Review Article: Care of the Hospitalized Patient with Cystic Fibrosis: A Summary of Current Practice Guidelines; Recommendations for the Hospitalist, Part 1 (Pulmonary Exacerbation)

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In the past, it was rare to see patients with cystic fibrosis (CF) on adult inpatient services as patients' lifespans were limited. In 1955, most children with CF were not expected to live long enough to attend elementary school. Today the predicted median survival is in the early 40's. This is largely due to the care provided through the national network of CF Foundation-accredited centers. This is a nationwide network of more than 110 centers where teams of experts in the care and management of CF treat people living with this disease. The CF Foundation's Care Center Network has been cited by the National Institutes of Health as a model of effective and efficient health care delivery for a chronic disease. Each center undergoes regular review of practices by the Foundation Center Committee prior to accreditation and funding. The national registry of the Cystic Fibrosis Foundation (cff.org), a registry that collects information from more than 27,000 people with CF who have agreed to share their medical data for research purposes, expects that the total number of adult patients will soon exceed the total number of patients younger than 18. Most CF patients receive care from CF specialty centers. CF specialty centers work in collaboration with local medical providers to deliver coordinated care for these complicated patients.

While pediatric providers have historically cared for this population's needs throughout their shortened lives, CF patients now rarely succumb to this disease in childhood and increasingly seek care from adult providers. We now expect to see CF patients for decades after they turn 18. It is for this reason adult Hospitalists should become proficient in recognizing the needs and providing for the management of the hospitalized CF patient. The existing literature puts forth well-reviewed and extensively studied clinical practice guidelines for the care of a hospitalized patient with symptoms of a Cystic Fibrosis pulmonary exacerbation. These are consensus reports based on the accumulation of evidence in Cochrane reviews as well as the cumulative experience of a number of experts representing the larger CF care community. The purpose of this series of articles is to summarize this body of work for the generalist and point out the resources available to the providers at the bedside. It will initially cover the basics of an admission, and in subsequent installments will expand the discussion of care to include the complications

Hospitalists see in caring for these patients. Below is an outline of the basic evaluation and management of a patient presenting with a pulmonary exacerbation:

1. Recognition of need for hospitalization
    a. Symptoms-pulmonary (GI symptoms predominate when patient presents with DIOS*)
        i. Hemoptysis
        ii. Cough
        iii. Changes in the character of the sputum
        iv. Chest pain
        v. Anorexia/vomiting
    b. Signs
        i. Increased work of breathing
        ii. Fever
        iii. Weight loss
        iv. Changes on pulmonary exam (abdominal exam)
    c. Data
        i. Hypoxemia
        ii. Decline in lung volumes as measured by pulmonary function testing (PFT) or spirometry
        iii. Change in CXR or other imaging
        iv. Leukocytosis
        v. Change in microbial inhabitants of the sputum
2. Rationale of treatment
    a. Based on pathophysiology of the disease (abnormal mucus)
    b. Guided by microbiology of airway
        i. Chronic colonizers
        ii. Viral infections
        iii. Mycobacterium
        iv. ABPA (allergic/inflammatory response to aspergillosis)
    c. Measured by;
        i. Symptom resolution
        ii. Recovery of lung volumes
3. Setting
    a. Home
    b. Hospital (specific floor)

- Special considerations

    a. IV access
    b. Infection control (private room and shower, rounding on patients)
    c. Exercise (DVT prophylaxis and another form of chest physiotherapy)

d. Access to calories (extra food, enzyme replacement)
e. IV fluids
f. Pregnancy testing

1. Therapies
    a. Oxygen
    b. Antibiotics
    c. Airway clearance therapies
    d. Nutrition
    e. Bowel program
2. Complications
    a. Hemoptysis

3. Pneumothorax
4.
    a. Pain
    b. Hepatic, renal and neurologic disturbances
    c. Nausea, vomiting, diarrhea, and/or steatorrhea
    d. CF-related diabetes
    e. Rectal prolapse
    f. Urinary incontinence
5. Monitoring/surveillance
    a. Weights
    b. Pulse oximetry
    c. Labs
    d. Culture data
    e. Blood sugars
    f. Imaging
    g. Immunizations and preventive care
6. Collaboration/consultation
    a. CF team, (CF doctor, CF dietician, CF nurse, CF respiratory therapist, CF social work, CF psychologist, pulmonologist and intensive care specialists)
    b. GI, ENT, Endocrinology
7. Transplant
8. End-of-life care

*Patients with cystic fibrosis can present for acute care for other reasons unrelated to lung disease, including; the development of DIOS, pancreatitis in the pancreatic-sufficient patient, pregnancy management, infertility workup and treatment, complications of cirrhosis as a result of CF-liver disease, and complications of CF-related diabetes.

