Burkholderia pyrrocinia in Cystic Fibrosis Lung Transplantation: A Case Report

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ABSTRACT

Infection with *Burkholderia* species is typically considered a contraindication leading to transplantation in cystic fibrosis (CF). However, the risks posed by different *Burkholderia* species on transplantation outcomes are poorly defined. We present the case of a patient with CF who underwent lung transplantation due to a severe respiratory failure from chronic airways infection with *Burkholderia pyrrocinia (B. cepacia genomovar IX)* and pan-resistant *Pseudomonas aeruginosa*. The postoperative course was complicated by recurrent *B. pyrrocinia* infections, ultimately lea ding to uncontrollable sepsis and death. This is the first case report in CF of *Burkholderia pyrrocinia* infection and lung transplantation, providing further evidence of the high risk nature of the *Burkholderia* species.

CYSTIC fibrosis (CF) is the most common life-threatening autosomal recessive condition affecting Caucasians; lung transplantation is currently the only definitive intervention available.

Although an increasing number of lung transplantations are being performed worldwide, the scarcity of available organs makes the timing of referral and subsequent transplant listing crucial. Preoperative infection by *Burkholderia cepacia* complex (BCC), particularly *B. cenocepacia,* is usually associated with poor transplantation outcomes. Recently, De Soyza and coworkers confirmed this but showed excellent long-term survival in a non–*B. cenocepacia* BCC group [1].

This case report describes, for the first time, lung transplantation in a CF patient with *Burkholderia pyrrocinia* infection.

CASE PRESENTATION

We describe the case of a woman affected by CF diagnosed at birth with meconium ileus. She carried the CFTR genotype F508del/CFTR dele 2,3. She was infected with *P. aeruginosa* from the age of 2 years. At age 15, she developed CF-related diabetes and CF-related liver disease associated with grade 1 esophageal varices. She became infected with *B. pyrrocinia* from the age of 13 years.

In the following years, the patient's nutritional status (body mass index, 18 kg/m^2) was poor and she required several hospital admissions for pulmonary exacerbations; all of which were successfully treated with a combination of intravenous temocillin and at least one other antibiotic. In January 2009 she started oxygen supplementation and began evaluation for pulmonary transplantation.

In May 2010 she was admitted to the hospital with acute dyspnea requiring increased oxygen supplementation. She was transferred to the intensive care unit and endotracheal intubation was performed due to lung failure. For the development of refractory hypercapnia, extracorporeal membrane oxygenation (ECMO) with venous-arterial support was started. After 4 days she underwent sequential bilateral lung transplantation. Because of the onset of primary graft dysfunction, the ECMO support was prolonged in the postoperative course and the patient was weaned on the day 8. Postoperative bronchoalveolar lavage (BAL) samples showed *P. aeruginosa, Achromobacter xylosoxidans,* and two strains of *B. pyrrocinia* of which one was resistant to all antibiotics.

She was discharged home on the postoperative day 80 and immunosuppression consisted of azathioprine (1 mg/kg/d), cyclosporine (5 mg/kg twice daily), and prednisone (0.5 mg/kg/d). Three months post-transplantation she developed nausea associated with generalized tremors. Cytomegalovirus (CMV) was isolated in gastric

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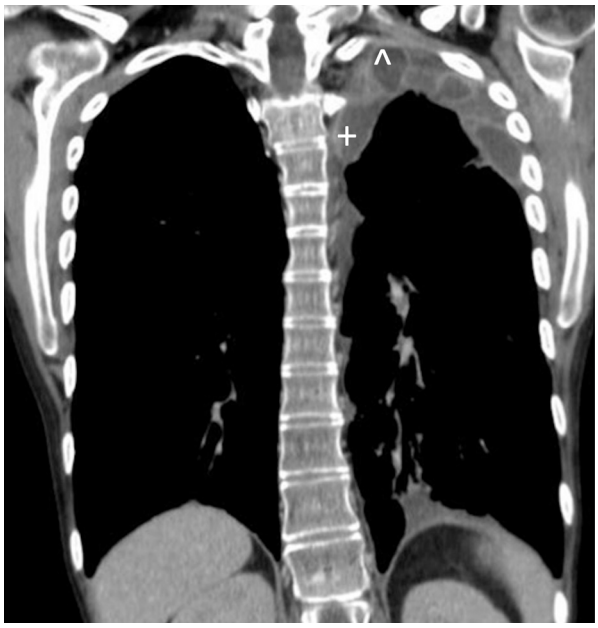

