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Relapsing life threatening community acquired pneumonia due to rare *Legionella* species responsive to ceftriaxone and aztreonam

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Summary
A 24 year old Saudi housewife was admitted thrice with life threatening community acquired pneumonia. Even though she responded to an initial cocktail of cefriaxone, erythromcin, rifampicin and flucloxacillin during the second admission, she relapsed within four days of discharge when she was on erythromycin only. During the third admission she was put on ceftriaxone and aztreonam and recovered fully without any relapse. Serology results received later showed *Legionella* IgM titres of more than 1:256 for *Legionella micdadei* and *Legionella bozemanii*, and IgG titres of *Legionella hackeliae*. This case demonstrates relapsing pneumonia due to *Legionella micdadei* and *bozemanii* infection, and previous exposure to *Legionella hackeliae*. Both species, that is, *Legionella micdadei* and *bozemanii*, are resistant to erythromycin, but responded very well to a combination of ceftriaxone and aztreonam have not been used previously for the treatment of Legionnaires diseases.

Keywords: *Legionella bozemanii, Legionella micdadei, Legionella hackeliae, Cefriaxone, relapsing pneumonia.*

Résumé
Une femme de menage Saoudienne de 24 ans a été admise 3 fois de suite d'une pneumonie menancant la comminautée. Quoique elle avait respondue au traitement initiale fait d'un cocktail d'antibiotique (ceftriaxone, erythromycin, rifampicine, flucloxacilin) pendant la seconde admission, mais elle n'a pas rechutée quartre jours apres sa decharge l'orsqu elle etait sous traitement d'erythromycine suelement. Pendant la troisieme admission, elle a été traitéduec du ceftriaxone et láctereonam. Elle a été complemetement querrier et n'a plus eu de pneamonie. Les resultats serologiques recut plutard ont montré que le titres des IgM ceontre les legionella a été 1:25 pour le legionella micdadec et leginella bazemannii et les titres de IgG de Legionella hackelia. Ce cas a demontré un cas de rechute de pneumonie due à une infection de legionella micdadei et bozemanii, et une exposition precedente due à la legionella hackeliae. Les deux especes (Legionella micdadei et bozemanii) sont resistant à l'erythromycine mais ont été sensible à une combinaison de ceftriaxone et aztreonam. A nobre connaissance, la ceftriaxone et la aztreonamie n'ont pas encore utilisé pour le traitement des maladies legionaires.

Introduction

Legionnaires' disease was first described in 1976 when a number of fatal cases of severe pneumonia were reported among persons attending American Legion Convention in Philadelphia, Pennsylvania, USA [1].

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Pneumonia caused by *Legionella pneumophila* and other *Legionella* species is known to occur globally in sporadic, endemic and epidemic forms [2].

Legionellosis is caused by a fastidious, aerobic, gram negative bacillus which is found commonly in the environment [3] and associated with surface water of lakes, streams, cooling towers, air conditioning systems, cold water storage tanks, shower systems and dusty atmospheres.

Epidemiologic studies of general populations indicate that legionella is a common cause of pneumonia. Prevalence rates between 1 and 15% have been attributed to legionella species for community-acquired pneumonia in USA, Canada and Europe [4].

Legionella pneumophila accounts for more than 95% of cases of Legionnaires diseas. *Legionnella micdadei* is the other important species that commonly causes human illness and has been a cause of major nosocomial outbreaks [5].

Halim *et al.* (1992). reported a series of 18 patients with *Legionella pneumophila*, community acquired pneumonia, in Riyadh [6].

Damash *et al.* (1994). from Riyadh, Saudi Arabia reported four cases of overwhelming respiratory failure due to *Legionella pneumophila* pneumonia [7].

We hereby report a case of life-threatening, community-acquired relapsing pneumonia which was caused by a concomitant *Legionella micdadei* and *Legionella bozemanii* infection with previous exposure to *Legionella hackeliae* and successfully treated with ceftriaxone and aztreonam. To our knowledge, ceftriaxone and aztreonam have not been used previously for the treatment of Legionnaire's disease.

