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Case report

A Malaysian ex-smoker with cough, breathlessness and nonresolving bronchospasm

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A 60-year-old, Malaysian ex-smoker with no known medical illness was referred from a district hospital for severe acute exacerbation of COPD secondary to pneumonia. He had a 40-pack-year history of smoking but had quit smoking for the past 2 years.

He was admitted with a fever and productive cough for 5 days, associated with breathlessness and wheezing. He had no other symptoms, including haemoptysis. There was no recent history of travel and no previous exposure to tuberculosis.

Upon review, the patient was tachypnoeic, speaking in short sentences with audible wheeze, suprasternal recession and intercostal recession. His respiratory rate was 40 breaths per min. He was febrile at 38.5°C with a blood pressure of 129/69 mmHg and heart rate of 130 beats per min. Oxygen saturation measured by pulse oximetry (S_{pO_2}) was 98% under oxygen supplementation. There was generalised rhonchi on auscultation and he had clubbed fingers. No murmur could be elicited and there was no sign of heart failure.

Task 1
What is your provisional diagnosis and immediate management?

The arterial blood gas immediately after intubation showed pH 7.25, carbon dioxide tension 68 mmHg, oxygen tension 377 mmHg, bicarbonate 30.1 mmol·L^{-1} and S_{pO_2} of 99.7% under an inspiratory oxygen fraction of 100%. Other blood tests showed white blood cells 8.8×10^9 per L (neutrophils 89%, lymphocytes 5.2%), haemoglobin 11 g·dL^{-1}, platelets 160×10^9 per L, urea 6.2 mmol·L^{-1} and creatinine 49.6 mmol·L^{-1}. Albumin was 25 g·L^{-1}, alanine aminotransferase was 47 U·L^{-1}, aspartate aminotransferase was 73 U·L^{-1}, alkaline phosphatase was 90 U·L^{-1} and creatinine kinase was 471 U·L^{-1}.

Answer 1
The provisional diagnosis was acute exacerbation of COPD. Intravenous hydrocortisone 200 mg and loading of *i.v.* aminophylline 250 mg was administered. Repeated nebulised ipratropium bromide and salbutamol were given. However, his condition did not improve and he was intubated for acute respiratory failure.

@ERSpublications
Repeated noisy breathing may be a tricky feature of lung infection. Recognising classical features in radiographs and CT scans may help in the diagnosis of severe lung infection and the start of life-saving treatment. http://bit.ly/2lQwe5y

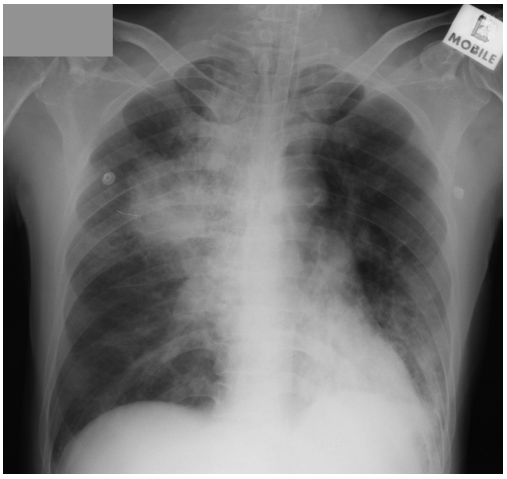

Figure 1 *Chest radiograph taken after the patient was intubated.*

Task 2
A chest radiograph, taken post-intubation, is as shown in figure 1. Can you describe the findings? What test would you like to do next?

Answer 2
The chest radiograph was rotated, and showed ill-defined heterogenous opacity in the right perihilar and right upper zones with the presence of air bronchogram within, suggestive of pneumonia.

Tracheal aspirate (TA) and blood samples were sent for culture and sensitivity testing (C&S). A TA for acid-fast bacilli (AFB) and *Mycobacterium tuberculosis* C&S were also tested. *i.v.* cefepime and *i.v.* azithromycin were started, and the patient was ventilated in the intensive care unit (ICU). Serial chest radiographs were performed over the next few days.

Task 3
Describe the serial chest radiographs (figure 2). What are your differential diagnoses and what tests would assist you in making the diagnosis?

