Improved lung function using Ceftaroline or Linezolid in a patient with Thymidine-Dependent Methicillin Resistant *Staphylococcus aureus*

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**Introduction:** Methicillin Resistant *Staphylococcus aureus* (MRSA) is an important respiratory tract pathogen in patients with cystic fibrosis (CF) that is known to contribute to progressive and ultimately fatal lung disease. Treatment with efficient antibiotics controls acute infections, however, once colonized, it is often difficult to clear from the bronchial system despite therapy. Persistence of *S. aureus* has been associated with the isolation of subpopulations with small colony variant (SCV) phenotypes that are both methicillin-resistant and methicillin-sensitive. These organisms grow as non-hemolytic, non-pigmented, and very small colonies that often exhibit auxotrophism for growth factors such as thymidine.

**Case Report:** 26 year old female with a history of CF (genotype dF508/R553X), severe obstructive lung disease, cystic-fibrosis related-diabetes (CFRD), pancreatic insufficiency with a normal BMI, iron-deficiency anemia, and chronic sinusitis presented with recurrent frequent exacerbations. The patient was on optimal CF therapy and adherent to her regimen. From May 2012 to May 2013, she had five hospitalizations and multiple outpatient antibiotic courses for CF exacerbations. FEV₁% declined from 47% (1.36 liters in May 2011) to 21.6% (0.62 L in May 2012) despite aggressive anti-bacterial treatment. Cultures were persistently positive for multi-drug resistant (MDR) *Pseudomonas aeruginosa*, thymidine-dependent MRSA, methicillin-sensitive *Staphylococcus aureus* (MSSA), and aspergillus species. Despite multiple outpatient regimens that had previously resulted in improved lung function and symptoms, as well as intravenous therapy (IV) with Vancomycin for MRSA, she continued to have a decline in lung function and exacerbate. During an admission in May 2013, IV Ceftaroline was initiated to treat the thymidine-dependent SCV MRSA species based on available literature and discussion with the infectious diseases service. Over the next several months, the patient has shown significant improvement in her overall clinical condition. Her FEV₁ has improved to a maximum of 47% (1.36 liters). She has not had any hospitalizations since and has needed only one outpatient antibiotic course which was treated with oral Linezolid. Her sputum cultures continue to be positive for thymidine-dependent MRSA.

**Conclusion:** The clinical and pathological significance of SCVs is not completely understood, but it is believed that these organisms are involved in the persistence of chronic infections in CF lung disease. Furthermore, there is some evidence that SCVs may be induced by frequent use of Bactrim. Here we describe a case of a patient with thymidine-dependent MRSA in our center that responded to inpatient therapy with IV ceftaroline and outpatient therapy with oral Linezolid demonstrated by an increase in lung function and fewer exacerbations. Identifying these SCVs in the microbiology lab and potentially tailoring antibiotics accordingly should be considered as alternative agents to standard therapies for this important pathogen in CF.

**Discussion points:**
- Thymidine-dependent MRSA and other SCVs - general overview, epidemiology, pathogenesis
- Known risk factors for SCV infections and implications in cystic fibrosis patients
- Literature review of SCVs in cystic fibrosis including treatment options
- Voids in current information and areas of potential future research