CASE REPORT
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COVID-19 and Cystic Fibrosis: Diagnostic Difficulties or Incorrect Methods?

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Abstract

Cystic fibrosis (CF) is a chronic lung disease with wide distribution worldwide. With the appearance of the Coronavirus Disease 2019 (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), difficulties arise when evaluating, diagnosing, and treating patients with other conditions, including CF. We present the case of a patient with CF who had a definite serological diagnosis, a CT scan suggestive of SARS-CoV-2 infection/COVID-19, and a negative molecular test (RT-PCR), with rapid resolution of symptoms and early discharge. CF/SARS-CoV-2 comorbidity needs to be adequately studied and assessed in the context of the COVID-19 pandemic.

Keywords: Cystic fibrosis, COVID-19, SARS-CoV-2, Serological tests, pandemic, Peru, Latin America

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INTRODUCTION

Until the year 2019, about 80,000 patients with cystic fibrosis (CF) corresponding to the United States and Europe were registered, the number of CF patients in America is not precisely known (1). CF patients have multiple events of viral, fungal, and bacterial infections throughout their lives, with chronic diseases due to Pseudomonas aeruginosa, Burkholderia cepacia, and Staphylococcus aureus being the most frequent. These recurrent infections are associated with pulmonary exacerbations (PE) that are the leading cause of death in CF1,2. Viral infections are estimated to cause between 10 to 60% of PE. Unfortunately, samples are not usually taken to assess the presence of viruses3. The infections described in the PE of CF patients are the respiratory syncytial virus, human rhinovirus, influenza types A and B, parainfluenza virus, human metapneumovirus, picornavirus, coronavirus, and coxsackie/echovirus, which are responsible for continually keeping inflammatory markers elevated during mixed exacerbations, causing antibiotic treatments to be prolonged2-5.

The Coronavirus Disease 2019 (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) begun on December 30 by the Wuhan health authorities, spreading to most countries of the world and as of May 19, 2020, it has affected more than 4.83 million people and caused the death of more 319 thousand cases6. However, there is very little literature that described the presence of this disease in patients with chronic lung diseases and specifically CF/SARS-CoV-2 comorbidity. The influence of chronic lung diseases on serological tests; therefore, we present the case of pulmonary exacerbation in a CF patient who tested positive for SARS-CoV-2 antibodies.

Case

A 20-year-old female patient diagnosed with CF from childhood through 2 tests for positive sweat chlorine and a genetic study with a homozygous DeltaF508 mutation. She is a continuous, home oxygen user. At the pulmonary level, he presented bilateral cystic and cylindrical bronchiectasis with marked derangement of the right upper and middle lobe. In the lower portions, she shows bronchoceles and compensatory emphysema, predominantly left. Additionally, she presents with chronic multidrug-resistant Pseudomonas aeruginosa infection, exocrine pancreatic insufficiency, and pulmonary hypertension. In stable PE-free periods, its treatment consists of inhaled tobramycin and colistin and azithromycin three times a week as an immunomodulator. The patient is treated in a national CF referral hospital.

At the beginning of the national health crisis in Peru, due to SARS-CoV-2, the patient was hospitalized on March 10, 2020, for a new PE. A SARS-CoV-2 infection was not considered probable because upon admission to Peru, there

Fig. 1. CT-scan and Chest X-ray of April 2020, with described findings.
were only 11 cases nationwide, and she did not meet the epidemiological criteria. The patient received intravenous antibiotic treatment with aztreonam, meropenem, and colistin, directed against Pseudomonas aeruginosa. After 21 days of treatment, on April 1, 2020, the patient was discharged after completing the antibiotic treatment, finding herself stable and improved.

On April 23, 2020, she went to a private clinic because she had three days of headache and dizziness, with a slight increase in dyspnea. She was clinically stable with normal vital functions except for a resting heart rate of 114 per minute, which is normal for her. There was no fever or pharyngeal pain. The most representative auxiliary tests were: Leukocytes: 15,190 cell/μL and hemoglobin: 8 g/dl. Platelets at 365,000 cell/μL, lymphocytes 2,278 cell/μL (15%), neutrophils 607 cell/μL (4%) and segmented 10,784 cell/μL (71%). The arterial gas study showed: ionic calcium 106 mmol/L. Chlorine 83.3 mmol/L, pH 7.34, PaCO₂ 75.5 mmHg. HCO₃ 48.3 mmol/L, lactate 1.9 mmol/L (normal range, 0.5-2.2). Base Excess: 0.91 μg/mL (normal range 0.0-0.5). LDH 125 U/L. C-Reactive Protein: 4.02 mg/dL (normal range 0.0-0.5). Procalcitonin: 0.04 ng/ml (normal range 0.0-0.5). Ferritin: 48.1 ng/ml (normal range 13.0-150.0). The marked elevation of PaCO₂ is highlighted, which is not usual in the patient.