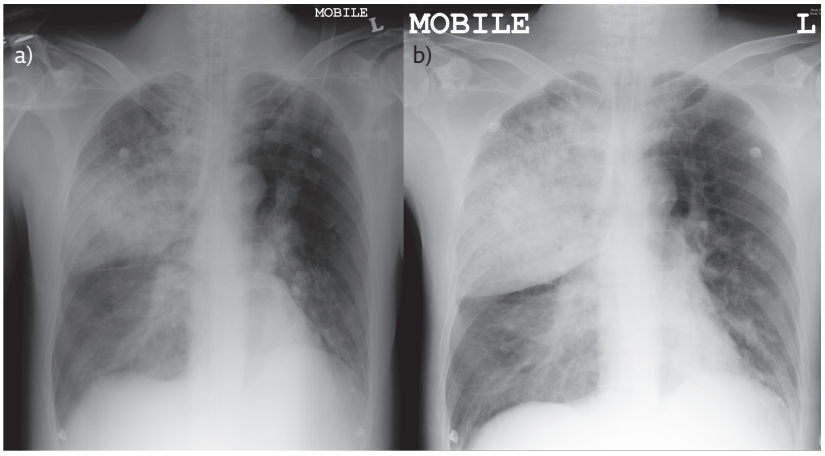

Figure 2 *Chest radiographs taken on a) day 5 and b) day 8 of mechanical ventilation.*

Answer 3
Subsequent chest radiographs showed lobar consolidation with a bulging horizontal fissure. Differential diagnoses include severe Friedlander pneumonia with sepsis, right upper lobe abscess and lung cancer. Contrast-enhanced (CE) computed tomography (CT) of the thorax was subsequently performed to rule out a space-occupying lesion.

Task 4
What did the CECT scan of the thorax show (figure 3)?

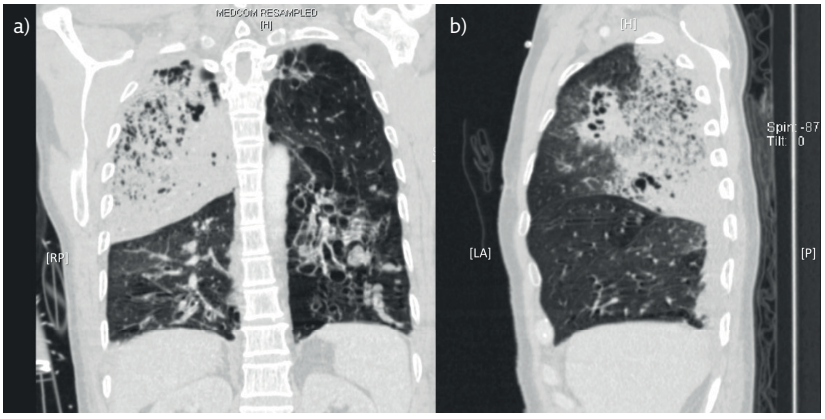

Figure 3 *CECT scan of the thorax: a) coronal view; b) sagittal view.*

Answer 4
The CECT scan of the thorax in the lung window showed a bulging horizontal fissure that was more marked at the posterior aspect. This "bulging fissure sign" is a classical feature of Friedlander pneumonia. There was also multiple cystic lesion of variable sizes indicating underlying cystic bronchiectasis.

Task 5
Based on the patient's history and radiological findings, which is the most common causative pathogen?

a. *Staphylococcus aureus*
b. *Klebsiella pneumoniae*
c. *Legionella pneumophila*
d. *Haemophilus influenzae*

Answer 5

b. *K. pneumoniae* is the most common pathogen causing the bulging fissure sign [1].

TA C&S taken after the patient was intubated grew methicillin-sensitive *S. aureus* on the third day of admission. It was sensitive to oxacillin and erythromycin. Epithelial cells were not seen and the polymorphonuclear (PMN) cell count was 1–5 per high-power field (HPF). Blood C&S, TA for AFB and *M. tuberculosis* C&S were all negative. Thus, *i.v.* cloxacillin was added. *i.v.* cefepime was discontinued after completing the course of 1 week.

Unfortunately, 2 days after the cefepime was off (*i.e.* 4 days after *i.v.* cloxacillin was started), the patient developed a fever, a hypotensive episode requiring the support of a vasopressor and C-reactive protein was raised to 145.9 mmol·L^{-1}. Antibiotics were changed to piperacillin/tazobactam to cover the spectrum of *K. pneumoniae* and *P. aeruginosa*. Subsequently, the patient's condition improved, and he was successfully extubated 4 days later and discharged home well after 4 weeks of hospitalisation. Follow-up chest radiography post-discharge showed resolution of the pneumonia (figure 4) (see figure 5 for timelines).

