CASE REPORT

Case Report: First report of *Elizabethkingia miricola* infection in a patient with cystic fibrosis [version 1; referees: 2 approved with reservations]

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**Abstract**

*Elizabethkingia miricola* is a rare non-fermenting Gram-negative rod that has previously been reported to be associated with blood stream and pulmonary abscess infections, but never before in cystic fibrosis (CF). Here we present the first reported case of *Elizabethkingia miricola* infection in a patient with CF and discuss the management options. We describe a patient with CF in whom we observed clinical and spirometric evidence of pulmonary exacerbation with the associated growth of *E. miricola* in sputum culture. The period of clinical instability was observed to coincide with the obtainment of four sputum samples from which *E. miricola* was cultured; improvement was seen following treatment with ciprofloxacin and the subsequent eradication of *E. miricola*. We conclude that *E. miricola* is able to survive in the CF lung and in this case was associated with pulmonary exacerbation. Empirical treatment with fluoroquinolones is appropriate, based on our experience.

**Keywords**

Cystic fibrosis, shortness of breath, chest infection, exacerbation, fluoroquinolone

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**Author roles:** Frost F: Conceptualization, Data Curation, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing; Nazareth D: Conceptualization, Writing – Original Draft Preparation, Writing – Review & Editing

**Competing interests:** No competing interests were disclosed.

**How to cite this article:** Frost F and Nazareth D. Case Report: First report of *Elizabethkingia miricola* infection in a patient with cystic fibrosis [version 1; referees: 2 approved with reservations] F1000Research 2018, 7:440 (doi: 10.12688/f1000research.14441.1)

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**Grant information:** The author(s) declared that no grants were involved in supporting this work.

**First published:** 10 Apr 2018, 7:440 (doi: 10.12688/f1000research.14441.1)
Introduction

*Elizabethkingia miricola*, a non-fermenting Gram-negative rod (NFGNB) was first identified following isolation from condensation water in the Russian space laboratory Mir. Originally identified as belonging to the *Chryseobacterium* genus, it has since been re-classified and is closely related to *Elizabethkingia meningoseptica* (previously *C. meningosepticum*). *E. miricola* has been demonstrated to be pathogenic, with reports of bacteraemia resulting in sepsis and pulmonary abscesses\(^2\). Here, we report the presence of *E. miricola* in the sputum of a patient with cystic fibrosis (CF). To our knowledge, this is the first reported case of *E. miricola* infection in CF; herein, we discuss the case itself and the literature surrounding this bacterium to help guide clinicians faced with similar clinical scenarios.

Case report

A 49-year-old male with a diagnosis of CF presented to his routine CF outpatient department complaining of feeling generally unwell. He reported increased cough, but this was non-productive. There was a drop in lung function, from a baseline forced expiratory volume in one second (FEV1) of 2.39 l (65% of the predicted volume) to 2.19 l (60% predicted). A sputum sample was taken and sent for routine culture, but given the non-specific symptoms and mild drop in FEV1, it was agreed that no immediate treatment was required and a follow-up in 4 weeks’ time was arranged.

Co-morbidities of the patient included osteoporosis and pancreatic insufficiency; he was also receiving treatment for allergic bronchopulmonary aspergillosis (ABPA). Cultured respiratory samples in the previous year had consistently grown non-epidemic *Pseudomonas aeruginosa*. The diagnosis of CF was made in adulthood and was based on the presence of bilateral bronchiectasis on a chest CT scan, a raised chloride level following a skin sweat test and genetic testing, which revealed that the patient was heterozygous for the CFTR F508del mutation. Family history included a younger sister who had died aged 23 years from pancreatitis.

A sputum sample taken at the clinic appointment was positive for *P. aeruginosa*, and extended incubation isolated *Elizabethkingia miricola*. At the next appointment, worsening symptoms were observed, including increasing shortness of breath, wheeze and productive cough. There was a further drop in FEV1 to 1.91 L (52% predicted) (Figure 1). On the basis of outcomes of previous infective exacerbations, an oral course of chloramphenicol (500 mg four times a day) along with prednisolone (30 mg daily) for 2 weeks was commenced and a further sputum sample was obtained. Sputum culture was again positive for *P. aeruginosa* and *E. miricola*.

A further 4 weeks later, symptoms were somewhat improved and FEV1 lung function had increased to 2.19 l (60% predicted). However, another 2 weeks later, symptoms deteriorated again, with an associated decline in lung function (FEV1, 1.95 l; 53% predicted). Sputum cultures from the previous admission were again positive for *P. aeruginosa* and *E. miricola*. Sensitivities from previous samples revealed *E. miricola* resistant to meropenem and ceftazidime, but sensitive to piperacillin/tazobactam and ciprofloxacin (CIP). A 2-week course of oral CIP (750 mg thrice daily) was therefore commenced.

The patient noted an improvement in symptoms and at the next clinic appointment FEV1 had improved to 2.08 l (57% predicted). Sputum then grew *P. aeruginosa* and yeast only. A further four subsequent sputum samples 1, 4, 8 and 12 months later have grown *P. aeruginosa* but no *E. miricola*, and lung function returned towards baseline.

