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Original Article

Achromobacter species in cystic fibrosis: Cross-infection caused by indirect patient-to-patient contact☆

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Abstract

Background and methods: Achromobacter species leads to chronic infection in an increasing number of CF patients. We report 2 cases of *Achromobacter ruhlandii* cross-infection between patients after well-described indirect contact.
Results: Both cases were young, stable, CF patients without chronic infections and with normal FEV_1, but experienced clinical deterioration after visits to the home of a CF patient with *A. ruhlandii* infection and after sharing facilities with an *A. ruhlandii* infected CF patient on a skiing vacation, respectively. Both cases became positive for *A. ruhlandii* in airway secretions and were colonized with *A. ruhlandii* in their sinuses.

Aggressive, long-term antibiotic treatment led to clinical stability. One of the cases developed chronic *A. ruhlandii* infection.
Conclusion: A. species can cause cross-infection even after a short period of indirect contact between infected and non-infected CF patients. Patients should be followed closely for several months before the possibility of cross-infection is ruled out.

Keywords: Cross-infection; *Achromobacter xylosoxidans*; Pulmonary infection

1. Introduction

In cystic fibrosis (CF) patients, chronic, pulmonary infection caused by *Achromobacter species* is an increasing problem. Antibiotic resistance is common in *A. species* infection and develops early, making antibiotic treatment difficult. Although the prevalence of chronic *A. species* infection is low in most CF centers, chronic *A. species* infection may lead to rapid clinical deterioration in affected patients [2,3].

In the case of other Gram-negative infections in CF patients, cross-infection has been shown to take place with *Pseudomonas aeruginosa* [4–8] and *Burkholderia cepacia* complex (BCC) [9–13] and recommendations are to avoid close contact between chronically infected patients and patients without chronic, Gram-negative infections [14–16].

Transmission of *A. species* between CF patients has previously been reported [17]. Studies have shown transmission between closely related CF patients, i.e. siblings [18], or patients known to have had close, prolonged contact [3,19–23].

We present 2 cases of cross-infection between CF patients with no direct, but well-described indirect contact.

2. Methods

2.1. Study design

Clinical data used in this study were collected prospectively and stored in the Copenhagen CF Centre database from time of diagnosis and onwards.

☆ Data have been presented at the 35th European Cystic Fibrosis Conference in Dublin, June 2012, as abstract number 353 [1].

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After discovering the incidences of cross-infection described in this work, data were gathered retrospectively from the database.

2.2. Patients

All CF patients are seen on a regular, monthly basis. At all visits, the clinical status of the patients is assessed by weight, height and lung function parameters, forced vital capacity (FVC) and forced expiratory volume in 1s (FEV_1) (Masterscreen Pneumo, Jaeger) are obtained according to the American Thoracic Society guidelines, using reference values from Wang [24] and Hankinson et al. [25]. Lower respiratory tract secretions for microbiological investigation are obtained by coughing or by endo-laryngeal suctioning. Specific, precipitating antibodies are obtained at least once every year, in patients with a chronic lung infection every third month. Chronic infection is defined as more than 50% of positive sputum samples and/or elevated levels of specific, precipitating antibodies [26]. Intermittent colonization is defined as isolation of a CF related Gram-negative rod in less than 50% of the investigated sputum samples in the present year (*P. aeruginosa*, *A. species*, *Pandoraeae apista* or a BCC species) in a patient with no increase in specific antibodies. The diagnosis of CF is based on abnormal sweat electrolytes, characteristic clinical features and CFTR genotype.

2.3. Segregation policy

In the clinic, patients with CF-related chronic Gram-negative, pulmonary infections are isolated from patients without chronic infections, and patients are encouraged to avoid social interaction with other CF patients with chronic Gram-negative, pulmonary infections.

All horizontal surfaces are cleaned after an infected patient has been in a room, and the hygienic procedures are in accordance with the recommendations of the department of infection control in the hospital.

2.4. Pulsed field gel electrophoresis (PFGE)

Strains isolated from individual patients are stored on a yearly basis, and PFGE [27,28], using Spe I as restriction enzyme, is performed regularly to discover possible cases of cross-infection.

2.5. Multilocus sequence analysis

Isolates from the 2 cases and from the 2 chronically infected CF patients were investigated using multilocus sequence analysis [17] and compared to a reference strain of *Achromobacter ruhlandii*, the Danish epidemic strain that has infected multiple patients at Danish CF centers in Aarhus and Copenhagen [3,17,23], as previously described.

3. Results

3.1. Case 1: A girl born in April 1999

Diagnosis was made shortly after birth due to meconium ileus. Her CFTR genotype is ΔF508 homozygous and she has been followed with monthly controls in the outpatient clinic since diagnosis. Daily treatment included pancreatic enzyme replacement since birth, lung physiotherapy and from the age of 21 months, also daily Pulmozyme® inhalation.

Monthly endolaryngeal suctioning revealed intermittent colonization with *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Haemophilus influenzae* and occasionally *Staphylococcus aureus*. All infections were treated with 2 week courses of oral antibiotics.

Case 1 had had 2 isolates of *P. aeruginosa*. First ever isolate of *P. aeruginosa* was cultured in April 2006 and treated with 4 weeks of inhaled colomycin and oral ciprofloxacin. Second isolate of *P. aeruginosa* was cultured in March 2007 and was treated with 3 months of inhaled colomycin and oral ciprofloxacin. This time, the patient had an asthmatic reaction to colomycin and received bronchodilator-treatment.

Measurement of lung function was performed since the age of 5.5 years and was stable with FEV_1 above 100 % predicted (Fig. 1).

The girl lives in a small village on an isolated island. In 2006, another CF patient moved to the village with her family, including 2 twin sisters (non-CF) of the same age as Case 1. The 3 girls became friends and Case 1 came in the home of the 2 twin sisters and their 9 years older sister with CF and chronic *A. ruhlandii* infection, the Danish epidemic strain. The parents took great care never letting the 2 CF patients stay in a room simultaneously.

After completion of 3 months of anti-*P. aeruginosa* treatment in June 2007, Case 1 experienced weight-loss and a dramatic decline in lung function and showed no effect of bronchodilator-treatment.

Within a few weeks, sputum samples became positive for multi-resistant *A. species*, only sensitive to sulfometoxazole. PFGE showed that the *A. ruhlandii* strains from Case 1 and from the older CF patient were identical, indicating patient-to-patient transmission, and multilucos sequence analysis confirmed that Case 1 harbored the Danish epidemic strain (Fig. 3).

In April 2008, functional endoscopic sinus surgery (FESS) was performed and *A. ruhlandii* was cultured from the sinuses.

Inhaled ceftazidime and oral sulfometoxazole and trimetoprim were started immediately after culture of first isolate of *A. ruhlandii*. Inhaled ceftazidime has been given continuously since then and supplemented with courses of oral antibiotics and/or iv. antibiotics. In August 2008, inhaled antibiotics were changed to colomycin, but again the patient had an asthmatic reaction with a dramatic decline in lung function. Lung function immediately stabilized when treatment was switched back to ceftazidime.

The patient is clinically stabilized, but sputum cultures remain positive for *A. ruhlandii* and specific, precipitating anti-*A. species* antibodies have increased to a steady level around 7–10, and the patient is considered chronically infected.