



Case report

A devastating cardiovascular event in an adult cystic fibrosis patient: An unforeseen outcome of increasing life expectancy

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ABSTRACT

The improving life expectancy for CF is known to be one of the biggest success stories in medicine. Life expectancy has increased from 6 months during the early 20th century to 42.7 years from in 2012–2016. As the life expectancy of CF patients has increased, it is important to consider other co-morbidities that these patients may encounter, and the impact this may have on their morbidity and mortality. We present a case of a 33-year-old male admitted to the hospital for a CF exacerbation who had an acute neurological decompensation due to an infarction of his right occipital and posterior temporal lobe.

1. Introduction

Cystic Fibrosis (CF) is a systemic disease affecting the lungs, sinus membranes, and pancreas. The advancement in therapy for CF is known to be one of the biggest success stories in medicine. Life expectancy has increased from 6 months during the early 20th century to 42.7 years from 2012 to 2016 [1,2]. This success has been attributed to a multi-disciplinary approach in the management and therapy of CF, which focuses on relieving airway obstruction, reducing inflammation and managing and preventing infections.² As the life expectancy of CF patients has increased, it is important to consider other co-morbidities that these patients may encounter and the impact this may have on their morbidity and mortality.

In the general population, cerebrovascular accidents (CVA) are usually attributed to disease processes such as atrial fibrillation, hypertension, and metabolic syndrome. In the pediatric population, although less common, they are usually seen in children with congenital and acquired heart conditions, hematologic conditions, vasculopathies, metabolic disorders, and drug ingestion [3]. As with non-CF patients, inflammation is a major risk factor for vasculopathies and CVAs in CF patients. In the past given the short life expectancy of CF patients, the management of modifiable risk factors for strokes may have been short sighted. Given the increasing life expectancy of these patients, and the fact that they are at increased risk due to inflammation, it is important to start considering modifiable risk factors. We present a case of a 33-year-old male admitted for management of a CF exacerbation who, on

the day of discharge, had an acute neurological decompensation due to an infarction of his right occipital and posterior temporal lobe.

2. Case report

A 33-year-old male with a history of CF, cystic fibrosis-related diabetes, chronic hypercapnia on nocturnal bilevel positive pressure ventilation, CF related pancreatic insufficiency, and CF related liver disease was admitted with increasing dyspnea and cough due to a CF exacerbation. His recent history included recent PEG tube placement due to pancreatic insufficiency, chronic malnutrition, multiple admissions for CF exacerbations (with a recent multi-drug resistant pseudomonas infection), and pulmonary hypertension due to CF-related lung disease (currently awaiting lung transplantation) with a baseline FEV1 of 79%. During his admission he was treated with inhaled and intravenous antibiotics as well as airway and nutritional support. His disposition plan included transfer to a lung transplant center after returning to his baseline respiratory status. The patient did not have a central line or port for access during this admission.

On the morning of his transfer, while undergoing an Albuterol treatment, he suddenly developed right-sided weakness and numbness in his upper and lower extremities, numbness, and left homonymous hemianopia. An in-hospital stroke alert was called, and after thorough examination by a neurologist, he was found to have persistent neurological symptoms, an extensor plantar response on the right with hyperreflexia and sustained clonus, and bilateral Hoffman's signs. A

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computed tomography (CT) scan of his head at the time did not show an acute bleed, and the patient was administered tissue plasminogen activator (tPA) due to his neurological findings. A CT angiography of the brain did not show large vessel occlusions. His symptoms had some improvement after receiving tPA, however he had some residual blurry vision and weakness on the right side.

The patient was transferred to a facility with a higher level of care with a plan for further neuroimaging and possible lung transplant when stabilized. A perfusion CT of his brain showed asymmetric perfusion with relative decreased cerebral blood flow and increased mean transit time in the right occipital lobe and posterior temporal lobe, compatible with a completed infarct to those areas. A *trans*-thoracic echo showed hyperkinetic left ventricular contractility, however the structure of the atria and ventricles could not be visualized adequately. An MRI of his brain showed increased T2/FLAIR signal intensity on the diffusion-weighted imaging involving the bilateral frontal, parietal, and occipital lobes as well as the bilateral cerebellum. There was scattered cytotoxic edema mainly surrounding the right frontal, parietal, and occipital lobes.