Fig 1. Chest HRCT showing left apical pleural thickening (+) with multiple areas of encapsulated fluid collections (^).

aspirates, so she received valganciclovir (30 mg/kg twice a day) and cyclosporine was switched to tacrolimus. Four months post-transplantation she became systemically unwell and developed pancytopenia (hemoglobin5.8 g/dL, white cell count 790 $\times$ 10^9/L); she was transfused and anti-CMV therapy was modified due to persistent high CMV viremia and foscavir was started. A computed tomographic (CT) scan showed a loculated empyema on the apical part of the left hemithorax; she underwent chest tube placement and intrapleural therapy with tobramycin and piperacillin was administered. In addition, she received intravenous administration of fluconazole and linezolid 600 mg twice a day. She developed acute rejection at 9 months post-transplantation which was treated with 1 g intravenous methylprednisolone for 1 day and 500 mg intravenous methylprednisolone over 2 consecutive days. Then prednisone (50 mg daily) was slowly tapering during the following 4 weeks. A routine BAL sample grew two strains of *P. aeruginosa* that were multidrug resistant; therefore, the antibiotic regimen administered consisted of intravenous doripenem, tobramycin, and vancomycin for 6 weeks. The patient developed acute renal failure and required hemofiltration.

One year post-transplantation, the patient developed pain on the fourth and fifth intercostal space on the left paravertebral line. On admission, thoracic CT showed a left apical fluid collection expanding to the posterior mediastinum and to the back, infiltrating dorsal muscle and subcutaneous tissues (Figs 1 and 2). A diagnosis of pleurocutaneous fistula was determined. BAL samples and wound swab both cultured *B. pyrrocinia.* An incision of subcutaneous fluid collection was performed and a large pleural drain was inserted; daily instillation of topical antimicrobial therapy (tobramycin and temocillin) was started. She received 21 days of an intravenous combination of meropenem, temocillin, and ceftazidime. The drain remained in site for 2 months in total, until there was complete sterilization of pleural fluid.

Twenty-three months post-transplantation, she attended a routine outpatient appointment and blood samples showed a high C-reactive protein (CRP) of 3.2 mg/dL. She received intravenous therapy with a combination of temocillin and at least one other antibiotic without improvement. During this period, immunosuppression was maintained with tacrolimus, azathioprine, and prednisone (20 mg daily). Her condition continued to worsen over the following days with an elevated CRP 19.7 g/dL and a repeat chest x-ray showed bilateral mediobasal parenchymal consolidations. A new sputum culture confirmed the presence of two strains of *P. aeruginosa* and *B. pyrrocinia*. During the next 2 days, respiratory function continued to deteriorate and chest x-ray showed multifocal bilateral consolidation (Fig 3). It was determined not to escalate treatment (ie, mechanical support) due to her poor prognosis after extensive discussion with the patient and with the patient's family. She died 48 hours later of sepsis and multiorgan failure.

DISCUSSION

This is the first case of a patient with CF chronically infected by *B. cepacia genomovar IX (Pyrrocinia)* and pan-resistant *P. aeruginosa rugosa* who died 2 years after lung transplantation. We contribute to a growing body of evidence that shows physicians should carefully consider access to a lung transplantation list for BCC non-cenocepacia–infected CF patients based on the patient's general clinical condition before listing for lung transplantation and the specific subspecies of BCC [2].

