Journal of Cystic Fibrosis 16 (2017) 499 – 502

www.elsevier.com/locate/jcf

Short Communication

Pleural effusions in non-transplanted cystic fibrosis patients☆,☆☆

Adam R. Belanger [a], Kimtuyen Nguyen [a], Umar Osman [b], Christopher R. Gilbert [c], Katie Allen [d], Ahmad Farid Al Rais [d], Lonny Yarmus [d], Jason A. Akulian [a,*]

[a] Division of Pulmonary and Critical Care Medicine, University of North Carolina, 8007 Burnett Womack Building, CB 7219, Chapel Hill, NC 27713, United States
[b] Division of Pulmonary, Allergy, and Critical Care Medicine, Penn State College of Medicine, 500 University Drive, Mail Stop H041, Hersey, PA 17033, United States
[c] Swedish Cancer Institute, Swedish Thoracic Surgery, 1101 Madison Street, Suite 900, Seattle, WA 98104, United States
[d] Division of Pulmonary and Critical Care, Johns Hopkins Hospital, Sheikh Zayed Tower, Suite 7-125, 1800 Orleans Street, Baltimore, MD 21287, United States

Received 30 August 2016; revised 17 November 2016; accepted 18 November 2016
Available online 12 December 2016

Abstract

Background: Pleural effusions are considered rare in cystic fibrosis (CF) patients. There is a paucity of available information in the literature concerning the nature and significance of pleural effusions in non-transplanted CF patients.
Methods: We conducted a multicenter retrospective evaluation of non-transplanted adult CF patients. Given the small sample size, only descriptive statistics were performed.
Results: A total of 17 CF patients with pleural effusion were identified, of whom 9 patients underwent thoracentesis. The crude incidence of pleural effusion was 43 per 10,000 person-years in hospitalized CF patients at large CF centers. All sampled effusions were inflammatory in nature. All samples submitted for culture grew at least one organism.
Conclusion: Pleural effusions are rare in adult non-transplanted CF patients. These fluid collections appear to be quite inflammatory with a higher rate of empyema than in the general population.

Keywords: Cystic fibrosis; Pleural effusion; Patient outcome assessment

1. Introduction

Cystic fibrosis (CF) is a disease stemming from impaired cellular transmembrane ion-transportation. This results in dysfunctional airway clearance leading to bacterial colonization and subsequent injury to the lung from repeated bouts of infection [1,2]. Patients with CF develop progressive airway obstruction with intermittent exacerbations driven by bacterial overgrowth, inadequate airway clearance and impaired epithelial defense [3,4]. Despite chronic colonization of the lung and recurrent flares of infection, pleural effusions are considered rare in the CF population [5–7]. There is a paucity of data regarding pleural effusions in patients with CF, here we present the first characterization of this disease process in patients with CF.

2. Methods

We performed a retrospective review at each participating institution (University of North Carolina in Chapel Hill, Johns Hopkins University, and Pennsylvania State University) after receiving Institutional Review Board approval. Patients were

☆ No conflicts of interest exist for the authors of this manuscript.
☆☆ Sources of Support: ARB is funded through the US National Institute of Health (NIH) – National Heart, Lung, and Blood Institute Fellowship Award T32 Research Training Program (HL007106-38).
* Corresponding author at: Division of Pulmonary and Critical Care, University of North Carolina at Chapel Hill, 8007 Burnett Womack Bldg., CB 7219, Chapel Hill, NC 27713, United States.
E-mail addresses: Adam.Belanger@med.unc.edu (A.R. Belanger), Knguyen.IM@gmail.com (K. Nguyen), Uosman@hmc.psu.edu (U. Osman), Christopher.Gilbert@swedish.org (C.R. Gilbert), Kallen43@jhmi.edu (K. Allen), ahmadalrais@gmail.com (A.F. Al Rais), Lyarmus@jhmi.edu (L. Yarmus), Jason_Akulian@med.unc.edu (J.A. Akulian).

http://dx.doi.org/10.1016/j.jcf.2016.11.006
1569-1993/

identified by querying the electronic medical records for patients with ICD-9 codes for CF with pulmonary exacerbation (277.02) and pleural effusion (511.9) or pleural effusion associated with pneumonia (511.89) or empyema (510). Patients with CF over the age of 18 who developed a pleural effusion or empyema between January 1, 2010 and December 31, 2015 were eligible for inclusion in the study. Patients with CF who developed pleural effusions after lung transplantation were excluded.

