Family case studies: absence of *Pseudomonas aeruginosa* transmission in bronchiectasis

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To the Editor:

Bronchiectasis, sometimes referred to as non-cystic fibrosis bronchiectasis (NCFB), is a chronic lung disease in which one or more bronchi become permanently dilated, resulting in mucus retention and airway inflammation [1]. It is characterised by repeated infective exacerbations and bacterial colonisation. In bronchiectasis, *Pseudomonas aeruginosa* is a significant pathogen, associated with increased mortality and acute hospital admission [2]. *P. aeruginosa* is an aerobic Gram-negative rod-shaped bacterium and a common nosocomial pathogen [3].

Cross-infection with *P. aeruginosa* in cystic fibrosis (CF) is well recognised, and has been described between CF patients, and from CF to non-CF individuals [4, 5]. This transmission occurs both in the community and nosocomially. Consequently, guidelines for CF advise strict segregation [6, 7]. However, the prevalence of cross-infection in NCFB is indeterminate.

To date, two single-centre studies identified *P. aeruginosa* cross-infection in NCFB through strain genotyping [8, 9]. De Soyza *et al*. [9] demonstrated one case of cross-infection in 36 nonsegregated NCFB. This finding was confirmed by a multicentre analysis of 91 NCFB patients in which whole-genome sequencing showed certain isolates had genetic similarity, implying cross-infection or common source acquisition [10]. Furthermore, Mitchelmore *et al*. [11] analysed *P. aeruginosa* in a nonsegregated NCFB population (n=46) and detected three cases of cross-infection in patients who shared a waiting room and lung function room.

The British Thoracic Society guidelines state that for NCFB, there is no evidence of *P. aeruginosa* transmissibility and that segregation is not routinely required [1], while the EMBARC Patient Advisory Group and the European Reference Network Bronchiectasis Network recommend that currently there is insufficient evidence to advise segregation [12].

We present two family case studies, all of whom have NCFB, in which household *P. aeruginosa* transmission does not occur, despite a significant contact history amongst the paired subjects. This supports the hypothesis that *P. aeruginosa* is less communicable in the NCFB population, compared to CF [10, 13].

In case 1, patient A was a 79-year-old man with an established diagnosis of severe idiopathic bronchiectasis (figure 1). His Bronchiectasis Severity Index (BSI) score was 17, indicating a 16.7–52.6% risk of hospitalisation at 1 year [14], and his Bronchiectasis Aetiology Comorbidity Index score was 2, indicating 5-year mortality of 11.7% [15]. He had multimorbidity, which included Parkinson's disease, percutaneous endoscopic gastrostomy (PEG) (weight 56.15 kg) and significant high-volume daily sputum production (estimated $\geqslant$60 mL·day^{-1}).

Patient A was colonised with *P. aeruginosa*. Over a 13-year period (2009–2022), he produced 50 purulent sputum samples for culture, with *P. aeruginosa* first isolated in 2009. *P. aeruginosa* has been isolated a further 28 times, with *in vitro* ciprofloxacin resistance developing in 2011. Additional bacteria isolated from sputum samples included the following. *Haemophilus influenzae:* 23 isolates with two isolates demonstrating co-trimoxazole resistance; *Escherichia coli:* six isolates; coliforms: four isolates; *Moraxella catarrhalis:* two isolates; *Streptococcus pneumoniae:* one isolate; and *Achromobacter xylosoxidans*: one isolate.

Shareable abstract (@ERSpublications)
Two case reports show lack of *Pseudomonas aeruginosa* transmission, despite household contact, in non-cystic fibrosis bronchiectasis (NCFB). This supports evidence that in NCFB, *P. aeruginosa* is poorly transmitted. This affects management strategies. https://bit.ly/3PeOcHy