Case report

First admission

A 24-year-old Saudi housewife was admitted with a history of dry cough and fever followed by shortness of breath and left sided pleuritic chest pain of two days duration. She later developed minimal mucoid sputum with occasional streaking of blood and anorexia.

On examination she looked ill, breathless, centrally cyanosed, anxious and febrile (temperature 38°C). Blood pressure was 110/70, while pulse was 120/minute regular. Ear nose and throat (ENT) examination was normal. Chest: bilateral late inspiratory crackles mid and lower zones posteriorly and anteriorly. Cardiovascular system (CVS), gastrointestinal system (GIT) and central nervous system (CNS) were unremarkable.

Investigations: Hb 13 g%, while blood cells (WBC) 12000/cmm, differential: polymorphs 88%, lymphocytes 10% monocytes 1.5% eosinophils 0.5%. Arterial blood gases (ABG) on room air pH 7.49, PCO_2 28 mm Hg, PO_2 43 mm Hg, O_2 saturation 83%. Chest X-ray: bilateral air bronchograms at both hila, bilateral mid and lower zones micronodular and alveolar shadows. She was treated with amoxycillin, erythromycin and 40% oxygen.

Because she was a little better on the fifth day she was discharged and advised to carry on with the above drug treatment for 10 days more.

Second admission

She was readmitted three days after discharge under the pulmonary service with anorexia, evening pyrexia, sweating and dyspnoea with severe cough productive of yellow sputum. On examination she was very ill-looking, breathless, cyanosed with a temperature of 37.7 °C and a respiratory rate of 40 per minute, pulse rate 130 per minute, regular, blood pressure 100/70 mm Hg. Chest examination revealed scattered late inspiratory bilateral crackles. CVS, GIT and CNS were unremarkable.

Investigations:

Hb 12.4 g%, WBC 13,420 per cu/mm, differential: polymorphs 90.4%, lympocytes 7.6%, monocytes 1.8%, eosinophils 0.2%. ABGs on room air: pH 7.42, PCO_2 32 mm Hg, pO_2 45 mm Hg, HCO_3 23 mmol/L, SaO_2 84% electrolytes, urea and creatinine were normal. Liver function tests (LFT) showed slightly raised transaminases and low albumin. HIV screen, Hepatitis B surface antigen (HbsAg), Anti-nuclear factor (ANF), LE cells, Rheumatoid factor, blood culture and Mantoux test were negative. Sputum acid fast bacilli (AFB) and Gram stain were negative. Chest X-ray: billateral extensive shadowing showing nodularity in mid and lower zones. Air bronchograms in the hilla as before. Some areas were showing alveolar pattern. Bone marrow showed no evidence of tuberculous granuloma. Mycoplasma and chlamydia pneumoniae serology results were also negative. She was admitted to the Intensive Care Unit and was started on 50% Oxygen along with erythromycin 1g six hourly iv and amoxycilling 1gm iv six hourly and was monitored by pulse oximetry, but her condition continued to deteriorate, with severe hypopxaemia, high fever and at this stage she required 60 – 70% Oxygen by non-rebreathing reservoir mask. [Fig. 1] She was provided full cover for tuberculosis till the results of sputum. Mantoux test and bone marrow were known. These being negative, the drugs, INH, pyrazinamide and ethambutol were stopped but rifampicin was continued in a dose of 600 mg bd for Legionella cover. Amoxycillin was stopped and it was replaced by ceftriaxone 2 gm iv 12 hourly and flucloxacillin 1 g iv six hourly was added to provide cover for Staphylococcus aureus. These changes were made four days after admission when her condition was found to be deteriorating. She started to improve, was afebrile while her oxygen requirements lessened and she was ultimately weaned off oxygen and chest X-ray also cleared. [Fig. 2] Flucloxacilling was stopped after five days treatment. Ceftriaxone and rifampicin were discontinued on day 14 of her admission having received 10 days course. She was discharged on day 14 when she was fully mobile and asymptomatic. The medication on discharge was erythromycin 500 mg six hourly for seven days.

