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Case Studies

Sinonasal persistence of *Pseudomonas aeruginosa* after lung transplantation

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ABSTRACT

We report on two CF patients who received double lung transplantation (LTX) due to *Pseudomonas aeruginosa* related pulmonary destruction. Prior to LTX we detected *P. aeruginosa* in nasal lavages (NL) and sputum cultures from both patients. Donor lungs of patient 1 became colonized within four weeks with *P. aeruginosa* identical in genotype with isolates from his pre-transplant sputum cultures and pre- and post-transplant NL.

In contrast, patient 2 remained *P. aeruginosa* free in lower airway samples (bronchial lavage/sputum) for now up to 30 months, despite persistent detection of *P. aeruginosa* that was identical in genotype with pre-transplant NL and sputum isolates in NL and even in throat swabs. For prevention of pulmonary re-colonization patient 2 has continuously inhaled Colomycin 1 MIU once daily during the preceding more than 36 months with the novel Pari Sinus™ nebulizer, which in scintigraphic studies was shown to deliver vibrating aerosols into paranasal sinuses, additional to bronchial antibiotic inhalation.

Discussion: Pulmonary colonization of transplanted donor lungs with identical clones previously colonizing the explanted lungs has been described previously and the upper airways were postulated as reservoir for descending colonization. However, this remained speculative, as upper airway sampling which does not belong to current standards, was not performed in these studies.

Our report demonstrates persistence of identical *P. aeruginosa* genotypes in CF upper airways prior to and after LTX underlining risks of descending colonization of transplanted lungs with *P. aeruginosa*, which increases risks of graft dysfunction. Therefore, we recommend regular assessment of sinonasal colonization prior to and after LTX. Sinonasal inhalation with antimicrobials should be investigated in prospective trials.
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Keywords: Cystic fibrosis; Paranasal sinus; Sinonasal; *Pseudomonas aeruginosa*; Genotype; Lung transplantation; BOS

1. Introduction

1.1. Case reports

Patient 1, a F508del homozygous male, was diagnosed to suffer from CF by the age of three years because of respiratory and gastrointestinal symptoms. After the respiratory tract had become chronically infected with *Pseudomonas aeruginosa* about the age of eight years, pulmonary function deteriorated continuously. Additionally, he had symptoms of chronic rhinosinusitis despite sinonasal surgery had been performed by the age of nine years.

By the age of 20 years a spontaneous pneumothorax occurred which did not stabilize with conventional drainage. Thoracoscopy was followed by serious complications including pulmonary leakages, infection and acute respiratory distress syndrome leading to mechanical ventilation and finally extracorporal membrane ventilation (ECMO). After four weeks of ECMO double lung transplantation was performed. Despite the need of prolonged intensive treatment including re-operation

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for hemorrhage, renal failure and symptomatic transitory psychotic syndrome the patient recovered considerably well. Pulmonary function improved from FEV 1.1 l (24% predicted) to presently 3.2 l (71%).

Already during the critical circumstances of post transplant treatment at the intensive care unit *P. aeruginosa* was detected in his BAL fluid samples from the transplanted lungs, which had not been colonized with the pathogen prior to LTX. The *P. aeruginosa* isolates were identical in their multimarker genotype [1] with isolates from his explanted lungs and NL sampled prior and after LTX (Figs. 1a and 2) and the pathogen persisted despite repeated intravenous antibiotic cycles and oral inhalation of Colomycin.

Patient 2, a F508del homozygous female, was diagnosed to have CF by the age of five months because of failure to thrive and recurrent bronchitis. She was fairly stable with CF standard therapy until an episode of distal intestinal obstruction syndrome required surgical intervention by the age of six years. During the stay at the hospital the patient acquired a persistent airway colonization with *P. aeruginosa*. Despite aggressive antipseudomonal chemotherapy lung function deteriorated substantially over the years so that she required double LTX with resection of the lingula of the donor organ by the age of 20 years. LTX was successful and FEV1 increased from 1.8 l (30% predicted) to 3.2 l (102%) at present.

