Title:
PSEUDOMONAS AERUGINOSA ANTIBODY RESPONSE IN CYSTIC FIBROSIS DECREASES RAPIDLY FOLLOWING LUNG TRANSPLANTATION

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What was your research question?
The aim of this study was to examine and characterize the antibody response against the bacteria \textit{Pseudomonas aeruginosa} (PA) in patients with cystic fibrosis (CF) after lung transplantation.

Why is this important?
PA antibodies and frequent bacteriology samples are used to diagnose PA infection and monitor disease progression in CF. Antibodies are part of the human defense against PA, but they also induce the bacteria to produce biofilm, i.e. a shield that makes the bacteria resistant to host defenses and antibiotics. As such, detection of rising antibodies is fundamental for early intervention with antibiotics to prevent biofilm formation and decreasing lung function. Despite this, there is a substantial lack of research in PA antibodies in CF after lung transplantation.
The five-year survival rate after lung transplantation is around 80 \% for Danish CF patients and post-transplant infection with PA is associated with death. Knowledge of the antibody response post-transplant could therefore potentially lead to a better prognosis for lung transplanted CF patients.
What did you do?
We examined the antibody responses and bacteriology samples in 20 CF patients with PA infection from the Cystic Fibrosis Center Copenhagen in the year prior to lung transplantation and up to five years after. We also examined the characteristics of the PA antibodies and compared individual antibody profiles from around the time of primary infection to after lung transplantation.

What did you find?
We found that:
1) The PA antibodies dropped dramatically after transplant and stayed significantly lower in the five-year observation period compared to pre-transplant levels for all patients.
2) Within one month post-transplant 45% of patients were reinfected with PA and this number increased to 70% in the observation period.
3) The antibodies analysed after transplant in each patient were similar to the antibodies at the beginning of their primary infection indicating a decades long memory of their immune response like an "immunological fingerprint".

What does this mean and reasons for caution?
We hypothesize that the antibody decline after transplant is due to removal of the sick lungs, immunosuppressive medications and that the PA antibodies are produced very locally in regional lymph nodes within and near the removed sick lungs. In addition, we observed a lack of protection against PA infection after transplant even though the high antibody counts should easily eradicate PA before it starts producing biofilm in a healthy pair of new lungs. We hypothesize that the antibodies are poorly functioning after transplant and that the remaining CF pathology/disease in the trachea, and thus surgical technique, could play a role in reinfection after transplant.

What's next?
Our study, which to our knowledge is the first of its kind, need further replication in larger studies and with other common CF pathogens in order to determine the antibody response post-transplant and potentially increase survival rates. In addition, the functional properties of antibodies against PA before and after transplant need further investigation and will be a focus of our future research.
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