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Burkholderia gladioli – a predictor of poor outcome in cystic fibrosis patients who receive lung transplants? A case of locally invasive rhinosinusitis and persistent bacteremia in a 36-year-old lung transplant recipient with cystic fibrosis

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There have been very few reports describing postlung transplant outcomes in patients' infected/colonized with *Burkholderia gladioli* pretransplant. A case involving a lung transplant recipient with cystic fibrosis who ultimately died as a result of severe rhinosinusitis due to *B gladioli* infection in the context of postlung transplant immunosuppression is reported.

Key Words: Bacteremia; Case report; Cystic fibrosis; Lung transplant; Opportunistic infection

Burkholderia gladioli are ubiquitous Gram-negative bacteria that are able to occupy diverse environments including soil, plants and the respiratory tract of humans (1). Although *B gladioli* have traditionally been recognized as plant pathogens, they are increasingly being reported to cause infections in humans. They are closely related to *Burkholderia cepacia* complex, which are well known for their ability to cause severe illness in cystic fibrosis patients. Based on poor postlung transplant outcomes, prelung transplant infection/colonization with *B cepacia* complex is currently an absolute contraindication for lung transplantation at many lung transplant centres in North America (2).

CASE PRESENTATION

A 36-year-old woman with advanced cystic fibrosis (CF) lung disease underwent bilateral lung transplantation in 2007. Her pretransplant history was notable for repeated pulmonary exacerbations involving methicillin-resistant *Staphylococcus aureus* (MRSA) and *Burkholderia gladioli*, but without clinically significant sinus disease requiring investigations and/or treatment. Ten months post-transplant, she presented with a right frontal headache. A computed tomography scan revealed severe paranasal sinus disease and she was diagnosed with severe rhinosinusitis. She required extensive sinus surgery, and sinus cultures demonstrated heavy growth of MRSA and scant growth of *B gladioli*. She was initially treated with intravenous and topical vancomycin. Her immunosuppressive regimen was modified with a reduction in her maintenance prednisone dose and continuation of both tacrolimus and azathioprine. Her initial postoperative course was promising; however, three weeks later, she developed fever, recurrent sinus symptoms and her blood cultures grew *B gladioli*, which demonstrated in vitro susceptibility to all antibiotics tested including amikacin, tobramycin, meropenem, piperacillin-tazobactam, ciprofloxacin

Le *Burkholderia gladioli*, un prédicteur de mauvaise issue chez les patients atteints de fibrose kystique qui subissent une greffe des poumons ? Un cas de rhinosinusite avec envahissement local et de bactériémie persistante chez un greffé de 36 ans atteint de fibrose kystique

Après une greffe pulmonaire, très peu de rapports décrivent les issues des patients qui étaient infectés ou colonisés par le *Burkholderia gladioli* avant la greffe. Est exposé le cas d'un greffé des poumons atteint de fibrose kystique qui est finalement décédé à cause d'une grave rhinosinusite causée par une infection à *B gladioli* dans le contexte de l'immunosuppression après la greffe pulmonaire.

and trimethoprim-sulfamethoxazole. She underwent additional sinus surgery that did not improve her symptoms. Sinus cultures at the time of her second sinus surgery demonstrated light growth of both MRSA and *B gladioli*. She was placed on intravenous vancomycin, meropenem, ceftazidime, oral trimethoprim-sulfamethoxazole and topical gentamicin. Although she initially improved following this treatment, she went on to develop bilateral purulent otitis media, mastoiditis and petrous bone apicitis (Figure 1). Subsequent sinus cultures demonstrated heavy growth of *B gladioli*. Her overall clinical condition progressively deteriorated, and she developed persistent *B gladioli* bacteremia, which developed resistance to all available antibiotics except piperacillin-tazobactam. Unfortunately, despite six months of continuous broad-spectrum intravenous antibiotics and six sinus surgeries, she eventually succumbed to the infection and died 18 months following lung transplantation.