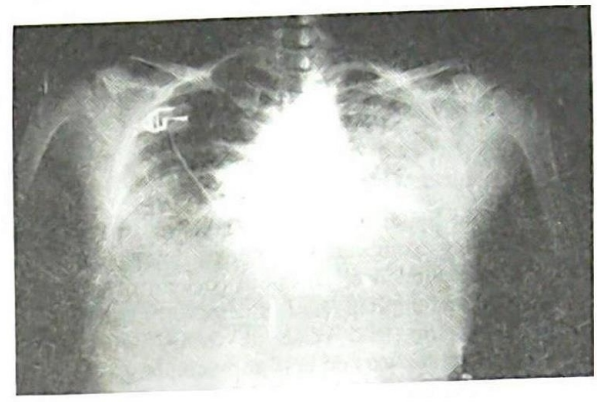

Fig. 1: Chest x-ray during second admission

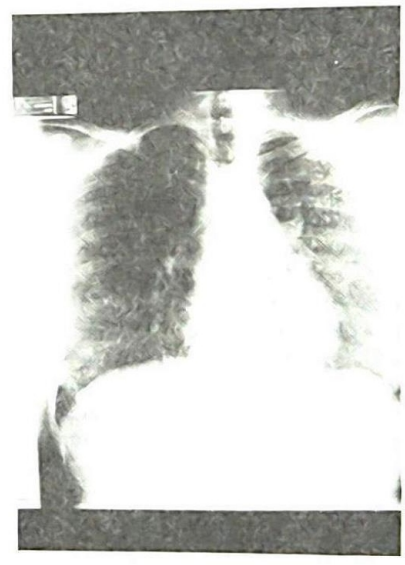

Fig. 2: Normal chest x-ray two days before discharge from her second admission

Third Admission

She returned five days after discharge when she had recurrence of symptoms of shortness of breath, cough and fever. She also developed weakness and diarrhoea.

On examination, she was orthopnoeic, cyanosed and looked very ill. Temperature was 38.7 °C, pulse 140/minute, regular. BP 90/60. Respiratory rate 45/minute Chest: scattered late inspiratory crackles both lung fields CVS, GIT and CNS were unremarkable.

Investigation: Hb 12.7 g%, WBC 12,000/cmm differential polymorphs 88%, lymphocytes 10%, monocytes 2%, with normal platelets. Electrolytes, urea, creatinine were normal. LFTs showed slightly raised transaminases. ABGs on 40% oxygen was pH 7.45, PCO_2 30 mm Hg, PO_2 49.9 mm Hg, HCO_3 20.7 mmol/L, O_2 saturation 87%.

Chest X-ray: findings were the same as in her first admission. [Fig 3]. Stool culture: no pathogens were grown. She was put on 70% O_2 by non-rebreathing reservoir mask and started on ceftriaxone 2 g iv 12 hourly and aztreonam 1 g iv eight hourly. These antibiotics were started empirically to give broadest possible cover and especially since ceftrizone probably had good effect during the last admission.