Discussion

Friedlander pneumonia is a severe form of community-acquired pneumonia with a high rate of mortality and morbidity [2]. It is commonly caused by *K. pneumoniae*, a Gram-negative bacterium that is frequently found in the alimentary tract and skin, as well as in natural environments. In 1883, this bacterium was first isolated by Friedlander from fatal cases of pneumonia; thus, the disease has also been known as Friedlander pneumonia. The potential risk factors for Friedlander pneumonia include diabetes mellitus, smoking, COPD and alcoholism [3, 4]. Characteristic radiological features of Friedlander pneumonia include a bulging fissure sign from chest radiography and thorax CT scan, which typically causes lobar infiltrates in the posterior aspect of the right upper lung. The bulging fissure sign has been regarded as a classical but nonspecific [5] feature of pneumonia caused by *K. pneumoniae*. It occurs due to exudates produced by the causative organisms that expand the lobe and cause a "bowing" or a "bulge" in the fissure. This can also be due to severe lung infection caused by *Streptococcus pneumoniae*, *P. aeruginosa* and *S. aureus* [6]. Other diseases that (less commonly) manifest a bulging fissure include pneumonia caused by *L. pneumophila* [7] or *M. tuberculosis* [1, 8], or any space-occupying process in the lung, such as pulmonary haemorrhage, lung abscess or tumour [9].

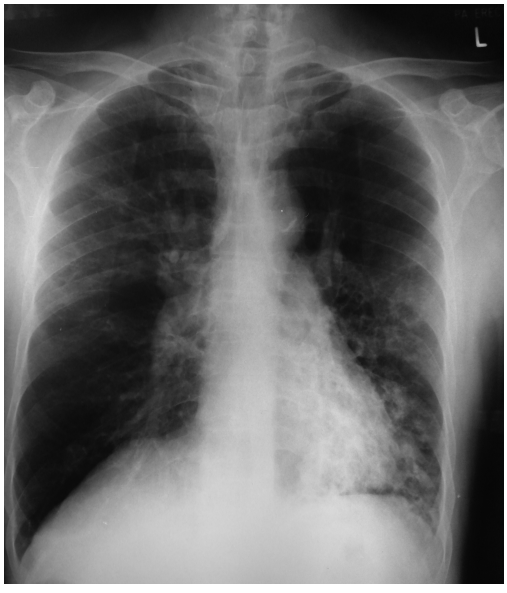

Figure 4 *Follow-up chest radiograph post-discharge showed resolution of right lung consolidation. Multifocal cystic lucencies representing cystic bronchiectasis can be seen in the right upper and left lower lobes with adjacent fibrosis.*

In this patient, sputum culture and sensitivity were first thought to grow *K. pneumoniae*. However, it turned out to be *S. aureus*, a Gram-positive bacterium, which was sensitive to erythromycin and oxacillin. Since *S. aureus* infection is also a causative agent of a bulging fissure sign [10], commencement of *i.v.* cloxacillin was justifiable. *i.v.* cefepime was off after 1 week.

Unfortunately, the patient did not respond well and his condition deteriorated 2 days later. He developed fever and hypotension requiring the commencement of vasopressor support, indicating a new bout of sepsis. Antibiotics was changed to piperacillin/tazobactam, which covers the spectrum of causative organisms associated with bulging fissure, *i.e. K. pneumoniae*, *P. aeruginosa* and *S. pneumoniae*. His condition improved even though the second blood and TA C&S did not yield any organisms.

Causes of false-positive and false-negative culture results should always be taken into consideration. In this patient, TA C&S were associated with a low PMN cell count (1–5 cells per HPF). This could be a false-positive result or misinterpretation of a "coloniser" as an "infection". This is because *S. aureus* is part of the normal flora found on the skin and mucous membranous area of the nose, mouth and throat, and is commonly encountered in daily living [11]. False-positive cultures of environmental organisms and other contaminants is not uncommon [12].

However, causes of false-negative culture results include inadequate samples, poor-quality samples and prior antimicrobial exposure. Bacterial counts may differ by 50-fold in areas of infected lung *versus* noninfected adjacent areas, which may also lead to a false-negative C&S finding of the second TA sample.

