CASE REPORT

Severe case of pneumonia with pleural effusion in an immunocompromised woman due to *Fusobacterium necrophorum*

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SUMMARY

Infections caused by fusobacteria have a wide clinical spectrum, and in certain patients, they can lead to severe systemic illness. We report the case of an immunocompromised young woman who presented with severe pneumonia complicated by parapneumonic pleural effusion, despite wide-spectrum antibiotic treatment. *Fusobacterium necrophorum* was isolated in the samples obtained after thoracentesis was performed. Apart from the pulmonary involvement, we could not identify the infectious focus, since the patient did not have poor dentition or Lemierre's syndrome. After an extended antibiotic regimen and placement of a chest tube, the patient fully recovered and was able to be discharged.

BACKGROUND

Lemierre's syndrome is the classic disease described 80 years ago¹ as an oropharyngeal infection complicated by thrombophlebitis of the internal jugular vein. This syndrome is commonly caused by *Fusobacterium necrophorum* and can spread septic emboli to the lungs and soft tissues. However, the clinical spectrum of infections produced by fusobacteria is wide, and it is not always possible to identify a primary focus or even an oropharyngeal infection. Fusobacteria are commensal, anaerobic, Gram-negative rods usually found in the oropharynx and gastrointestinal tract. They can penetrate the mucosal surfaces only in certain situations, most of which are associated with altered host defence mechanisms.²

CASE PRESENTATION

A 25-year-old woman was admitted to our hospital with right-sided chest pain with pleuritic characteristics, dyspnoea, dry, non-productive cough and fever. The patient had a history of Crohn's disease and was on infliximab. She had been diagnosed with pharyngitis and a cold by her general practitioner a couple of weeks earlier. At that time, she had a runny nose, nasal congestion, headache and cough. Although she had been on amoxicillin 500 mg three times per day for 7 days and azithromycin 500 mg daily for 3 days, our patient did not improve.

On physical examination, she had a fever (38.6°C), heart rate of 94 bpm, respiratory rate of 18 breaths/min, blood pressure of 104/60 mm Hg and oxygen saturation of 96% on room air. The

oropharyngeal examination was normal and she had no periodontal disease. The otoscopic examination was also normal. On auscultation, heart sounds were normal, but we found crackling sounds in the base of the right hemithorax.

INVESTIGATIONS

Laboratory tests revealed a white cell count of $19\,400/\mu\text{L}$, with 87% neutrophils and 13% bands, haemoglobin 126 g/dL and platelet count of $233 \times 10^9/\text{L}$. C reactive protein was 264 mg/dL (normal level: <5 mg/dL). Kidney and liver panels were normal.

The chest X-ray showed an opacity in the right lower lobe (figure 1A), leading us to the diagnosis of community-acquired pneumonia. Given the patient was immunocompromised, we considered drug-resistant pathogens, so we decided to initiate ceftriaxone 2 g daily and levofloxacin 500 mg daily.³ However, after 72 hours of antibiotic treatment, the fever was still present and the patient did not improve. She had chills, and was pale and sweaty on examination. We found dullness to percussion, and decreased breath sounds in the right hemithorax. In addition to this clinical worsening, we performed a repeat chest X-ray, which showed right pleural effusion (figure 1B), which was not present in the previous X-ray. Ultrasound confirmed the effusion in a pleural space of 9–11 mm, with a consolidation which appeared isoechoic with the liver and was referred to as lung hepatisation by the radiologist. We tried to place a percutaneous pigtail catheter for pleural drainage, but given the small amount of effusion, we were unable to do so.

Given the new onset of effusion and the clinical worsening, we decided to add linezolid in order to provide antibiotic coverage for resistant Gram-positive bacteria. However, 24 hours later, the patient presented with cough, malaise, dyspnoea and right-sided chest pain. Oxygen saturation on room air was 87%, heart rate was 100 bpm and blood pressure was 90/57 mm Hg. We then decided to perform a repeat chest X-ray, which showed that the right pleural effusion had worsened (figure 1C). The patient was therefore referred to the intensive care unit (ICU) and a chest tube was placed. The pleural fluid had the following characteristics: pH 7.42, white cell count $11 \times 10^9/\text{L}$ (neutrophils >95%), glucose 50 mg/dL and proteins 2.8 g/dL. Adenosine deaminase and lactate dehydrogenase were normal.

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Figure 1 Slide A shows the consolidation in the right lower lobe (arrow). Despite the antibiotic treatment, the repeat chest X-ray showed right pleural effusion (slide B, arrow). The pleural effusion worsened (slide C). Given the respiratory insufficiency, the patient was referred to the intensive care unit for a chest drainage tube to be placed. A chest CT scan, performed to rule out complications, showed bilateral pleural effusion, but no necrotising pneumonia or abscesses (slide D).

Culture of *Mycobacterium* species in Löwenstein-Jensen medium was negative. However, the pleural fluid culture revealed the isolation of *Fusobacterium necrophorum*. It showed antibiotic sensitivity to metronidazole, clindamycin, imipenem and piperacillin-tazobactam.

Although the initial diagnosis was a parapneumonic pleural effusion, given that pH >7.20 and glucose >60 mg/dL, the final diagnosis was changed to thoracic empyema since we confirmed an evident bacterial infection of the pleural liquid.