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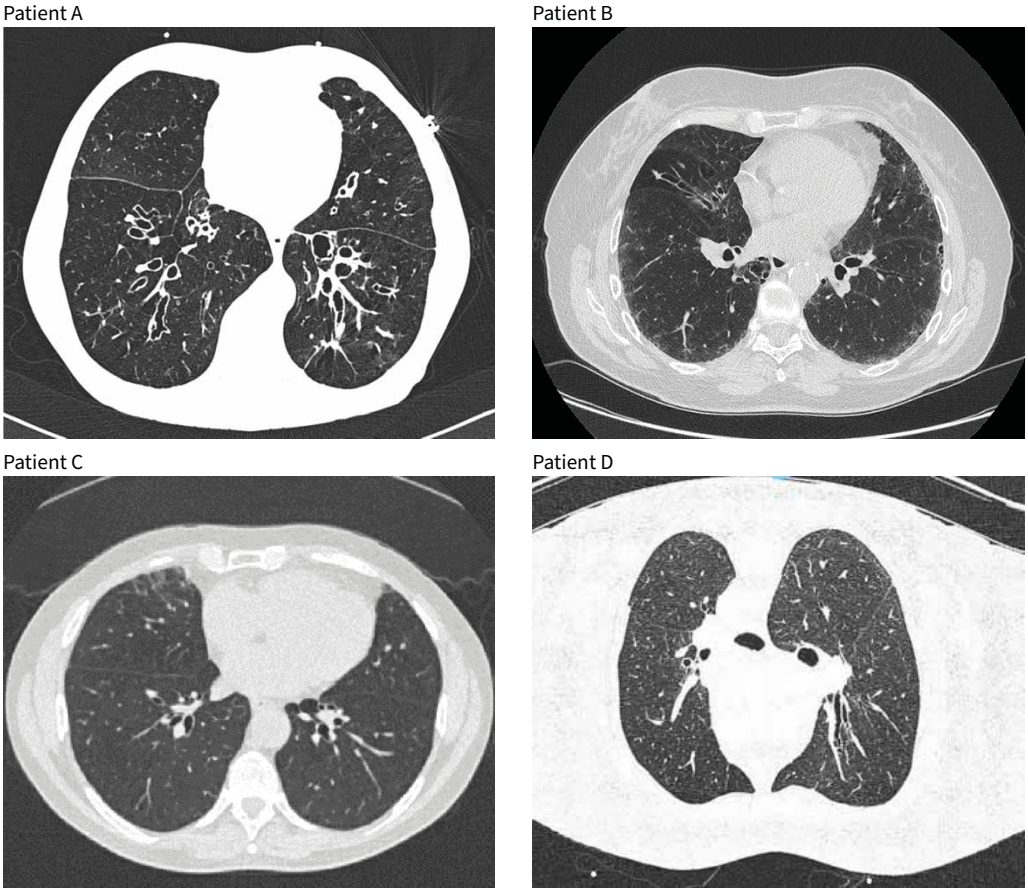

FIGURE 1 Computed tomography image slices demonstrating bronchiectasis.

His bronchiectasis was managed with inhaled beclomethasone/formoterol, carbocisteine and prophylactic co-trimoxazole, reflecting an intolerance of azithromycin.

In November 2016, patient A was noted to have a weak cough and a reduced mean peak cough flow of 145 $L \cdot min^{-1}$ (<270 $L \cdot min^{-1}$ indicates ineffective airway clearance). Lung function testing demonstrated forced expiratory volume in 1 s (FEV_1) 1.4 L (49% of predicted) and forced vital capacity (FVC) 3.1 L (80% of predicted). This was initially managed with a lung volume recruitment bag (2017) and flutter valve but as his symptoms progressed, he was prescribed a cough assist device in 2020. Due to the patient's frailty, his wife assisted him with this device.

Patient B, the wife of patient A, was a 74-year-old female who also had a diagnosis of idiopathic bronchiectasis, diagnosed in 2013 on computed tomography (CT) (figure 1). Her lung function was FEV_1 2.33 L (102% of predicted) and FVC 2.77 L (102% of predicted), and her weight was 73 kg. She had produced 27 sputum samples from 2012–2022 and was colonised with *H. influenzae* (19 isolates), which twice demonstrated co-trimoxazole resistance. The following additional bacteria were isolated from her sputum. *M. catarrhalis*: fours isolates; and *S. pneumoniae*: one isolate. She was the main carer for her husband, assisting him with his PEG feeding and his cough assist device. Additionally, in 2020, she shared her husbands disused flutter valve.

We conclude that despite cohabiting and close daily contact (including handling a cough assist device with purulent sputum within) that patient A has not infected patient B with *P. aeruginosa*. This is despite a 12-year period of *P. aeruginosa* isolates, daily close proximity and 2 years of handling a cough assist device.

