



A Case of Post-Infectious Bronchiolitis Obliterans Developing after Covid-19 Infection

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Introduction

Bronchiolitis obliterans (BO) is a chronic irreversible, non-progressive and obstructive lung disease that is characterized by inflammatory reaction, and that develops following severe injury to the lower respiratory tract [1]. The condition should be considered when making a diagnosis in the presence of persistent wheezing and cough and auscultation findings 6–8 weeks after an episode of pneumonia [1,2]. We present here a case diagnosed with post-infectious bronchiolitis obliterans after a cough and wheezing developed following the identification of COVID-19 positivity in the family.

Case

A 5.5 month-old male patient presented with complaints of wheezing and cough for 1.5 months to the outpatient pediatric pulmonary diseases clinic, due to an increase in the severity of the complaints over the last 2 weeks. It was learned from prenatal history that the patient had been born to a 19 year-old G1P1A0 mother at 38 weeks and 2 days by Cesarean section, with a birth weight of 3435g. In the absence of spontaneous respiration, positive pressure ventilation (PPV) was applied and the patient was admitted to the intensive care unit for 5 days for respiratory and nutritional follow-up. The patient was placed on intravenous antibiotics for 5 days. When oxygen support was no longer needed, the patient was discharged with a nonspecific chest X-ray. The family history revealed no cigarette smoking in the family, and the mother was regularly followed-up during the pregnancy with no history of infection. There was no history of consanguinity between the mother and father. A physical examination revealed a height of 64 cm (3-10 p), a weight of 7700 g (25-50 p) and a head circumference of 43 cm (25-50 p). Tachypnea and intercostal retractions were observed during the examination of the respiratory system. No rales or ronchi were present on auscultation. No pathological findings were present when questioning the other

systems. The vital values of the patient were as follows: Body temperature: 36.40C, heart rate: 147/min, respiratory rate: 48/min, blood pressure 85/45 mm Hg and oxygen saturation: 92%. Among the laboratory tests, the total WBC:12950 u/L, ANS:2180 u/L, ALS:9700 u/L, HGB:11g/dl, Platelets:342.000 u/L, CRP:0,42mg/L, Sedim:4mg/h and serum electrolyte values were within the normal range. The ferritin level was 86.8ug/L, 25-OH vitamin D: 47.3 ug/L, D-dimer: 110 ng/mL and Fibrinogen 163 mg/dL (200-400). The patient's immunoglobulin values were within normal ranges for his age IGG: 473(374-789), IGM: 42 (29-107), IGA: 24 (5-48); IGE<16.9. It was learned that the father of the baby had a history of COVID-19 infection, and the patient's COVID-19 (SARS-COV-2) total antibody was 60.23 and positive. The patient had presented to the emergency service 43 days earlier with fever and reduced sucking, but was released with nonspecific laboratory results, since the family reported no history of COVID-19. The patient was admitted to the ward due to the presence of a ground glass pattern and a mosaic appearance in a thoracic tomography. The patient's viral respiratory tract panel was normal, and no other agent was detected, and so the patient was considered to have post-infectious bronchiolitis obliterans (PIBO), developing after a COVID-19 infection. Oxygen support was started through a mask with a reservoir bag, since the oxygen saturation of the patient was borderline low. He was treated with azithromycin for 5 days and methylprednisolone at a dose of 1 mg/kg/day. No need for oxygen was identified starting from the third day of the treatment, and the patient's retractions resolved. Blood was drawn for peripheral lymphocyte subgroup measurements prior to the start of methylprednisolone treatment, and the results were within the normal range. The patient underwent oral methylprednisolone treatment for 14 days and azithromycin prophylaxis on three days a week was prescribed as a discharge treatment. Inhaler fluticasone propionate was planned after the 14-day methylprednisolone treatment was concluded (Figures 1 and 2).

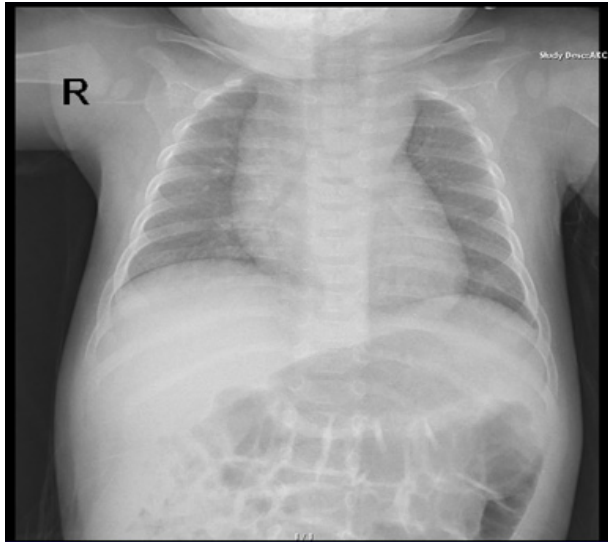


Figure 1: PA Chest X-ray: normal.

