**Background**

- The effective management of cystic fibrosis (CF) patients with recurrent pulmonary and sinus infections caused by MDR- and XDR-Pa are challenge due to the emergence of antibiotic resistance.
- Combination of inhaled, and or oral and intravenous antimicrobial therapy for prolonged durations are often required.
- We applied MBST with DDA to guide combination antibiotic therapy in an 18-year-old woman with CF that underwent bilateral lung transplantation.
- We investigated if this approach can assist in choosing effective antibiotic regimens against XDR pseudomonas aeruginosa.

**Methods**

- Consecutive MDR- and XDR-Pa respiratory isolates were collected.
- Duration: December 2016 to March 2018 (pre and post lung transplant).
- Isolates were initially screened with Vitek and antibiotic commercial discs.
- Further antibiotics were sequentially added to create double (DDD) or triple disc diffusion assays (TDD) based on resistance mechanisms.
- Composites of anti-pseudomonal antibiotics, β-lactamase inhibitors, and cell membrane agents were utilized to achieve MBST.
- Whole genome sequencing of isolates subsequently performed.

**Results**

- During therapy, 1859 antibiotic-days were administered.
- Isolates with varying AST patterns were found (Timeline).
- MBST with DDA revealed active combinations for resistant isolates.
- Combinations led to a microbiological response allowing transplantation.
- Regimens were also informed by allergies, clinical and radiologic findings.

**Conclusion**

- Strains with evolving resistance profiles recapitulate the dynamic nature of respiratory infections in CF.
- Double or triple DDAs identified potential treatment options e.g. vs. MDR-XDR Pa. MBST can support the management of challenging infections.
- Treatment of XDR pseudomonas aeruginosa is extremely challenging in immunosuppressed patients.
- Antimicrobial options could be expanded with appropriate stewardship of testing multiple combinations based on the mechanisms of resistance and synergy.

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