In case 2, patient C was a 60-year-old male diagnosed with idiopathic bronchiectasis in 2009. He was a heavy smoker of cigarettes and had regularly smoked cannabis, and high-resolution CT showed upper-lobe predominant emphysema in addition to bronchiectasis (figure 1). He had well maintained lung function:

FEV_1 3.05 L (87% of predicted) and FVC 4.80 L (103% of predicted). His BSI was 5, indicating moderate bronchiectasis, and he was managed with inhaled beclomethasone/formoterol and carbocisteine [14]. His main symptom was persistent cough with high sputum volumes; however, his bronchiectasis exacerbated only infrequently (approximately one exacerbation per year).

Between 2018 and 2022, patient C produced five purulent sputum samples. He had been colonised with *P. aeruginosa* since 2020. Culture had also grown *S. pneumoniae* once.

Patient D was an 84-year-old female and the mother of patient C. She had a long-standing history of bronchiectasis (figure 1) with a background of recurrent pneumonia, sinusitis and otitis media. She had a BSI of 11 and a comorbid diagnosis of asthma. Spirometry showed FEV_1 1.25 L (77% of predicted) and FVC 1.68 L (83% of predicted). In contrast to her son, she had never smoked and had regular exacerbations requiring three to four antibiotic courses per year. She had high sputum volumes, and was managed with nebulised hypertonic saline, high-dose inhaled budesonide/formoterol, montelukast and carbocisteine.

From 2014–2019, patient D produced 13 sputum samples that predominantly showed *Staphylococcus aureus* colonisation. Nontuberculous mycobacteria (*Mycobacterium chimaera* and *Mycobacterium avium*) were also isolated twice, but never *P. aeruginosa*.

Since undergoing a total hip replacement in February 2019, patient D required increasing care from patient C. This included daily visits and manual labour to assist in household refurbishment. Despite this daily contact and both patients having significant cough, patient D has not become colonised or infected with *P. aeruginosa*.

We have demonstrated two separate cases where *P. aeruginosa* transmission has not occurred despite significant household contact. Understanding the transmissibility of *P. aeruginosa* in NCFB is important. These patients did not segregate in waiting rooms, inpatient wards or during therapy, *i.e.* pulmonary rehabilitation, and meta-analysis demonstrates *P. aeruginosa* in NCFB is common (21.4%) [2].

UK studies have demonstrated that there is no prevalent infectious *P. aeruginosa* strain in NCFB [10] and Cramer *et al*. [13] showed low risk of *P. aeruginosa* transmission in an outpatient clinic: no evidence of patient-to-patient transmission in 49 patients. It has been proposed that due to decreased time spent in inpatient settings, NCFB patients have reduced time to cross-infect in hospital [9]. Additionally, people living with NCFB attend outpatient clinics at a reduced frequency compared with CF patients.

This case report series has some intrinsic limitations. The absence of cross-infection described can be accounted for by a number of different reasons (*i.e.* both host and pathogen factors). Possible explanations for the results found are that *P. aeruginosa* is poorly transmitted in the NCFB cohort, that the strains of *P. aeruginosa* seen in this series were not readily transmissible or that the hosts were not sufficiently susceptible. The latter is particularly important as most bronchiectasis patients are not colonised with *P. aeruginosa* (despite *P. aeruginosa* being widespread in the environment). It is therefore important to note our findings cannot be generalised to the whole NCFB community.

In conclusion, large-scale longitudinal studies are required to determine the incidence of cross-infection in NCFB [12]. Previous work has demonstrated that cross-infection is rare, and in some instances, the primary source from a CF patient [4]. We have provided evidence showing lack of transmission of *P. aeruginosa* in NCFB, in patients with a significant exposure history. To our knowledge, these are the first cases demonstrating this, supporting evidence that in NCFB, *P. aeruginosa* is poorly transmissible by direct contact. This is of interest to the bronchiectasis community, with implications for inpatient and outpatient management strategies.

Ruth Sobala [1], Kristian Brooks[1], John Davison[1], Joanna Lumb[1] and Anthony De Soyza [1,2]

[1]Freeman Hospital, Newcastle Upon Tyne, UK. [2]Population Health Science Institutes, Newcastle University, Newcastle Upon Tyne, UK.

Corresponding author: Ruth Sobala (ruth.sobala1@nhs.net)

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