



Covid-19 Infection on Asthma in an Immunocompromised Child: A Rare and Unusual Case

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Summary

Introduction: Autoimmune lymphoproliferative syndrome is an immune system deficiency secondary to a disorder of lymphocyte homeostasis, the diagnosis of which is based on major and minor criteria. The combination of Asthma and COVID 19 has been described in numerous studies and several information has been disseminated on the presumed risk factors for COVID-19. Among these, the idea has emerged that people with autoimmune diseases have a higher risk of infection with COVID 19. The objective of our study is to assess the severity of COVID 19 infection in a patient with underlying pathologies. **Observation:** We report the case of an 8-year-old patient known to be asthmatic and followed for autoimmune lymphoproliferative syndrome since the age of 6 years. The patient presented to the Pediatric Infectious Diseases Department with exacerbation of asthma due to Covid-19 infection. She presented with wheezing dyspnea associated with fever and dry cough and was found to have febrile respiratory distress with wheezing rales on auscultation and signs of respiratory struggles requiring salbutamol nebulization. The evolution was marked by the improvement of dyspnea and cough with regression of fever after a therapy combining inhaled corticosteroids, antibiotics and hydroxychloroquine. **Conclusion:** This case study demonstrated that the occurrence of COVID 19 in an asthmatic and immunocompromised child was benign, and highlighted the dual benefit of hydroxychloroquine on COVID infection as well as on autoimmune lymphoproliferative syndrome.

Keywords: Asthma, autoimmune lymphoproliferative syndrome, COVID 19, hydroxy chloroquine, child.

INTRODUCTION

Autoimmune lymphoproliferative syndrome (ALPS), or Canale-Smith syndrome, first described in 1967 by Canale and Smith, is a rare disease that occurs mainly in early childhood (1), it is a disorder characterized by immune dysregulation due to an inability to regulate lymphocyte homeostasis through abnormalities in lymphocyte apoptosis or programmed cell death (2). Leading to chronic non-malignant lymphoproliferation

ALPS is an incurable disease, and its treatments are primarily aimed at eliminating adenopathy, autoimmune deficiency, lymphoma, and other concomitant diseases (3). Although some patients with ALPS require no treatment, many require immunosuppression, particularly to treat cytopenias (3).

Coronavirus 2019 (COVID-19) is a respiratory tract infection caused by a newly emerged coronavirus around December 2019 in Wuhan, China and is now an unprecedented global pandemic. Thus, we report the rare case of COVID 19 Infection on Asthma in an immunocompromised child with a review of the literature after free and informed parental consent

OBSERVATION

We report the case of an 8-year-old child, known to be asthmatic, with a history of autoimmune lymphoproliferative syndrome (AIS). She had a brother who was followed for autoimmune lymphoproliferative syndrome, repeated respiratory infections since the age of 6 months and bi-cytopenia, and presented with febrile respiratory discomfort, productive cough, dyspnoea and a fever of 38.7 C° for 5 days. The clinical examination found a hemodynamically and respiratory stable conscious patient with polypneic skin pallor at 32 cycles/min, tachycardia at 127 beats/min, fever at 38.7 C°, her free air saturation was 97%, her weight at 21kg (-1DS) and her height at 127 cm (M). Pleuropulmonary examination revealed a symmetrical chest with diffuse bilateral crackling and sibilant rales without signs of respiratory struggle. The ENT examination showed a clean throat without signs of otitis and the abdominal examination did not find hepatosplenomegaly and the lymph nodes were free. The diagnosis of asthma exacerbation by pneumonia was evoked by the febrile polypnea with crackling and sibilant rales on auscultation. Chest X-ray showed thoracic distension with a right peri hilar focus (Figure 1).

The infectious workup showed an elevated CRP of 133 mg/l and bi-cytopenia with normocytic anemia of 7.7 g/dl associated with leukopenia of 2570. The patient was put on amoxicillin clavulanic acid 80mg/kg/day for 8 days with nebulized salbutamol 0.6 mg/kg/6h and background treatment of asthma based on inhaled corticosteroid 125ug 2 puffs* 2/day and short-acting bronchodilator if needed.

Given the context of the COVID 19 pandemic and in view of the respiratory symptoms and the lack of improvement under treatment, we performed a COVID PCR, which proved positive and the diagnosis retained was an exacerbation of asthma due to COVID 19 infection in an immunocompromised environment.

A thoracic CT scan to assess the degree of parenchymal involvement showed a focus of parenchymal condensation associated with ground glass areas with signs of micronodules and mediastinal adenopathy with minimal involvement 10%.

(Figure 2)

The patient was put on azithromycin 20mg/kg/dr at d1 and then 10mg/kg/dr from d2 to d5, Vitamin C 1cp/dr and zinc 2cp/day and under hydroxy chloroquine with a starting dose of 10mg/kg/day for 10 days then 6mg/kg/day for 3 weeks; this was started after a normal pre-therapeutic check-up made of ECG, renal and liver check-up and ionogram.

After 15 days, the evolution was favorable under treatment without any side effect.

She was seen every 15 days after discharge, the evolution was favorable and her asthma was well controlled.

DISCUSSION

Autoimmune lymphoproliferative syndrome (ALPS) is a rare disease in children, In the majority of patients, ALPS is due to inherited mutations in genes encoding proteins of the Fas pathway, which is involved in programmed cell death or apoptosis (4). It has a very low incidence and its exact prevalence is still unknown. According to the revised criteria for the diagnosis and classification of ALPS from the 2009 National Institutes of Health (NIH) International Workshop, only about 500 patients with ALPS from more than 300 families have been examined worldwide (5).