Figure 1. Lung function before and after positive sputum culture for *Elizabethkingia miricola*. Lung function was measured using forced expiratory volume in one second (FEV1). Dotted lines represent the time period between which four sputum cultures were positive for *E. miricola*.
Discussion

*E. miricola* has been described in a number of healthcare settings, but not previously in CF. One of the first reports of *E. miricola* infection was of positive growth in blood and sputum cultures of a septic patient whom had recently undergone a stem-cell transplant for mantle-cell lymphoma. Since then it has been reported in only a handful of cases, including septicaemia in a young patient with alcoholic pancreatitis and in the sputum of a septic patient with pulmonary abscesses. More recently, *E. miricola* was identified as causing a UTI in an immunocompetent adult.

Here, we describe a patient with CF in whom we observed clinical and spirometric evidence of pulmonary exacerbation, with associated growth of *E. miricola* in sputum culture. The period of clinical instability was observed to coincide with four sputum samples culturing *E. miricola* and improvement was seen with treatment. This is the first report of *E. miricola* in an individual with CF, meaning this report should therefore be relevant to all CF clinicians and microbiologists involved in the care of people with CF.

All case reports of *E. miricola* infection mentioned above report identification by MALDI-TOF (matrix-assisted laser desorption/ionisation time-of-flight) mass spectrometry. MALDI-TOF has been widely adopted for bacterial identification, facilitating diagnosis quickly and reliably. In the CF setting, MALDI-TOF has also been shown to be particularly useful in identifying non-fermenting gram-negative bacteria, for which classification can be difficult using conventional phenotypic approaches. Given the increasing use of MALDI-TOF in clinical microbiology laboratories, identification of NFGNB infections is likely to rise. Hence, establishing the optimal initial management strategies for these infections is important.

In this case, initial empirical treatment with oral chloramphenicol did not clear the infection, but treatment with oral CIP (based on culture sensitivities) successfully treated the exacerbation.

Eradication of *E. miricola* was also observed, with contemporaneous clinical improvement. Notably, the sputum culture sensitivities revealed that *P. aeruginosa* was resistant to CIP, further supporting the idea that *E. miricola* had a pathogenic role. Our experience of treatment with a fluoroquinolone is in keeping with that of previous reports, in which *E. miricola* bacteraemia has been associated with sensitivity to levofloxacin and/or CIP, both of which resulted in successful treatment. Susceptibility to co-trimoxazole (SXT) has also been reported, and it would seem that treatment with fluoroquinolones or SXT is an appropriate empirical strategy.

Conclusion

*E. miricola* appears to have the potential to grow in the CF lung and can be associated with pulmonary exacerbation. Given the paucity of information on *E. miricola* infection in CF, we hope that the case report and literature review herein are relevant to CF clinicians and microbiologists alike. Treatment based on culture sensitivity is recommended, but empirical treatment with fluoroquinolones may be an appropriate initial strategy if there is suspicion of pathogenicity.

Consent

Written informed consent for the creation and publication of this report was obtained from the patient.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

References


Open Peer Review

Current Referee Status:  

Version 1

Referee Report 30 April 2018

doi: 10.5256/f1000research.15719.r33065

Andrew M. Jones
Manchester Adult Cystic Fibrosis Centre, University Hospital of South Manchester, Manchester, UK

This is the first case described as far as I am aware of Elizabethkingia mircola in a patient with cystic fibrosis. The authors describe isolation of Elizabethkingia mircola in association with clinical deterioration of a patient, and subsequent clinical improvement and eradication of the organism following quinolone therapy.

The report could be further improved by addressing the points below:

- The authors state in the first paragraph that the patient had a cough that was unproductive, but in contrast also state that a sputum sample was obtained.
- The report states that the patient was receiving treatment for ABPA; it is important to know what exactly the treatment was and in particular if this could have caused immunosuppression and lead to increased susceptibility to unusual infections.
- The authors state the patient was heterozygous for F508del; did they identify the other CF gene?
- The authors state Elizabethkingia mircola was isolated after extended incubation: what culture media was used and how long was the extended incubation before Elizabethkingia mircola was isolated?

Is the background of the case's history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.
I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Referee Report 23 April 2018

doi:10.5256/f1000research.15719.r33066

Simon C. Langton Hewer
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I agree that this appears to be the first report of this organism in CF and as such this is a relevant and important article and so should be published. The Case Report para 2 states the patient was heterozygous for CFTR mutation F508del but does not give the other mutation. Readers (including me) would be interested to know the second mutation so this should be stated.

Para 4 states treatment of P aeruginosa and E miricola took place with oral chloramphenicol. This is an unusual choice as P. aeruginosa would usually be treated with ciprofloxacin or IV therapies and/or nebuliser amino glycoside. It would be helpful to know why chloramphenicol was chosen and whether any neb antibiotics were used as well (which is likely the case).

These details should be included to give a more complete picture of the case.

Is the background of the case’s history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
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