CASE 4.2
Cystic Fibrosis | Level 2

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1. What is the subjective and objective evidence for the diagnosis of CF acute pulmonary exacerbation in this patient?

SUBJECTIVE FINDINGS: One-week history of increased cough, increased sputum production; sick contacts at home; increased work of breathing, respiratory distress; patient more tired in the last few days, missed school days due to illness, decreased appetite

OBJECTIVE FINDINGS: Significant decline from baseline FEV_1% predicted (from 98 to 82); increased respiratory rate (24 breaths per minute), crackles and rhonchi on RLL and LUL; increased WBC; clubbing of upper extremities indicating chronic poor oxygenation, reduced oxygen saturation (SpO_2 87% on room air)

Sputum culture results, although used in guiding antimicrobial therapy selection, are not indicative of CF acute pulmonary exacerbation. Patients with CF are often colonized with pathogens in their airways. Thus, presence of pathogens as part of routine workup of patients with CF (e.g., during quarterly clinic visit) does not determine presence of CF acute pulmonary exacerbation. Patient presentation (as noted in the above subjective and objective findings) and changes in spirometry (when applicable, infants and young children are not capable of coordination for standard spirometry) are most commonly used to determine whether a patient is presenting with CF acute pulmonary exacerbation.

2. Describe recommended nonpharmacologic therapy as part of treatment for this patient's CF acute pulmonary exacerbation.

Airway clearance is an important aspect in the maintenance of lung health in patients with CF. This patient, like most of those diagnosed with CF, produces thick mucus, which is difficult to clear due to cilia dysfunction and increased viscosity. The airway obstruction, mucous plugging, and consequential airway inflammation warrant the use of physiotherapy (i.e., airway clearance) to help loosen the mucus to expel it from the airways. This patient uses a "vest," which is a high-frequency chest wall oscillation (HFWO) vest. This device works by generating airflow velocities that lead to shear forces similar to a strong cough, decreasing mucous viscosity. Airway clearance helps to move secretions, including mucus, to the larger airways so that a patient may cough the mucus up (expel). Patients with CF require complete airway clearance therapy daily as part of chronic treatment, with a recommended frequency of twice daily. With an acute

CF pulmonary exacerbation, the frequency of airway clearance should be increased to 3 or 4 times daily at home to help expel the increased volume of sputum production during the course of an exacerbation. In the case of admission for treatment of an exacerbation, airway clearance should be done 4 times daily, because there is less of a scheduling issue with availability of the patient for more frequent physiotherapy during a hospital admission.

3. Develop a pharmacologic regimen for the treatment of CF acute pulmonary exacerbation for this patient, including goals of therapy and monitoring parameters.

The overall treatment goals of CF acute pulmonary exacerbation in CF are to recover the acute decline of lung function (i.e., FEV_1) with return to baseline lung function, reduce pulmonary symptoms including frequency of cough and sputum production, while also minimizing adverse drug reactions.

Antimicrobial Therapy

The overall goal of this patient's antimicrobial therapy is not necessarily the eradication of bacteria; however, treatment with systemic antimicrobials help in decreasing bacterial burden and growth as these may be increased during CF acute pulmonary exacerbation. Different from systemic antimicrobial therapy (e.g., IV or oral antibiotics), the use of inhaled antimicrobials (i.e., Tobi Podhaler®) as part of chronic therapy (i.e., every 28 days on and off) is to chronically suppress bacterial growth in the airways. The standard of care for treatment of a CF acute pulmonary exacerbation includes the use of systemic antimicrobials (if suspect bacterial etiology) in conjunction with increased frequency of airway clearance.

Antimicrobial therapy should be targeted against MRSA and *P. aeruginosa* based on his recent sputum culture and history of these pathogens. Recommended therapy includes two agents (from different classes) for *Pseudomonas* coverage and single drug coverage for MRSA, based on guidelines and standard of care in CF centers. The choice of antibiotics should be based on various factors, including patient-specific pathogen susceptibility data, patient medication allergies or intolerances, organ function (renal and hepatic), and concurrent drug therapy. This patient is allergic to sulfa agents with a reaction of hives and also has a noted allergy to penicillin; however, the patient is able to tolerate cephalosporins.

Larger overall doses for antimicrobials are warranted in patients with CF due to the need for higher serum concentrations for optimal pulmonary tissue penetration and increased clearance of antimicrobials noted in this population. Based on this patient's sputum culture susceptibilities and known allergies, an appropriate therapy selection for *Pseudomonas* coverage would be cefepime (50 mg/kg/dose IV q 8 hr; 1,300 mg IV q 8 hr) plus once daily dosing tobramycin (10 mg/kg/dose IV q 24 hr; 260 mg IV q 24 hr). For MRSA coverage starting vancomycin (15 mg/kg/dose IV q 6 hr; 400 mg IV q 6 hr) would be appropriate based on culture data and patient allergies. Linezolid should be reserved for cases of poor clinical response (i.e., failure to improve in respiratory symptoms after at least 3 days of therapy or improved lung function on spirometry after 1 week). A tetracycline, such as doxycycline or minocycline, could be considered second line because there are greater data supporting use of vancomycin in patients with CF acute pulmonary exacerbations. Duration of therapy is typically 10 to 14 days and will vary depending on clinical response (e.g., respiratory symptoms such as cough and sputum production, spirometry).

General clinical response should be assessed daily and includes assessment of frequency of cough, sputum production, respiratory rate, oxygen saturation, and need for oxygen supplementation. In addition, spirometry/pulmonary function tests to evaluate lung function (e.g., FEV_1) can be used to assess efficacy of treatment, to be done approximately each week. Therapeutic drug monitoring is necessary and includes tobramycin serum concentrations to be drawn after the second dose of tobramycin at two postdose times, such as 2 and 8 hours postdose. These serum concentrations are used to calculate peak and trough, with goal peak of 20 to 30 mcg/mL and trough of less than 1 mcg/mL, with C_{peak} calculated to 30 minutes after end of