COVID-19 infection in two children with cystic fibrosis in two prevalent regions of the globe

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Introduction:

Cystic Fibrosis (CF) is a genetic disease with progressive lung disease, malnutrition, liver disease and CF-related diabetes (1). Viral infections are a major factor causing pulmonary exacerbations in CF (2). COVID-19 has caused a worldwide pandemic with high death rates. As science suggests, patients with CF would be severely affected with a high rate of morbidity, hospitalization and mortality. In a recent study published by Cosgriff et al. (3) people with CF who were 15 years and older, infected with COVID-19 appear to have better outcomes than initially anticipated. We report the only two cases of CF in literature less than 15 years of age with better than expected outcomes post COVID-19 infection and discuss the possible effects of hypertonic Saline as a plausible explanation.

Clinical Data:

Two cases with CF affected by COVID-19 are presented; one a COVID-19 positive and the only hospitalized case of patient with CF in Iran, a country of 82 million with an estimated CF carrier rate of 1 in 8,000 and an epicenter of COVID-19 in the Middle-East, and a second case in New York City, an epicenter of COVID-19 in the United States, of a patient with CF with past history of frequent exacerbations due to viral infections who required no hospitalization despite two positive COVID-19 parents.

Case 1 is a 3-month old male, the second child of a family with consanguineous marriage, with pancreatic insufficient CF, who was born at full term gestation with birth weight of 3.25 kg status post two operations for intestinal obstruction at 3 and 46 days of life. Sweat test were 98 mmol/L and 90 mmol/L. He was admitted because of fever, tachypnea and hypoxia, with oxygen saturation of 78% in room that increased to 97% on 4 L/min of oxygen via oxyhood. He weighed 3.5 kg. Lungs were remarkable for bilateral crackles and presence of bilateral lower limb edema. On admission, WBC was (16.9 x 109)/L (21% neutrophil, 62% lymphocyte and 10% monocyte), Hb 9.4 g/L, platelet of (412 x 109)/L. Electrolytes and liver function tests were normal. Chest radiograph and chest CT showed patchy infiltrates and increased interstitial markings bilaterally. EKG was normal with QT interval of 0.37. G6PD level was normal. He was treated with Meropenem and Vancomycin until the deep throat culture results showed Klebsiella pneumonia that was sensitive to Meropenem. Vancomycin was discontinued. Hydroxychloroquine was started at 3mg/kg/dose, twice a day for 10 days. On the third day of admission, he was started on aerosolized albuterol and hypertonic saline (5%) three times daily with improvement in oxygen requirement and respiratory symptoms. After five days of inhalation therapy, his clinical status improved with resolution of respiratory distress and oxygen requirement. His bilateral lower limb edema was attributed to hypoalbuminemia and treated with nutritional supplementation and appropriate pancreatic enzyme dosing.

Case 2 is a 10 years old girl with pancreatic insufficient cystic fibrosis (delta F508/W1282X) with moderate bronchiectasis, G-tube for nutritional support, and port for frequent IV antibiotics. In March of 2020, her BMI was 50th percentile, FVC 1.35 L (72% of predicted value), FEV1 0.89 L (53% of predicted value), FEV1/FVC ratio 79% and FEF25-75% of 0.46 L/s (20% of predicted value). Her family's apartment is located in an urban neighborhood of New York City that is among the most affected geographical location by COVID-19. Her parents both developed symptoms including fever, chest congestion and cough and tested positive for SARS-CoV-2 by nasopharyngeal RT-PCR. Although isolation precautions were recommended, because of space limitations, it was essentially impossible to keep the child with CF isolated while her parents recovered. Additionally, because of delays in reporting of test results, her parents did not learn they were positive until about 1 week after symptoms started. This individual with CF requires frequent courses of oral and IV antibiotics for CF pulmonary exacerbations, and often they are triggered by common viral infections, based on PCR viral respiratory panels tested on admission. With this in mind, our team anticipated that she would be at risk for respiratory complications with COVID-19. Remarkably, she developed a mild pulmonary exacerbation characterized by cough and increased sputum production without hypoxemia or associated weight loss that was managed at home with oral sulfamethoxazole/trimethoprim, frequent chest vest therapy, nebulized albuterol, 7% hypertonic saline, and alfa dornase. She recovered clinically about a week after starting these therapies.

Discussion:

Based upon our findings, COVID-19 does not significantly affect individuals with CF. This can be due to infection control measures and minimizing contact that hold true in many regions of the world but does not apply to these two cases. One explanation for this observation can be the CF medical therapy regimen that includes hypertonic saline. Previous studies have shown that salt can affect viruses. In a study by Zhang et. al. (4), high salt was identified as a crucial regulator of signaling. In another study by Siber and Podgornik (5) the influence of salt was shown on encapsidation of single- stranded viral RNA molecules. This influence was also shown on double stranded RNA at 250 mM sodium chloride. 5% hypertonic saline is equivalent to 0.85 mM NaCl. More studies are needed to answer the therapeutic role of hypertonic saline in treatment of COVID-19.

There can be additional protective factors in CF such as genetics or immunological factors that remain to be identified. It appears that patients with CF need an additional risk factor such as malnutrition or severe airway obstruction that puts them at risk from COVID-19 infection. There is still significant unknowns in dealing with the COVID-19 infection and there is no place for complacency. Until there is more scientific data, social distancing and infection control measures should be continued.

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