract/diarrhea-in-my-lung-a-rare-case-of-clostridium-difficile-empyema/>.



Fig. 1. Transverse view of fluid collection in the right lower chest cavity.

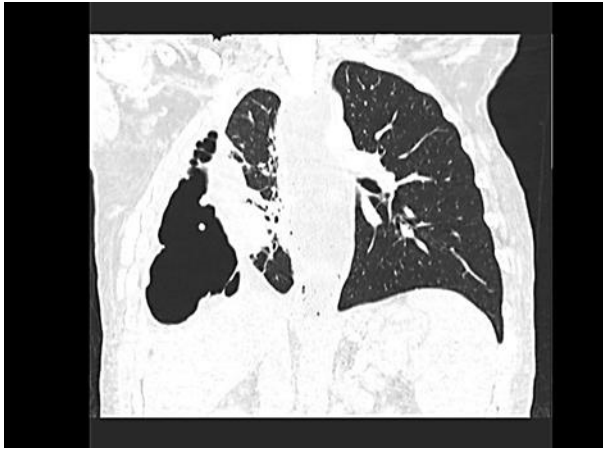


Fig. 2. Coronal view of fluid collection in the right lower chest cavity.

Table 1. Pleural fluid analysis

Date	Pleural fluid analysis of previous thoracentesis	Pleural fluid analysis of current thoracentesis
Appearance	Cloudy	Turbid
Color	Orange	Orange
Fluid RBC	8,730	23,200
Fluid WBC	2,295	166,400
Fluid PMN, %	1	91
Fluid lymph, %	66	1
Fluid monocytes, %	12	8
Fluid eosinophils, %	18	0
Fluid histiocytes, %	3	0
Glucose fluid	106	–
Total protein fluid	4.2	4.4
LDH fluid	194	7,337
Cholesterol fluid	57	46
Triglyceride fluid	21	20
ADA	Neg	–
Albumin fluid	1.8	1.1
Albumin serum	2.4	1.5
LDH serum	124	104

First column from the initial thoracocentesis and second column from subsequent pleural fluid analysis.

Table 2. Previously reported cases of *C. difficile* empyema

Ref.	Sex/ age	Predisposing condition	Stool	Outcome	Other organ- ism isolated	Possible transmis- sion
5	65/M	Pleurisy	Not Recorded	Not recorded	None	Aspiration
5	58/M	Pneumothorax	Not Recorded	Not recorded	None	Aspiration
14	52/F	Pleural effusion	Not Recorded	Improved	None	Aspiration
7	65/M	Pleural effusion	Negative/+history of <i>C. difficile</i>	Improved	None	Aspiration
8	53/M	Pleural effusion	Negative	Improved	None	Aspiration
6	46/M	Pleural effusion	Negative	Improved	None	Contamination from chest tube insertion