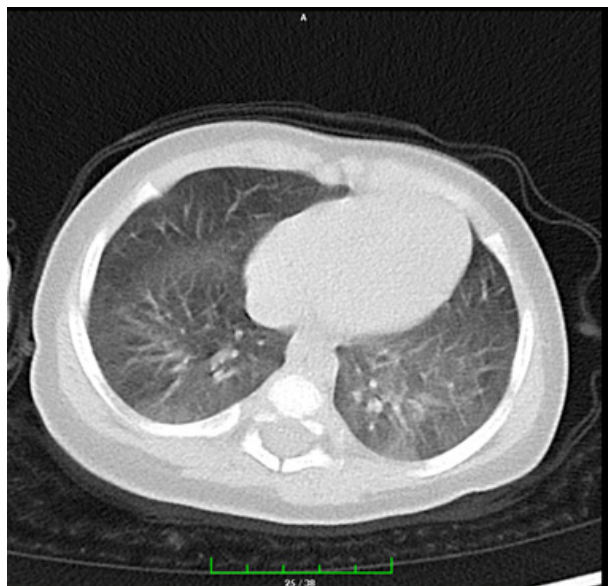


Figure 2: Thoracic CT: ground glass pattern and mosaic appearance.

Discussion

Cases of viral pneumonia started to appear in Wuhan, China at the end of 2019, and the World Health Organization (WHO) declared the outbreak a pandemic on March 11, 2020, the effects of which we are still enduring today. Viral bronchiolitis is the most common cause of presentation to hospital among children in the winter each year, but in 2020, compliance with the rules related to the wearing of masks, as well as social distancing and hygiene recommendations amid the COVID-19 pandemic, decreased the rate of presentations by 90% [3].

Bronchiolitis obliterans refers to the partial or total obstruction of the respiratory and terminal bronchioles through inflammation and fibrosis. It may develop after bone marrow or lung transplants, and less frequently after the respiration of toxic materials, being a condition associated with aspiration and connective tissue diseases [1,2]. The most common type, known as post-infectious bronchiolitis obliterans (PIBO), is seen secondary to respiratory tract viral pathogens. The most frequently detected viral pathogens are adenoviruses [4]. In the case presented here, the causative pathogen was considered to be COVID-19, given the family history of COVID-19 in the patient's father 6-8 weeks earlier, the fact that no other viral pathogen grew on the viral respiratory tract panel, and the positive COVID-19 antibody test. To the best of our knowledge, this is the first case of COVID-19-associated PIBO to be presented in literature.

The outset of the disease mimics viral bronchiolitis clinically. The presence of tachypnea and fever, the development of a supplemental oxygen requirement, and the auscultation of diffuse rales on physical examination for 6–8 weeks should bring PIBO to mind [5]. In the present case, the complaints of wheezing and cough that had started at the beginning of the infection had continued for 6 weeks. Disease diagnosis is supported by thoracic CT findings, with areas of air trapping, mosaic attenuation, peribronchial thickening and a ground glass appearance, and central bronchiectasis at advanced stages being detected [6]. In the present case, the ground glass appearance and the mosaic pattern associated with areas of air trapping was seen.

Anti-inflammatory agents are suggested for treatment, since the obliteration in the lungs is considered to be due to inflammation, although there are a lack of studies investigating PIBO treatments [7]. The first choice agents are corticosteroids, since they prevent fibrosis, while pulse corticosteroid treatment has been used in some studies as an alternative to long-term oral corticosteroids, and is considered to cause less exposure to the long-term side effects of oral steroids [1]. The present case was started on oral corticosteroids, given his a very young age and the low severity of the disease, and the treatment was planned to be changed subsequently to inhaler corticosteroids.

The presence of an inflammatory response in the sputum, bronchoalveolar lavage (BAL) and serum is known in the pathogenesis of PIBO disease. The use of macrolides has been suggested for the prophylactic treatment of patients with BO in order to benefit from the anti-inflammatory properties of such proinflammatory neutrophilic biomarkers as IL-1 β , IL-6 and IL-8 [8,9]. Accordingly, the patient was started on azithromycin for the maintenance treatment.

Clinical findings have identified a high level of inflammatory response in the presence of a SARS-CoV-2 infection, and this has been found to be associated with fatal uncontrolled pulmonary

inflammation with genetic sensitivity. More than 40 candidate genes, including ACE2, interleukin 10 (IL-10), tumor necrosis factor (TNF) and vascular endothelial growth factor (VEGF), have been suggested to establish a ground for ARDS, while increased IL-6 and IL-8 levels have also been shown to be associated with adverse results of ARDS [10,11]. The similar pathogenesis of PIBO and SARS-CoV-2 infections facilitated the development of BO in the patient with the COVID-19 infection.

Molecular tools such as TNF-alpha blockers, montelukast, hemopoietic stem cell transplantation and microRNA have been considered as new treatment protocols for the treatment of BO, although more studies are required [1]. The selected treatment was not among the new generation treatment methods in the present study, since our patient was young.

Conclusion

The development of post-infectious bronchiolitis obliterans is frequently seen following viral bronchiolitis, especially in the winter months. Post-COVID-19 PIBO should be considered in children younger than 1 year of age and with long-standing respiratory symptoms, especially in families with a history of COVID-19 infection, although the presentation of viral infections has decreased since the announcement of the pandemic.

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