**Pandoraea pulmonicola** chronic colonization in a cystic fibrosis patient, France

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**Abstract**

Pandoraea are considered emerging multidrug resistant pathogens in the context of cystic fibrosis. We report herein for the first time the case of a 30-year-old woman with cystic fibrosis, living in France, who was chronically infected with Pandoraea pulmonicola and who died of *Pseudomonas aeruginosa* sepsis 3 weeks after bilateral lung transplantation.

**Keywords:** Antibiotic resistance, lung transplantation, multi-drug resistant bacteria, Pandoraea, pulmonary infection

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**Introduction**

Pandoraea species are non-fermentative, Gram-negative bacteria that are considered emerging multi-drug resistant pathogens in the context of cystic fibrosis (CF) [1]. The genus *Pandoraea* was created in 2000 and now comprises at least five validated species, i.e. *Pandoraea apista*, *P. norimbergensis*, *P. promenusa*, *P. pulmonicola* and *P. sputorum* [1] (Fig. 1). Conventional phenotypic laboratory methods remain problematic for the accurate identification of these bacteria at the species level and misidentification with bacteria of the genus *Burkholderia* and *Ralstonia* has been reported [2]. Although these bacteria are emerging pathogens in CF patients, there are very few clinical data on the clinical course and outcomes for patients colonized with these bacteria especially in the context of lung transplantation [2]. We report herein for the first time the case of a 30-year-old woman with CF, living in France, who was chronically co-infected with *P. pulmonicola* and *Pseudomonas aeruginosa* and who died of *P. aeruginosa* sepsis 3 weeks after bilateral lung transplantation (BLT).

**Case Report**

A 30-year-old woman who was diagnosed with CF at 3 months of age with a homozygous ΔF508 mutation had been infected with *P. pulmonicola* at least since October 2009. She was also chronically infected with *P. aeruginosa* and was placed on the active waiting list for BLT from January 2009. From October 2008 to March 2010, the patient had a dramatic deterioration of her pulmonary functional tests with a chronically persistent septic status and intermittent fever. During this period, apart from *P. aeruginosa* (resistant to all antibiotics except colistin), a colistin-resistant Gram-negative bacterium was isolated seven times from Cepacia agar. *P. pulmonicola* was eventually identified by routine analysis by matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF) [3] and confirmed with 16S rDNA gene sequence analysis (99.9% of similarity with GenBank accession number AF139175) (Strain 9405935, Fig. 1). The susceptibility profile of this organism demonstrated that the organism was initially susceptible only to tigecycline and rifampin, and resistant to ticarcillin, ticarcillin/clavulanic acid, tazocillin, ceftazidine, imipenem, gentamycin, tobramycin, fosfomycin, rifampin, trimethoprim/sulfamethoxazole, colistin, ciprofloxacin and ceftipirome.

In March 2010 the patient was admitted to the adult CF reference centre in Marseille for persistent haemoptysis and worsening of pulmonary infection. On examination she had fever (38°C), and had lost 4 kg in weight during the previous 6 months. She presented stage III NYHA dyspnoea, cough and purulent expectoration. Axial lung computed tomography (CT) scan showed a large parenchymal cavity that occupied almost all the right upper lobe, with a thick lobulated wall (maximum thickness 7.5 mm) interpreted as an infarct pneumonia (Fig. 2A). Relevant laboratory findings included a white blood cell count of 17, 78 G/L, a platelet count of 405 G/L, C-reactive protein at 36 mg/L, and fibrinogen at 4.8 g/L. She had a new procedure of therapeutic bronchial artery embolisation.

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Utilization and an intravenous antibiotherapy with tigecycline 50 mg × 2/day, colistin 2M × 3/day, meropenem 2 g × 3/day and tobramycin 450 mg/day was started. The patient received continuous oxygen therapy and intermittent non-invasive ventilation but there was poor progress after 14 days with such therapy. The patient finally underwent BLT 3 weeks after her admission. Her condition worsened 5 days after lung transplantation and *P. aeruginosa* was isolated from blood cultures, lymph nodes, bronchoalveolar lavage, liquid drains and pleural liquid whereas *P. pulmonicola* was cultured only from one bronchoalveolar lavage on postoperative day 19. A CT scan of the lung showed diffuse bilateral alveolar opacities and a parenchymal cavity 40 mm in diameter in the left upper lobe (Fig. 2B). The patient died 3 weeks after the BLT from multi-organ failure in septic shock despite intravenous antibiotherapy.

**Conclusions**

During the last decade, many new and/or emerging multidrug resistant pathogens (especially bacteria resistant to colistin) have been described in CF patients including *Burkholderia cepacia* complex, *Inquilinus limosus* [4], *Acetobacter indonesiensis*...
Brevundimonas diminuta, Ochrobactrum anthropi [6], and bacteria of the genus Pandoraea [7] (Fig. 1) suggesting that these bacteria may be selected during therapy with colistin for chronic colonization with P. aeruginosa. This hypothesis is strongly supported for Pandoraea species since in all published cases, CF patients were co-colonized with P. aeruginosa [2,8–10]. In our report we eventually identified P. pulmonicola by a molecular method and also we have demonstrated the accuracy and usefulness of MALDI-TOF as a routine technique for rapid identification of this bacterium as previously described [3,11]. The pathogenicity of Pandoraea species remains controversial and there are only a few reports concerning lung transplant patients in the literature. However, there is evidence of lung function decline as well as patient-to-patient transmission of these bacteria in CF patients, at least for P. apista [8]. Whether this bacterium has contributed to the poor outcome of the patient before and/or after BLT remains unclear since P. aeruginosa was also repeatedly isolated during this period and our patient eventually died of P. aeruginosa sepsis. In our review of the literature we found only four cases of transplantation in CF patients chronically colonized with bacteria of the genus Pandoraea [2] including three cases of P. apista (one case from Denmark and two cases from the USA), and one case of P. pulmonicola from Ireland. In the case report from Australia, one CF patient was chronically colonized by P. sputorum and this patient was not considered to be a suitable candidate for transplantation [2]. For the four CF transplanted patients reviewed, the three patients previously colonized with P. apista and the patient with P. pulmonicola survived after BLT. There is only one case of a 30-year-old man suffering from end-stage pulmonary sarcoidosis who died from P. pnomenusa sepsis after lung transplantation, suggesting that Pandoraea species may lead to severe infections in patients with chronic lung diseases [12]. To the best of our knowledge, our case of a CF patient chronically colonized with P. pulmonicola is the first human case reported from France. The lack of available effective antibiotics for the treatment of such infections due to the pan-resistant phenotype and the possibility of transmission between patients re-emphasizes the need to implement control strategy policies to protect the CF community, especially contact isolation procedures during follow-up visits and hospitalizations [8].

References