BCC refers to a group of at least 17 closely related bacterial species (genomovars) that vary considerably in the frequency with which they cause infection in patients with CF. It is recognized that some patients apparently infected with the same strain of *B. cepacia* can suffer varying degrees of accelerated lung damage, but relatively few develop cepacia syndrome [3]. In the United States, 50% of all BCC patients were infected with *B. cenocepacia* (formerly genomovar III), 38% with *B. multivorans* (formerly genomovar II), 5% with *B. vietnamiensis* (formerly genomovar V), and fewer than 5% with either genomovar I or *B. stabilis* (formerly genomovar IV). Genomovars VI to IX appear to be rare, but in Italy the

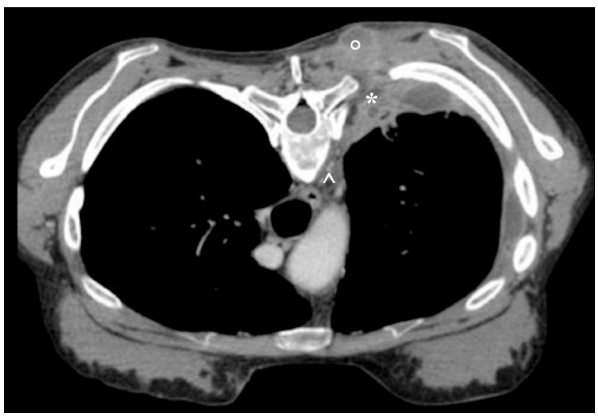

Fig 2. Chest high-resolution CT scan showing left pleural apical collection (*) extending to dorsal subcutaneous tissues (°) with the presence of fluid collection in the posterior mediastinum (^).

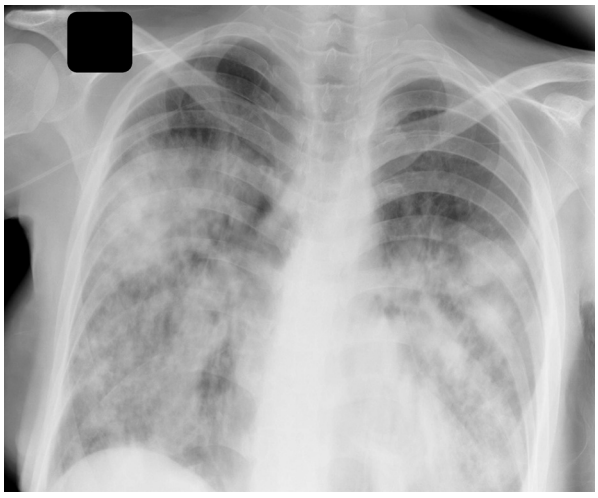

Fig 3. Chest plain x-ray showing multiple mediobasal opacities.

B. pyrrocinia infection rate is approximately 3% [4]. So, the clinical relevance of genomovar IX in transplantation is emerging and still to be defined.

De Soyza et al [1] as well as Aris et al [5] described their experiences in CF lung transplant recipients who had preoperative *B. cepacia* complex infection. They reported significant differences in survival among patients who were infected preoperatively with *B. cenocepacia* versus patients infected with other species (mostly *B. multivorans* and *B. vientamiensis*). These data have led some centers to revise their transplantation eligibility criteria to exclude *B. cenocepacia*–infected patients while offering transplantation to patients infected with other *Burkholderia* species.

To date, the lack of knowledge about the relative risks of infection with different rare *Burkholderia* species (ie, genomovar IX) made the decision to transplant this patient difficult. The patient had several important factors (ie, diabetes, pancreas insufficiency, malnutrition, liver cirrhosis, gastroesophageal reflux) present before transplantation that probably affected her post-transplantation survival, and therefore her risk from the *B. pyrrocinia per se* is difficult to define.

This case report highlights the continual challenge of understanding the variable pathogenicity of BCC infections and their relative high risk in lung transplantation. Specifically, this case suggests that transplantation outcomes with *B. pyrrocinia* may be poor; however, more data are needed before definitive conclusions can be drawn.

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