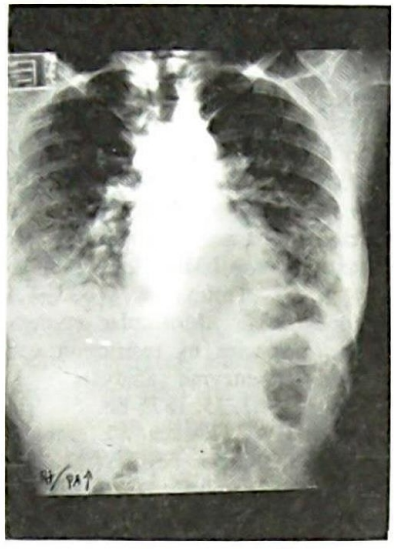

Fig. 3: Reappearance of bilateral infiltrates, third admission

Patient started showing signs of improvement after 48 hours and her O_2 requirement gradually came down over the next seven days. She was off O_2 and her chest X-rays ultimately came back to normal [Fig. 4] after two weeks of antibiotic treatment and she was allowed to go home. She was reviewed in the follow-up clinic after two weeks and when she was in excellent condition and had a normal chest X-ray. Serology was received by this time which showed Legionella antibody titre of more than 1:256. Immunofluorescent typing also demonstrated IgM antibody as *Legionella bozemanii* and *Legionella micdadeii*. Immunofluorescent typing demonstrated IgG antibody as *Legionella bozemanii, Legionella micdadei,* and *Legionella hackeliae*.

Environmental sampling from the house of the patient did not reveal any organisms on culture.

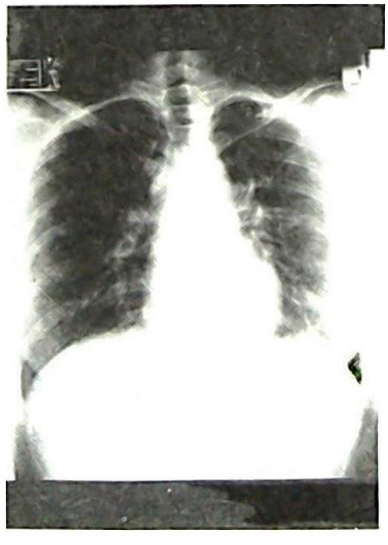

Fig. 4: Normal chest x-ray in clinic two weeks after discharge from third admission.

Discussion

This case presented some unusual features of relapsing pneumonia, especially when the patient was placed on erthromycin after discharge. *Legionella bozemanii* infection is characterised by progression of pneumonia despite therapy and relapse when treatment is stopped [8]. *L. micdadei* and *L. bozemanii* are resistant to erythromycin as reported by many workers [9,10,11,12]. Infection by more than one species is reported by other workers [13,14,15]. The species usually involved were *L. pneumophila* and *L. micdadei*. This case demonstrated positive serology for acute infection with *L. micdadei, L. bozemanii* and previous exposure to *L. hackeliae*. Tompkin *et al* (1987) reported a case with pneumonia in a cardiac transplant patient infected simultaneously with *L. pneumophila, L. dumoffii* and *L. micdadei* [16]. The severity of the illness in our case who was otherwise healthy is most probably the result of synergistic interaction between two species. Our case is the first with infection of three species of legionella in Saudi Arabia. During her third admission, we started the patient with ceftriaxone and aztreonam. By this time the serology results had not yet been received. To our surprise she had a dramatic response after 24 hours and within 36 hours her temperature came down, and from then onwards she kept on improving. After completing two weeks of intravenous antibiotic therapy she was discharged with normal chest X-rays. [Fig 4].

This antibiotic therapeutic regimen has not been reported previously in legionellosis. There are anecdotal reports of successful treatment of legionnaire's disease by cephalosporins like cefamendole in *L. hackelia* pneumonia [17]. Our patient was receiving ceftriaxone during her second admission in addition to erythromycin and rifampicin. We believe she responded to ceftriaxone and not to erythromycin as she relapsed when she was sent home on the same treatment. The mere fact that she didn't relapse after receiving a two-week course of ceftriaxone and aztreonam is indicative of the fact that she responded to ceftriaxone during the second admission. Whether or not aztreonam has any role in her treatment is an open question. We believe it probably did play some role as she didn't relapse after treatment during her third admission.

This is the first case report of legionellosis due to *L. micdadei* and *L. bozemanii* in an immunocompetent patient who had previously been exposed to *L. hackeliae* in Saudi Arabia.

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