PATHOPHYSIOLOGY

For an detailed discussion about the pathophysiology of cystic fibrosis, I will refer to the resource information. In brief, cystic fibrosis is a complex genetic disease affecting many organs, although 80-90% of the mortality is a result of lung disease. Cystic fibrosis lung disease begins early in life and is a result of mutations in the CFTR (cystic fibrosis transmembrane conductance regulator) protein. CFTR functions as a chloride channel in epithelial membranes. Insufficiency of the protein leads to pathologic changes in organs that express CFTR. These include secretory epithelial cells of many organs including; sinuses, lungs, pancreas, liver, the reproductive tract and sweat glands in the skin. The most striking change occurs in the airway surface liquid. Electrolyte changes in the airway lead to the following complex interactions:

1. Abnormal mucus resulting from dehydration of the airway surface liquid layer
2. Impaired mucociliary clearance
3. Colonization of the airway with multiple organisms **
4. An exaggerated, sustained, and extensive inflammatory response to the pathogens in the airway

** Pseudomonas aeruginosa (Ps a.) has long been recognized as a significant pathogen in disease progression. Other recognized agents include methicillin-resistant Staphylococcus aureus (MRSA), Achromobacter species, Stenotrophomonas maltophilia, Burkholderia cepacia and non-tuberculosis mycobacteria (NTM). Studies have shown that these strains lead to worsening symptoms and can speed the decline in lung function.

PULMONARY EXACERBATION

Recognizing the need for treatment is the first step in management of a pulmonary exacerbation. Most patients with cystic fibrosis can recognize a change in symptoms and will either present to the outpatient clinic with new complaints (increased cough, increased amount of sputum with thickening and difficulty in airway clearance, chest pain, dyspnea, fatigue, new oxygen need, etc.) or contact the Cystic Fibrosis Center to report changes from baseline. Physical examination and pulmonary function testing will often confirm an exacerbation of lung disease. Patients can be treated with an outpatient course of antibiotics if symptoms are not too severe; however, with more significant symptoms such as hemoptysis, weight loss, fevers, hypoxemia or failure to recover after a course of oral antibiotics, patients will require hospitalization. Treatment of a pulmonary exacerbation is largely based on three elements: antimicrobial treatment, aggressive airway clearance, and adequate nutrition.

ANTIMICROBIAL TREATMENT

As previously mentioned, treatment therapies are based on the pathophysiology of the disease and the presence of abnormal mucus in the airway. The microbiology of the airway also guides the choice of therapies. The airway in CF is often chronically colonized by more than one bacterial agent and is also susceptible to periodic infection by viral agents as well as Mycobacterial species. In addition, the CF airway can demonstrate the allergic/inflammatory response of ABPA (allergic bronchopulmonary aspergillosis). For this reason, sputum is generally collected at every clinic visit and at the onset of a hospitalization for culture and sensitivities. Generally, AFB is checked approximately every 6-12 months and total IgE is

monitored yearly. If the patient is unable to expectorate a sample for culture, bronchoscopy should be considered. Choice of initial antibiotic therapy is based on the identity and sensitivities of the organisms known to be present in the airway until new culture data can be obtained. In addition, most CF care providers double cover Pseudomonas (use two different active agents against the bacterium). Trials with single antibiotics have not shown equal efficacy. There is insufficient evidence to recommend for the simultaneous use of inhaled and IV antibiotics; however it is frequently practiced. There are currently no studies which define the optimal duration of antibiotics for a pulmonary exacerbation of cystic fibrosis. The practice is generally to let symptoms and lung volume measurements guide duration of therapy.

Patients with Ps a. and strains of NTM are frequently on chronic oral antibiotic treatment. In general, these agents should not be discontinued during a hospitalization but continued along with appropriate IV antibiotics. CF care center physicians should provide assistance with choice of antimicrobial agents. Pharmacists at CF centers also play a crucial role in the care of these patients. At our center we ask for pharmacy dosing assistance to achieve appropriate dosing of aminoglycosides and vancomycin.

Access for IV antibiotics may require the placement of a PICC line in those without an existing port. Patients with cystic fibrosis should be housed on a hospital floor where staff members are experienced in the care of these patients. This includes attention to infection control procedures, private rooms and showers, opportunities for exercise, consistent care of PICC lines and ports, access to supplemental nutrition, a knowledgeable team of respiratory therapists, and a supportive environment of staff familiar with this chronic illness.

Recently, new infection and control guidelines have been drafted by the Cystic Fibrosis Foundation. The latest medical data show that the risk of spreading destructive bacteria among people with CF is greater than was previously believed. New findings include evidence that strains of different bacteria, such as Pseudomonas aeruginosa, MRSA, and NTM, have been spread between people with CF. Research also suggests that the risk of some germs spreading through the air is greater than was previously known. For these reasons it is now standard of practice to gown and glove when entering a patient's room to examine the patient or provide care. Masks are used when the patient has infections spread by respiratory droplets (i.e. influenza). This is especially important when traveling between multiple CF patients' rooms.