DISCUSSION

We contribute to a growing body of evidence that *B gladioli* infection in CF patients prelung transplant can result in significant post-transplant morbidity and mortality (3-5). Our described case of a CF patient with chronic respiratory infection involving *B gladioli* prelung transplant tragically resulted in locally invasive sinus disease, persistent bacteremia and death 18 months post-transplant. Although MRSA may have contributed initially to her sinus disease, *B gladioli* became the primary pathogen because her clinical deterioration correlated closely with heavy growth of *B gladioli* from the sinuses and subsequent bacteremia. Her sinus infection was exceedingly difficult to control despite continuous intravenous antibiotics in the face of underlying immunosuppression, challenges achieving local source control and

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eventual development of antibiotic resistance. Interestingly, she did not grow *B gladioli* in her transplanted lungs and did not demonstrate evidence of allograft dysfunction based on symptoms, spirometry or chest imaging. The present case report follows a recently documented case of a CF lung transplant recipient with a mediastinal abscess due to *B gladioli* diagnosed postlung transplant that was also difficult to control but eventually responded to a prolonged course of intravenous antibiotics and surgical debridement (3).

Although there is general consensus of poor post-transplant outcomes in CF patients harbouring *Burkholderia cepacia* complex (Bcc) (2), experience with *B gladioli* infection is limited. Several distinct species constitute what is now referred to as Bcc, with apparent considerable variation with respect to their virulence in CF patients. Based on small studies, some centres have revised their lung transplant eligibility criteria to exclude *B cenocepacia*-infected patients, while offering transplant to patients harbouring other Bcc genomovars (5). Although *B gladioli* are phenotypically very similar to genomovars of Bcc, they are molecularly distinct and, therefore, have been classified as an independent species due to the availability of advanced molecular identification techniques (1). Studies have suggested more transient infection, less antibiotic resistance and absence of patient-to-patient transmission with *B gladioli* compared with Bcc (1).

Kennedy et al (4) conducted a review investigating postlung transplant outcomes in CF patients' infected/colonized with *B gladioli*, summarizing three new cases and four previous cases from the literature. One of seven patients died as a direct result of *B gladioli* infection; however, that patient exhibited evidence of disseminated disease before lung transplant. The remaining six patients responded favourably to antibiotic therapy post-transplant. In light of these findings, the authors concluded that caution should be exercised, but that pre-transplant infection with *B gladioli* should not contraindicate lung transplantation in patients with CF. A more recent retrospective review by Murray et al (5), utilizing data from the United States CF Foundation Patient Registry, demonstrated greater post-transplant mortality in 14 CF lung transplant recipients infected with *B gladioli* compared with noninfected recipients, with an HR of 2.23 (P=0.04).

The present case adds to the growing body of evidence characterizing considerable morbidity and mortality related to opportunistic *B gladioli* infection in CF lung transplant recipients. This information suggests that the identification of *B gladioli* in pretransplant CF patients warrants reconsideration as a possible important relative contraindication to lung transplantation, similar to Bcc.

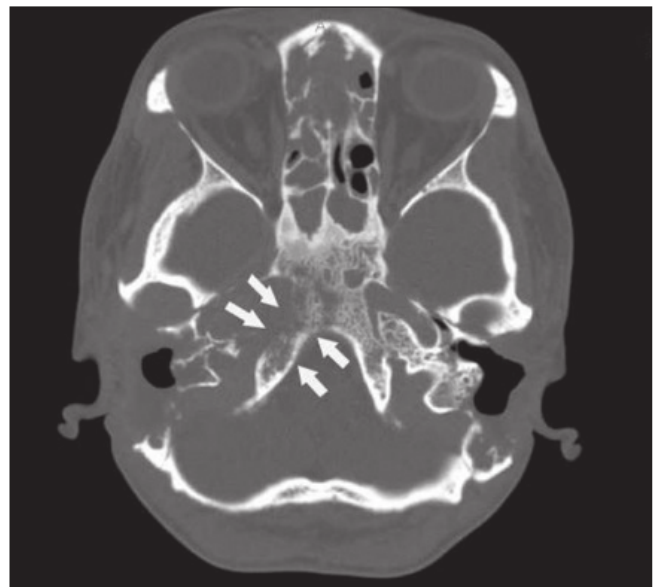


Figure 1) Extensive sinus opacification and petrous bone osteomyelitis caused by *Burkholderia gladioli* and methicillin-resistant *Staphylococcus aureus* infection in a lung transplant recipient with cystic fibrosis. The solid white arrows indicate the moth-eaten petrous aspect of the right temporal bone

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