Pulmonary Clostridium perfringens: Seeding beyond the gastrointestinal tract

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Pulmonary *Clostridium perfringens*: Seeding Beyond the Gastrointestinal Tract

Thilini Delungahawatta,*, Shiavax J. Rao, Marcos Wolff, Christopher J. Haas

Abstract

*Clostridia* perfringens infection outside the gastrointestinal system is rare. Here, we report on a 75-year-old man with history of end-stage renal disease presenting after a syncopal event with lactic acidosis, leukocytosis, and mild hyperbilirubinemia. Chest imaging revealed a loculated, left-sided pleural effusion; diagnostic thoracentesis identified *Clostridia perfringens*, consistent with an empyema. Video-assisted thoracic left lung decortication was performed; tissue culture also speciated *Clostridia perfringens*. Further imaging revealed concomitant acute cholecystitis, suggesting hematogenous seeding or transdiaphragmatic extension of *Clostridia perfringens* to pleural space from an abdominal source. The patient was successfully managed with laparoscopic cholecystectomy and discharged on a one-month course of amoxicillin-sulbactam. This case highlights the potential for *Clostridia perfringens* to produce a pleuropulmonary infection, necessitating timely diagnosis and intervention, to improve patient outcomes.

Keywords: *Clostridium*, *Clostridium perfringens*, Empyema, Lung abscess, Pleuropulmonary infection

1. Introduction

*Clostridium* bacteria are anaerobic, spore-forming bacilli commonly found within soil and as part of the normal bacterial composition of the human and animal gastrointestinal tract. Certain *Clostridia* species have also been reported to colonize the skin of hospitalized patients. Infection of the lung and pleural space by *Clostridium* bacteria however, are rare occurrences. In fact, only 4 cases have been reported in the English literature over the past 10 years. Among these studies, proposed etiologies included underlying lung malignancy, cirrhosis complicated by hepatic hydrothorax, and aspiration of oropharyngeal contents. Other etiologies of pleuropulmonary infection from *Clostridium bacteria* previously reported included trauma or iatrogenic contamination of chest wall and pleural cavity, chronic disease or immune system impairment, pulmonary embolization and lung infarction, and bacteremia from a secondary focus of infection. The most commonly identified species of *Clostridium* is *Clostridium perfringens*, however infection with *C. sordellii*, *C. sporogenes*, *C. paraputreficum*, and *C. bifermentans* have also been reported. Disease pathogenesis is attributed to release of potent extracellular toxins that provoke vascular leukocytosis and limit polymorphonuclear leukocyte response to invading microorganisms, leading to tissue necrosis with abscess formation or empyema. Given that *Clostridia* bacterial infection is an infrequently observed pathogen in pulmonary disease and early symptomatology may mimic features of an acute pneumococcal pneumonia, delays in diagnosis and management are common. Herein, we report a rare case of pulmonary empyema secondary to probable hematogenous seeding or transdiaphragmatic extension of *C. perfringens* from complicated cholecystitis. We aim to aid clinicians in promptly identifying the disease and etiology to promote timely intervention and favourable health outcomes.
2. Case presentation

A 75-year-old man with history of end-stage renal disease (secondary to long-standing diabetes mellitus and hypertension) presented to the hospital from his outpatient dialysis center after a syncopal episode. He was in his normal state of health the evening prior to presentation; however, upon awakening in the morning he had experienced left-sided chest discomfort, described as non-radiating, worse with deep inspiration, that was reproducible on palpation. He attended his scheduled dialysis session during which he experienced shortness of breath, chills, and a witnessed syncopal event. On presentation, he denied further complaints including abdominal pain, nausea, vomiting, fevers or chills, but he did have one episode of emesis. He denied any recent falls or antecedent trauma.

Vital signs on presentation revealed tachycardia (100 beats per minute) and hypertension (170/70 mm Hg), but he was otherwise afebrile and saturating adequately on room air. Physical examination was notable for lethargy with no focal deficits and absent breath sounds across the left lung fields. The abdomen was also soft, non-distended, without tenderness to palpation. Initial laboratory diagnostics demonstrated an elevated lactic acid (3.3 mmol/L; reference range 0.7–2 mmol/L) and leukocytosis (17.6 k/uL; reference range 4–10.8 k/uL). Liver function tests were mostly unremarkable - aspartate aminotransferase (AST) of 8 units/L (reference range 0–33 units/L), alanine aminotransferase (ALT) of 9 units/L (reference range 10–49 units/L), and alkaline phosphatase (ALP) of 75 units/L (reference range 46–116 units/L) - except for mild hyperbilirubinemia with total bilirubin of 1.2 mg/dL (reference range 0.2–1.1 mg/dL). Given suspicion for acute infection, blood cultures were obtained, and he was subsequently initiated on broad-spectrum antibiotics (vancomycin and piperacillin-tazobactam). A plain film radiograph of the chest revealed total opacification of left hemithorax suggestive of possible pleural effusion or pneumonia. Respiratory viral panel was negative. He was admitted to the medicine floor for further management.