ALPS has been diagnosed in both sexes and in individuals of diverse racial backgrounds. It is a genetic disorder with a median age of first onset of 24 months; however, ALPS patients have recently been reported to appear at 3 weeks of age and 36 weeks of gestation in utero (5)

APLS is characterized by splenomegaly, massive lymphadenopathy, autoimmune phenomena such as thrombocytopenia, neutropenia, hemolytic anemia, and accumulation of double-negative T cells (CD3+CD4-CD8-) in the blood (2)

ALPS patients may present initially with episodes of fatigue, pallor, and jaundice due to hemolytic anemia. They may also develop easy bruising and mucocutaneous bleeding due to thrombocytopenia. Bacterial infections may occur due to neutropenia. It is also possible to develop multiple autoimmune problems of other organs, including the liver, kidneys and eyes (2)

The diagnostic criteria for ALS were created by consensus in 1999 and revised in 2010 by a group of international investigators (5).

NIH (National Institute of Health) 2009 consensus diagnostic criteria for ALS:

- ▶ Major: 1) Lymphadenopathy and/or splenomegaly
2) Double negative T lymphocytes: >1.5% of total lymphocytes
- ▶ Minor: Primary: 1) Abnormal LT apoptosis by flow cytometry
2) FAS or CASP10 transfer

- Secondary: 1) Cytopenia (anemia, neutropenia, thrombocytopenia)
2) Family history of ALS
3) IL 10 >20 pg/ml or IL 18 >500 pg/ml

Based on this set of criteria, a definitive diagnosis is based on the presence of two required criteria and one primary ancillary criterion. A probable diagnosis is based on the presence of two required criteria plus one secondary ancillary criterion (2)

In our patient's case, the diagnosis was made at the age of 6 months, she had a family history of ALS and presented with chronic lymphadenopathy, pancytopenia, and normal double negative T cells. And the diagnosis retained in her was SLAI-like since she had normal double negative T lymphocytes (DNT).

ALPS is an incurable disease, Overall, management is focused on treating the primary manifestations of the disease and its complications, since it is not possible to cure the genetic defect at this time. Treatment is for disease-specific complications, including lymphoproliferation and autoimmune cytopenias with immunosuppression (2).

Initial treatment of multilineage autoimmune cytopenia is similar to that of other immune-mediated cytopenias and consists of high-dose corticosteroids with or without intravenous immunoglobulin injection (IVIG). Bolus therapy with solumedrol starting at 5-10 mg/kg, followed by low-dose oral prednisone (1-2 mg/kg) as maintenance therapy, has been successfully applied in many patients (4).

Our patient had not previously received any specific treatment for APLS but only a macrolide-based antibiotic prophylaxis every other day since she had recurrent infections since birth.

The only curative therapy for ALPS is hematopoietic stem cell transplantation (HCT). However, cases of ALPS that have undergone stem cell transplantation are extremely limited in currently published case reports (4).

Despite the many underlying lymphoproliferative abnormalities and immune system disturbances, the clinical course of ALS is generally relatively benign. With the exception of patients who undergo splenectomy, serious infectious consequences of ALS-associated immunosuppression are surprisingly uncommon (6)

The risk of secondary malignancies, most commonly non-Hodgkin's lymphoma, is estimated at 10-20% (3).

The current outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), began in December 2019 in Wuhan. On January 30, 2020, the World Health Organization (WHO) declared COVID-19 as a pandemic health emergency. Since then, COVID-19 has continued to spread rapidly and has become the most dangerous pandemic in over 100 years.

The first pediatric case in the literature was reported in January 2020 in a 10-year-old boy from Shenzhen, China, whose family had visited Wuhan.

Symptoms of COVID-19 are generally milder in children, with mild pneumonia. Although there is little literature on pediatric risk factors, we have demonstrated in our patient that COVID-19 can present a clinical picture of asthma or asthma exacerbation in asthmatic children, with coughing, wheezing, and difficulty breathing, Fever is more commonly associated with COVID19, but may be present in asthma exacerbation triggered by infection (7)

Global Initiative for Asthma (GINA) recommends avoiding the use of nebulizers because of the increased risk of dissemination of COVID-19 to other patients and health care personnel; therefore, it recommends the use of inhalers as the preferred delivery system during asthma attacks (8and9) therefore, our case was managed with inhalers.

Oral steroids are not recommended to treat COVID19-associated lung disease because of possible increased viral replication. However, in asthmatic patients, current recommendations are to use oral steroids for moderate to severe asthma exacerbations that respond poorly to bronchodilators (7) in our case we did not administer oral steroids.

Various reports have shown that hydroxychloroquine has an immunomodulatory effect by inhibiting autophagy in memory effector T cells, thus inducing apoptosis of these cells. Hydroxychloroquine also has anti-inflammatory, antiproliferative and photoprotective effects (10), this double action will have an impact on the two pathologies that our patient presents, i.e., the autoimmune lymphoproliferative syndrome and the COVID 19 infection. For this purpose, we put the patient on hydroxy chloroquine for three weeks.

All epidemiologic evidence to date suggests that SARS CoV-2 infection is less severe in children than in adults (11).

A recent statement from the EAACI Pediatric Section stated that "patients with asthma (particularly severe or uncontrolled) and immunodeficiency have been classified as being at increased risk of developing severe COVID-19, based more on common sense than on mounting evidence."(8)

In our study we noticed that the COVID infection was benign even in the presence of immunosuppressed terrain and chronic respiratory pathology

CONCLUSIONS

Our study showed that COVID 19 infection in the pediatric population remains mild even in the presence of an underlying immune deficiency and asthma.

Hydroxy chloroquine has proven to be of dual benefit in both COVID and autoimmune lymphoproliferative syndrome.

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