Alternatively, it could be a case of concomitant *S. aureus* and *K. pneumoniae* or *P. aeruginosa*

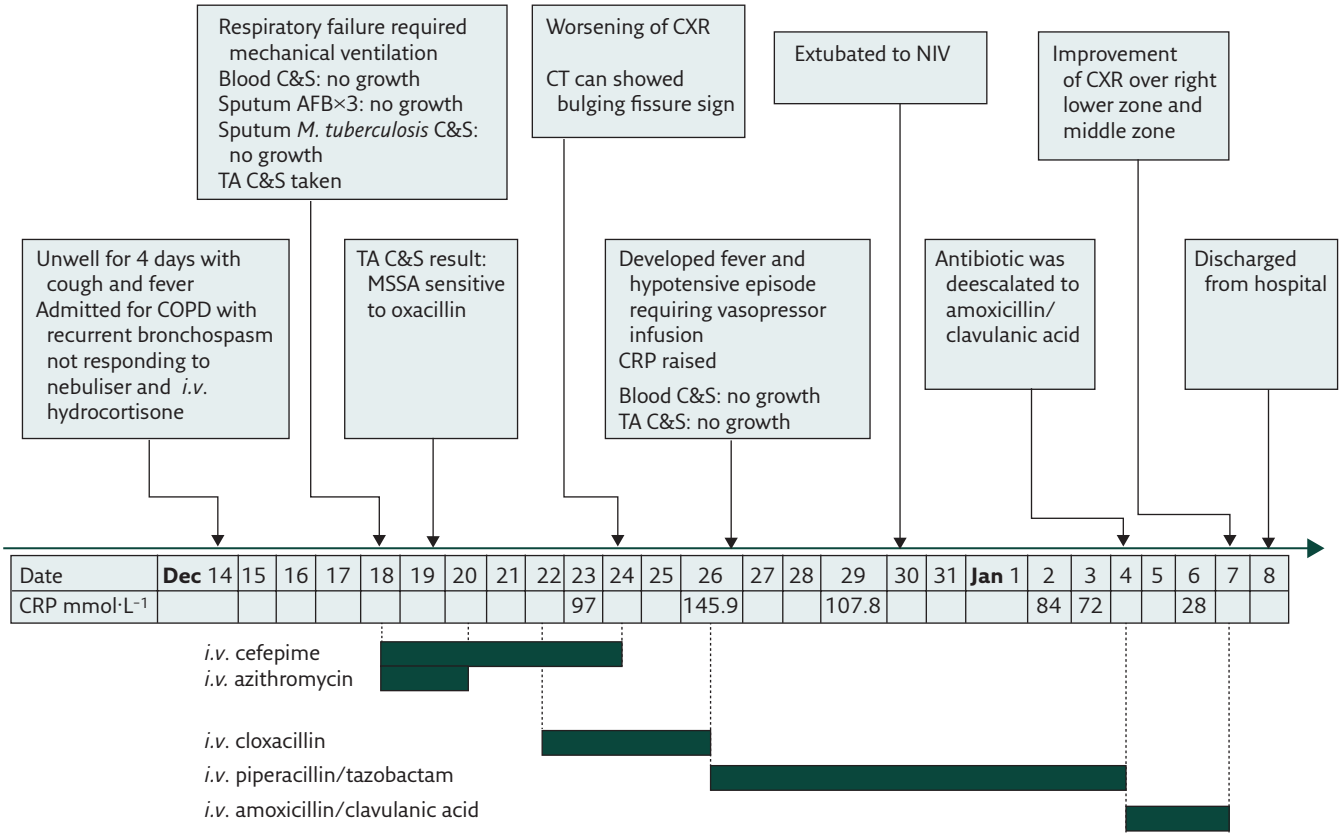

Figure 5 *Timeline of presentation, events, treatments and progress of patient with Friedlander pneumonia. MSSA: methicillin-sensitive Staphylococcus aureus; CXR: chest radiograph; CRP: C-reactive protein.*

infection. Cases of concurrent *K. pneumoniae* and methicillin-resistant *S. aureus* infection had been reported [13]. Concurrent infection occurs more frequently among patients with underlying comorbidities such as COPD and reported has a significantly higher mortality rate [13].

From the CT scan of the thorax, this patient had underlying bronchiectasis, which explains his clubbed fingers. Chronic lung disease is a risk factor for the occurrence of severe Friedlander pneumonia with sepsis in this case. A high index of suspicion is the key to management of similar patients.

Conclusion

Recurrent bronchospasm may be a presenting feature of lobar pneumonia. Recognising classical features of Friedlander pneumonia in radiological investigations may help in the diagnosis and life-saving treatment of similar patients.

Affiliations

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Conflict of interest

J.A. Lim has nothing to disclose. N. Caruppaiya has nothing to disclose. N. Zainol Abidin has nothing to disclose. B.T. Khor has nothing to disclose. T. Palanivelu has nothing to disclose. S.D. Hukam Gopal Chand has nothing to disclose. A. Ibrahim has nothing to disclose.

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