Unfortunately, the patient's respiratory status worsened, and he was intubated upon arrival to the facility. He was placed on veno-venous (VV) ECMO a week after transfer and was managed in the intensive care unit. He was treated with prophylactic anti-epileptic medications, underwent tracheostomy placement, and treated for infections with *Pseudomonas* and *Aspergillus* species found on his most recent sputum culture. A repeat of his MRI did not show any change from his initial MRI the day following the event. The patient was eventually weaned off ECMO, and he underwent a bilateral pulmonary transplant for his CF. He was discharged home in a stable condition after about 8 weeks after his initial neurologic decompensation.

3. Discussion

Cystic Fibrosis is a genetic disorder that results in recurrent sinopulmonary infections, pancreatic insufficiency, diabetes, and liver disease. The mainstay of therapy aims to prevent airway infection and inflammation, along with nutritional support. The pathophysiology of CF itself predisposes patients to thrombosis and increased risk of cardiovascular disease.

Risk factors for thrombophilia included protein C abnormalities, transient lupus anticoagulants, indwelling central lines, CF-related liver disease, Vitamin K deficiency, immobility, and diabetes [4]. In a study by Balfour-Lynn et al., 204 CF pediatric patients had undergone thrombophilia screening, and 20% of patients had abnormalities. These included activated protein C resistance (5%), anti-thrombin deficiency (1%), protein S deficiency (5%), protein C deficiency (4%), and lupus anticoagulant (9%) [4]. The exact mechanism for these thrombophilic abnormalities in the population studied was unclear, however it was thought as not likely to be associated with the CF transmembrane conductance regulator (CFTR) defect. Vitamin K deficiency is found in CF patients and is associated with protein C and S deficiency and is even seen in patients with pancreatic insufficiency [5].

Cardiovascular involvement in patients with CF, such as pulmonary hypertension or heart failure, usually occurs at later stages in life [6]. Most studies focus on right ventricular dysfunction as a result of CF-related lung disease; however, more recently subclinical dysfunction of the left ventricle has been described along with increased arterial stiffness in adult and pediatric patients [7–10]. Again, it is unknown if cardiovascular changes in CF patients are due to the defect in the CFTR protein or if they are secondary changes. It is generally agreed that the presence of elevated circulating levels of pro-inflammatory mediators in CF patients with recurrent pulmonary infections likely affect cardiac contractility and stiffness of blood vessels [11,12]. Other mechanisms

of cardiovascular changes due to comorbidities in CF patients that have been discussed include cardiomyopathy as a result of diabetes, myocardial fibrosis due to longstanding hypoxia, and ventricular dysfunction due to pulmonary hypertension [11,12].

Another potential etiology for young CF patients that should be considered for stroke would be a paradoxical stroke. A paradoxical embolism occurs when there is the presence of a patent foramen ovale (PFO), and a blood clot from the venous system traverses a PFO and enters the systemic circulation [13]. Echocardiography is the diagnostic imaging modality, where the presence of saline contrast bubbles from the right to left atrium within 5 cardiac cycles confirms its diagnosis [13].

It is well known that cystic fibrosis patients have increased systemic inflammatory levels putting them at risk for cardiovascular diseases. Additionally, with the increasing life expectancy in these patients, extra-pulmonary risk factors such as diabetes, hypertension, and other components of the metabolic syndrome may now need to be considered. The etiology of our patient's thrombotic event was less likely as a complication of metabolic syndrome given his low BMI of 19 and his chronic malnutrition, however it is worth noting that he did suffer from CF-related diabetes.

Chronic malnutrition is a major issue in CF patients, and the current multidisciplinary approach does attempt to address this. Given the increasing life expectancy, we suggest including adult-risk factors mentioned in this paper in the dialogue for primary prevention of CF related events. Prevention of these conditions should be emphasized with just as much importance, if not more, in the adult cystic fibrosis population as compared to the general population.

Conflicts of interest

The authors have no conflict of interest with this work and report no funding sources for this work.

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