In order to obtain a crude incidence of pleural effusion in CF patients we asked each CF center to report their average number of CF patients ≥18 years of age over the last several years. We then obtained a measure of person-years at risk by summing the average number of CF patients over 18 years of age for each center and multiplying by 5 years, the duration of the study period. We calculated a crude incidence rate by dividing the total number of CF patient-pleural effusions detected during this study by the estimated person-years at risk.

All data were stored and analyzed within a Microsoft Excel (Seattle, WA) database. Data analysis consisted of descriptive statistics; specifically, the absolute counts and percentages for qualitative data and median with 25th and 75th percentile values for quantitative data.

3. Results

A total of seventeen CF patients with pleural effusion were identified. (Table 1) The crude incidence of pleural effusion was 0.0043 or 43 per 10,000 person-years. The median age of the patients was 25 (22–31) years. The majority of patients were Caucasian (94%), and the most common comorbid condition was diabetes (41%). A wide range of baseline forced expiratory volumes in 1 min was noted (0.89 L to 3.06 L).

All patients had a sputum culture positive in the 6 months prior to the identification of the pleural effusion. (Table 1) *Pseudomonas aeruginosa* was the most frequently isolated organism (82%). Other organisms isolated from the sputum included mold or fungus (47%), methicillin-sensitive *Staphylococcus aureus* (41%), and methicillin-resistant Staphylococcus aureus (24%).

Nine patients underwent sampling and analysis of their pleural fluid with a median volume of 40 (18–55) mL of fluid removed (Table 2). The pH was 7.2 (7.2–7.5). All effusions analyzed were inflammatory with an elevation in lactate dehydrogenase (LDH) of 927 (422–2119) units/mL and a total protein of 4.8 (4.2–5.4) g/dL [8]. In addition, there was a neutrophilic predominance in the cell count of 83% (17–88%). Six pleural fluid specimens were submitted for culture; no organisms were detected on gram stain. All six patients subsequently had positive cultures of the fluid (Table 3). Three cultures were polymicrobial and three of the six contained organisms also present on sputum culture.

All patients were managed in the hospital with IV antibiotics. Four patients underwent chest tube placement; three in the setting of positive pleural fluid culture. Chest tube size ranged from 14 to 28F and the chest tubes were present for a median of 5 (4–9) days. No patients underwent surgical intervention. The median length of stay for all patients was 8 (3–13) days, 7 (3–12) days in patients in whom pleural fluid sampling was performed and 8 (4–11) days for patients with a positive pleural fluid culture. There were no deaths during the index hospitalization, however 3 patients died within the year following the detection of the pleural effusion.

4. Discussion

We report the first characterization of pleural effusions in the non-transplant CF population. The data presented appears to

Table 1
Pre-effusion characteristics.

	N = 17
Age (years)	25 (22–31)
Sex	
Male	9 (53%)
Female	8 (47%)
Race	
Caucasian	16 (94%)
Asian	1 (6%)
Comorbid diabetes	7 (41%)
Other significant comorbidities	
Acute Lymphoblastic Leukemia	1 (6%)
Cirrhosis	1 (6%)
Liver Transplant	1 (6%)
Lung function	
Baseline FEV1 (Liters)	1.36 (1.04–1.77)
Baseline FEV1 (percent of predicted)	41% (30%–61%)
Sputum culture results by organism in 6 months prior to pleural effusion	
Methicillin-sensitive *Staph aureus*	7 (41%)
Methicillin-resistant *Staph aureus*	4 (24%)
Pseudomonas aeruginosa	14 (82%)
Stenotrophomonas maltophilia	2 (12%)
Burkholderia cenocepacia	1 (6%)
Fungus or mold	8 (47%)
Cultures positive for only one organism	3 (18%)

Data are presented as the absolute number and percentage or as median and (25th and 75th percentile values). FEV1 = Forced expiratory volume in 1 min.

Table 2
Pleural Effusion characteristics.

Effusion laterality	
Unilateral	16 (94%)
Bilateral	1 (6%)
Thoracentesis	
No	8 (47%)
Yes	9 (53%)
Volume of pleural fluid removed (mL)	40 (18–55)
White blood cell count (mL)d	990 (490–1975)
Neutrophil percentage	83% (17–88)
Lymphocyte percentage	13% (12–23)
pH	7.26 (7.2–7.5)
Glucose (mg/dL)	130 (111–169)
Protein (g/dL)	4.8 (4.2–5.4)
LDH (Unit/L)	927 (422–2119)
Bacteriology	
Positive culture	6 (35%)

Data are presented as the absolute number and percentage or as median and interquartile range. LDH = Lactate dehydrogenase.