Fig. 1. Non-contrast CT scan of the chest revealing a large, loculated, left-sided pleural effusion concerning for empyema with gas-forming infection and consequent complete left lung collapse (A-C), as well as diffuse gallbladder wall thickening (D).
Computed tomography (CT) of the chest without contrast demonstrated a large, loculated, left-sided pleural effusion concerning for empyema with gas-forming infection and consequent complete left lung collapse (Fig. 1). It also showed diffuse gallbladder wall thickening, thought to be an unrelated finding given no clinical association from examination or history. A left pleural pigtail catheter was placed by interventional radiology, from which diagnostic thoracentesis yielded 30 mL of cloudy fluid. Pleural fluid gram stain (Fig. 2) grew Gram positive rods, subsequently identified as pan-sensitive *C. perfringens* consistent with an empyema. Acid-fast bacilli smear and fungal stains were negative. At this time, the antibiotic regimen was narrowed to amoxicillin-sulbactam. The patient’s respiratory status remained stable; he was able to tolerate dialysis and the thoracostomy tube was subsequently removed. A video-assisted thoracoscopic surgery for left lung decortication was performed and lung tissue cultures also speciated *C. perfringens*, confirmed by matrix-assisted laser desorption/ionization-time of flight mass spectrometry. Surgical pathology was negative for malignancy. Blood cultures, however, remained negative.

Given the rarity of pleural/pulmonic *C. perfringens*, a contrast-enhanced CT scan of abdomen and pelvis was obtained to rule out occult abdominal infection. CT revealed cholelithiasis, thickening and enhancement of the gallbladder wall concerning for acute cholecystitis, as well as a fluid collection adjacent to the gallbladder fundus concerning for contained perforation (Fig. 3). Hepatobiliary iminodiacetic acid (HIDA) scan confirmed acute cholecystitis and cystic duct obstruction. The patient continued to deny any abdominal pain, nausea, or vomiting, and was tolerating a regular diet. There was no tenderness on examination and Murphy’s sign was negative. He remained hemodynamically stable with no laboratory evidence of leukocytosis at the time; liver enzymes remained within normal limits. There was high clinical suspicion for bacterial spread from diseased gallbladder and subsequent seeding of left pleural space, and thus, the patient underwent laparoscopic cholecystectomy for source control. Surgical pathology of the gallbladder showed mucosal responses to acute and chronic inflammation with a focus of ulceration and hemorrhage.

Following surgery, liver function tests remained within normal limits. Pain was well controlled, and the patient was advanced to a solid diet within 48 h. He was discharged to acute rehab with the recommendation to continue amoxicillin-sulbactam for 1 month from the time of decortication and planned outpatient surgical follow-up.

### 3. Discussion

Clostridia empyema is a rare phenomenon. In a population-based surveillance study involving a sample of 1 million individuals in Calgary over 3 consecutive years, authors failed to identify any cases of *C. perfringens* empyema. In an earlier literature review of thirteen cases of Clostridia empyema, authors highlight middle-age, male sex, and underlying pulmonary disease as potential risk factors, and also show how lung involvement was multilobar but often spared the upper lobes. Presenting symptoms of *C. perfringens* empyema are typically non-specific, as they can share features of an acute pneumonia and systemic symptoms are only present in a few cases.
Several etiologies of C. perfringens empyema have been previously proposed. In our patient, given the evidence of contained perforation of a diseased gallbladder, C. perfringens empyema secondary to hematogenous or transdiaphragmatic seeding were the most probable causes. In the former theory, this case remains unusual considering that the patient’s blood cultures remained negative. Nevertheless, transient bacteremia in patients with acute abdominal inflammatory processes or following endoscopic procedures has previously been described. On the other hand, bacteria may have followed a pressure gradient from high abdominal cavity pressure to the lower pressure of the pleural space through hepatic and diaphragmatic fenestrations. Previously reported cases of pleural abscesses and empyema have typically presented ipsilateral to the concomitant abdominopelvic process, but in rare cases, the contralateral lung has solely been affected, as seen in our case. Furthermore, while most cases of C. perfringens empyema result from trauma or iatrogenic introduction of skin flora into the pleural cavity, our patient had no history of trauma or procedures involving the chest wall prior to admission. Our patient may be of higher risk however, given the disturbances of the immune

Fig. 3. Contrast-enhanced CT scan of the abdomen and pelvis revealing thickening and enhancement of the gallbladder wall, as well as a 1.6 cm x 4 cm x 2 cm fluid collection adjacent to the gallbladder fundus.
system associated with end-stage renal disease. Aspiration has also been described as a common source of infection, as *C. perfringens* can colonize the oral microbiome and, in a few cases, endotracheal intubation procedures may lead to reflux and migration of bacteria into lung fields. However, mixed organisms are usually isolated from these patients; no other common oral microorganisms were cultured from the pleural fluid in our patient and there was no report of dysphagia or recent intubation.

Treatment of *C. perfringens* empyema generally involves pleural drainage and antibiotic therapy with penicillins. Use of hyperbaric oxygen has been proposed to be effective given its bactericidal properties via a phagocytic oxygen dependent intracellular killing mechanism and acts rapidly given the ease of diffusion to tissues. Clinical evidence for these theories, however, is lacking. Containment of exotoxins within the borders of the pleural space may help to minimize systemic toxicity, and therefore mortality associated with *C. perfringens* pleuropulmonary infection is relatively low when compared to other bacterial empyemas. However, in rare cases, distributive shock has been reported to occur. In those that recover from the disease, minor pleural thickening is often the only residual finding.

4. Conclusion

In conclusion, *C. perfringens* is a rare cause of pleuropulmonary infection, arising most commonly from iatrogenic contamination, aspiration, or bacteremia — the latter of which is suggested in our case. Despite its rarity, there is potential for systemic complications and as such, clinicians must be cognizant of this phenomenon to aid in early diagnosis and timely treatment. Standard management involves pleural drainage and antibiotic therapy with favourable outcomes. Further epidemiological studies are needed to identify risk factors and evaluate therapeutic alternatives.

Patient consent

Informed consent was obtained.

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Conflicts of interest

All authors declare no conflict of interest.

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