A SARS-CoV-2 infection study was performed using immunochromatographic methods to detect antibodies in serum. Positive IgG and negative IgM antibodies were found. She was admitted to a personal isolation room and started antibiotic treatment with intravenous colistin and oral hydroxychloroquine.

The findings on the CT-scan of April 23, 2020, were described as signs of cystic fibrosis with primary involvement in the right upper lobe and results suggestive of moderate degree coronavirus pneumonia due to the presence of patchy opacities in ground glass of subpleural distribution that compromises mainly the right lower lobe and to a lesser extent in the segments of the lingula and the anterior segment of the left upper lobe (Fig. 1).

The RT-PCR took at the admission was negative, and on April 25, 2020, three days later, she was discharged, with significant improvement in the symptoms of admission. She was instructed to continue with colistin for seven days and to stop hydroxychloroquine.

The patient lives with a sister, a grandmother, and her mother. The study of antibodies against SARS-CoV-2 and the nasopharyngeal sample for RT-PCR of the mother were negative. No tests were done to the sister or grandmother, and they remain asymptomatic.

DISCUSSION

There is very little information about SARS-CoV-2 infection in CF patients. To date, very few cases have been reported in Europe: five patients in France, 7 in Great Britain, 5 in Germany, 3 in Spain and 1 in Italy, most of the adults and with a mild SARS-CoV-2 infection, without a marked
impact on the functional status of CF patients\textsuperscript{7,8}, therefore we cannot establish or identify risk factors or protective factors.

It is recognized that viral infections in patients with cystic fibrosis are a factor of poor prognosis and deterioration of lung function and increased frequency of PE and its severity\textsuperscript{2,7,9,10}. The symptoms of a SARS-CoV-2 infection differ from the symptoms of PE that most patients with cystic fibrosis know how to recognize\textsuperscript{5,7}. Another question is to understand what is the role of azithromycin as a treatment since CF patients use it for long periods as immunomodulators\textsuperscript{4,7,11}.

The evolution of the symptoms suggests that the patient did not present a SARS-CoV-2 infection because at admission the patient only had three days of symptoms and suggestive tomography, so the RT-PCR should be positive since the viral RNA is positive up to 3 weeks after acute clinical manifestations\textsuperscript{12-14}, the detection of antibodies also negative or only positive IgM antibody. On the contrary, she had a positive IgG antibody, negative IgM, and negative RT-PCR or recovery phase of the disease.

The presence of ground-glass opacities may indicate an early acute phase of COVID-19, however, in patients with chronic lung diseases such as CF, they may also indicate an acute inflammatory process within PE or the disease’s chronic lesions, becoming a confounding factor when treating and evaluating evolution in patients with this comorbidity. When comparing the tomography of September 2019 with the tomography of April 2020 (Fig. 2), we found that both present chronic lesions typical of cystic fibrosis and patches of ground glass patches of subpleural distribution in the basal lobes, which corresponds to the process chronic inflammatory\textsuperscript{2,9,15}.

Another important fact is that the mother, in direct contact with the patient, presented RT-PCR and negative antibodies, being the only person who could have infected the patient. Additionally, the sister and grandmother were asymptomatic.

We believe that the acute symptoms of the patient and their rapid resolution are probably secondary to the severe elevation of PaCO\textsubscript{2} that she presented, in addition to chronic infection with \textit{Pseudomonas aeruginosa}, with a positive serology perhaps due to viral infections other than SARS-CoV-2 but of the Coronaviridae subfamily\textsuperscript{3-5,14}. COVID-19 continues to be a diagnostic challenge\textsuperscript{16,17}; clinical suspicion should be high\textsuperscript{18}. However, emerging situations, such as the possibility of false-positive serological tests\textsuperscript{15} have been raised with other conditions overlapping, especially immunological and infectious, as happen with dengue\textsuperscript{20}, which in certain regions, such as Asia and Latin America is highly endemic\textsuperscript{19,21-23}.

Viral infections are recognized causes of pulmonary exacerbation in CF patients. The SARS-CoV-2 pandemic is a new challenge for both doctors and CF patients, mainly its diagnostic and therapeutic approaches. Strict social isolation is the best preventive measure we have to avoid SARS-CoV-2 infection.

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None.

**CONFLICT OF INTEREST**

The authors declare that there is no conflict of interest.

**AUTHORS’ CONTRIBUTION**

SPS and ACNS participated in the conception of the report and performed the interview, SPS, KAL, VPC, and AJRM developed the manuscript preparation, reviewed the bibliography, and made the critical revision of the manuscript. KD reviewed the bibliography, and made a critical revision of the manuscript. All the authors approved the final version.

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**ETHICS STATEMENT**

Written informed consent was obtained from the patient.

**DATA AVAILABILITY**

Not applicable

**ICMJE STATEMENT**

All authors meet the ICMJE authorship criteria.
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