P. aeruginosa has not been detected in post-LTX bronchoealveolar lavages or in sputum until now, despite of regular detection of the pathogen in sinonasal lavages and in three deep throat swabs (Fig. 1b). For the prevention of the colonization of the donor lung with *P. aeruginosa* from the sinonasal segment, we instructed the patient to continuously inhale Colomycin 1 MIU twice daily into the lower airways and to administer Colomycin 1 MIU once daily into the upper airways (UAW). The utilized device is the Pari Sinus™ nebulizer which has been shown to deposit vibrating aerosols into the paranasal sinuses [2,3].

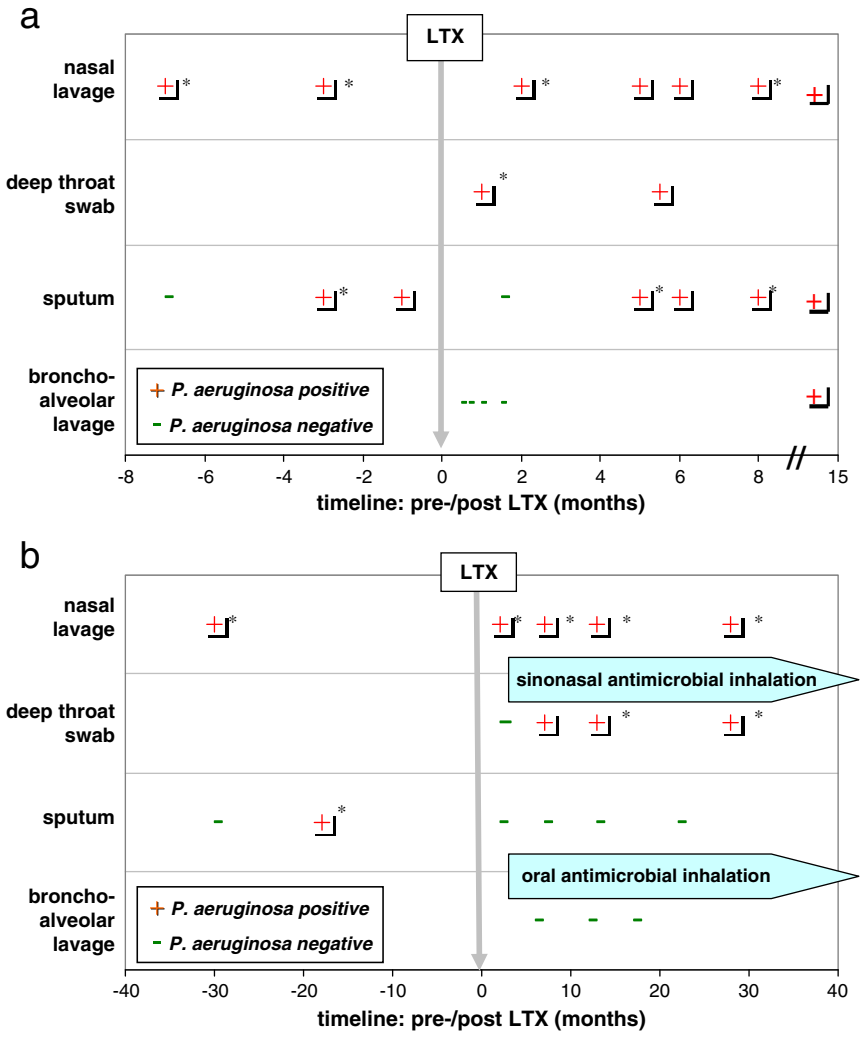

Fig. 1. a and b: Colonization of different airway levels with *P. aeruginosa* prior and after lung transplantation (LTX). Chronic sinonasal and bronchial inhalation of antipseudomonal agents since 2 months post LTX ( ). (a: patient # 1; b: patient # 2). (*) Genotypes of selected indicative *P. aeruginosa* clones from pre- and post LTX periods from each patient were assessed and in each patient they resulted to be identical in genotype.

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