OUTCOME AND FOLLOW-UP

In the ICU, the patient underwent a neck and chest CT scan to assess complications and to rule out further complications such as abscesses or necrotising pneumonia (figure 1D). CT scan ruled out Lemierre's syndrome and septic emboli. Meropenem was initiated and ceftriaxone and levofloxacin were withdrawn. After the isolation of *F. necrophorum*, linezolid was also withdrawn. Our patient was on meropenem for 10 days. The duration of antibiotic therapy for bacterial empyema was determined based on the improvement of the patient. Factors that influenced our decision included the isolation of the pathogen, response to initial therapy and adequacy of drainage as assessed by radiographic resolution.⁴ The chest tube was able to be removed 48 hours after the ICU admission. She was referred to the admissions ward to complete the treatment and to undergo monitoring of her clinical progress and laboratory tests. In a repeat chest X-ray, the day before discharge, both the effusion and the lung consolidation had almost disappeared. The patient had fully recovered by the time of an outpatient follow-up 2 weeks later.

DISCUSSION

Although Lemierre's syndrome is the most widely recognised infection involving fusobacteria, the clinical spectrum can be wide, and clinicians can attend to patients with severe infections without any obvious oropharyngeal involvement, as with the current case.^{2 5 6} However, it is worth noting that *F. necrophorum* causes quite a distinct spectrum

of respiratory tract infections when compared with *F. nucleatum*. Therefore, findings from studies involving several fusobacterium species are not necessarily applicable on *F. necrophorum* infections. In two large studies focusing on invasive, disseminated infections with *F. necrophorum*, underlying conditions were rare in Lemierre's syndrome and other infections involving the upper respiratory tract.^{7 8} On the other hand, in elderly patients with fusobacterium disseminated disease with gastrointestinal or urogenital focus, severe underlying conditions such as malignancy are common both for *F. nucleatum* and for *F. necrophorum*. Concerning *F. nucleatum*, poor dental hygiene has to be considered.⁶

We would like to highlight immunosuppression as our patient's underlying condition. According to the above-mentioned statements, *F. nucleatum* cannot easily penetrate the mucosal barrier, unless there is a condition which facilitates the disruption, such as poor dental hygiene, periodontal disease, diabetes mellitus, malignancy, oropharyngeal infections or immunosuppression.⁶ However, the isolated pathogen was *F. necrophorum*. Our hypothesis was that our immunocompromised patient had an oropharyngeal infection that caused the disruption of the mucosal barrier which facilitated the penetration of *F. necrophorum*, or that the microorganism was somehow involved in the development of the upper respiratory tract infection. Either way, our hypothesis was that the infection was accompanied by lung involvement probably due to haematogenous seeding.^{6 9}

Pulmonary involvement caused by fusobacteria is uncommon. The most common finding is the presence of septic emboli and secondary lung abscesses caused by septic thrombophlebitis of the internal jugular vein. The presence of pneumonia and parapneumonic pleural effusion is rare if Lemierre's syndrome is not present.⁵

We would like to focus on the unusual finding of *F. necrophorum* in the pleural fluid. This pathogen requires a work-up in which Lemierre's syndrome should be ruled out. The neck and chest CT scan confirmed the absence of septic thrombophlebitis of the internal jugular vein and septic emboli. Also, if possible, molecular detection or culture for *F. necrophorum* from the tonsils should be performed. Although our young patient had a pharyngitis and a cold a few weeks prior to admission, which can be a common presentation of Lemierre's syndrome, we could rule out such a diagnosis.

Despite the severity of the infections, mortality rates are low if treatment is promptly initiated with an antibiotic regimen, and surgical treatment, such as abscess drainage, if needed. If empyema is present, a chest tube must be placed. In some cases, intrapleural fibrinolysis may be needed.^{9 10}

Finally, we would like to emphasise that clinicians are often faced with common infections caused by uncommon microorganisms. Therefore, only a high clinical suspicion based on the patient's predisposing conditions can lead us to consider the causative pathogen. In our patient, antibiotic treatment was initiated, taking into account the most common causative microorganisms of community-acquired pneumonia and the immunosuppression. Worsening of the patient's condition and the new onset of pleural effusion made us consider other alternatives, and the isolation of *F. necrophorum* confirmed the final diagnosis.

Since *F. necrophorum* can form abscesses, physicians should be aware of the risk for prolonged or returning fever, and be prepared to look for abscesses despite correct antibiotic treatment and to treat them surgically if necessary.

Learning points

- ▶ *Fusobacterium necrophorum* is an anaerobic Gram-negative bacterium, often involved in Lemierre's syndrome. It is found as part of the normal genital, gastrointestinal and oral flora. Certain predisposing conditions may disrupt the mucosal barrier and allow the infection by fusobacteria.
- ▶ Infections caused by *Fusobacterium* species are uncommon, but they have a wide clinical spectrum. Some of them can be severe and can lead to sepsis or admission to an intensive care unit (ICU).
- ▶ Pneumonia with empyema may be part of the clinical spectrum, even in the absence of Lemierre's syndrome.
- ▶ Certain underlying conditions, such as malignancy, immunosuppression and diabetes mellitus, may predispose the patient to severe infections such as pneumonia and parapneumonic pleural effusion, which can lead to ICU admission or surgical management.
- ▶ Collecting samples for cultures, when possible, is a key factor in the selection of an antibiotic regime, especially when the clinical condition is worsening despite treatment for the most common pathogens.
- ▶ In the presence of *F. necrophorum*, prolonged or returning fever should alert clinicians to initiate a work-up to search for abscesses or other complications.

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