On June 20th, 2014 the Cystic Fibrosis Foundation announced that updated guidelines for infection prevention and control have been endorsed by the Society for Healthcare Epidemiology of America (SHEA) and the Association for Professionals in Infection Control and Epidemiology (APIC). The updated guidelines will be published online in Infection Control & Hospital Epidemiology, the official journal of SHEA, within the next several weeks.

AIRWAY CLEARANCE THERAPY

Along with systemic antibiotics, airway clearance or pulmonary toilet is critical to the recovery of the CF patient. This includes a "package" of treatments referred to as airway clearance therapy (ACT). The treatment consists of specific aerosolized medications combined with mechanical airway clearance. This treatment package has been specifically intended for the abnormal airway

of a cystic fibrosis patient with impaired mucociliary clearance. (A component of reactive airways disease often exits as well). ACT begins with a bronchodilator, such as albuterol, followed by either a mucolytic or a mucous hydrator, Pulmozyme, and hypertonic saline (7% saline). During these inhaled treatments, patients use chest physiotherapies such as external high-frequency chest compression ("the vest") or airway oscillating techniques such as flutter, Acapella, Coronet, EZpap or IPPV. This mechanical clearance is cycled and interspersed with intermittent "huff-cough." The purpose of these techniques is to stimulate clearance of mucus from the airway. These therapies are "stepped up" or intensified during the hospital stay with a goal of 4-5 treatments per day (the well CF patient may only do 2 treatments per day). A combination of ACT modalities is often used. Hospitalization may provide an opportunity for patients to be introduced to new forms of airway clearance therapy. The respiratory therapy department or hospital practice must also provide equipment cleaning or replacement of tubing, handsets and other "contaminated" equipment regularly to prevent further contamination and spread of infection. CF teams have respiratory therapists well-versed in ACT and management of equipment. A review of home and hospital ACT equipment maintenance and cleaning procedures should be performed with patients regularly. To assist in infection control, it is best that patients bring their own vest with them to each hospitalization to ensure proper fit. This also decreases the risk of transmission of infectious agents between patients who share equipment. It is only after airway clearance has been effectively completed that it is appropriate to deliver inhaled antibiotics to the airway.

NUTRITION

The CF Foundation has been collecting data from the accredited CF Centers for many years. There is strong evidence that lung health is best maintained by achieving and maintaining adequate nutrition in CF patients. Target BMI values have been determined for adult male and female patients in addition to children. Weight loss is directly associated with a decline in pulmonary function. Caloric needs far exceed that of a healthy young person (2-3 times), even during wellness. Caloric needs are even greater during illness. Extra calories compensate for malabsorption and meet the greater energy needs in pulmonary disease. Pancreatic enzymes are critical for those patients who have pancreatic insufficiency. Fat-soluble vitamin supplements (vitamins A, D, E, and K) are also needed due to poor absorption. Vitamin K may be deficient in those with hemoptysis and is used routinely in massive hemoptysis even before lab values confirm a deficiency. CF teams always have a dietician trained in the management of CF malnutrition.

IMAGING:

A two view chest x-ray does not consistently demonstrate detectable infiltrates. It is often not informative of a pulmonary exacerbation. This is due to several reasons, including:

1. The extent of disease and resultant damage to the anatomy with extensive scar in the lungs which may obscure infiltrates.
2. A chest film seems to have less "sensitivity" to a pulmonary exacerbation than lung volumes and patient-reported symptoms.

3. The chronicity of bacterial colonization, which is often not localized to a particular part of the lung but is scattered throughout the anatomy. There may be many "small pneumonias."
4. CF disease is in the airway (bronchi, bronchiole) and the alveoli are the "innocent bystanders" of inflamed tissues of the airway.

(For billing purposes, it is our practice to refer to pulmonary exacerbations as "broncho-pneumonia" along with the terminology "pulmonary exacerbation of cystic fibrosis" to aid billing and coding personnel).

Other imaging performed for CF patients include: a yearly abdominal ultrasound as a screen for hepatic and renal disease, periodic bone scans due to poor absorption of vitamin D and malnutrition associated with this disease, and CT scans of sinus and lungs.

LABORATORY STUDIES:

*General chemistry to include renal and liver panels

*Complete blood count to evaluate for leukocytosis or anemia

*Sputum culture labelled with "Cystic Fibrosis" and yearly AFB

*Pregnancy testing in females

* Testing for influenza may be indicated

*To meet guidelines, patients may need additional testing such as vitamin levels, PT/INR, total IgE, Hgb A1C, GGTP

Our next discussion article on CF will quiz the reader over the preceding information and point out "pearls" to remember.

RESOURCES

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