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SARS-CoV-2 infection in an adolescent with X-linked agammaglobulinemia

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SARS-CoV-2 in X-linked agammaglobulinemia

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SARS-CoV-2 in X-linked agammaglobulinemia.

Abstract

We present a case of a 17-year-old boy with X-linked agammaglobulinemia who had mild disease when initially infected with SARS-CoV-2 but after recovering from acute infection developed fevers and a raised ESR that persisted for several weeks without any ongoing respiratory symptoms. Multiple nasopharyngeal swabs were found to be negative for SARS-CoV-2 during the febrile period, but typical changes of COVID-19 on chest high resolution CT to the detection of SARS- COV-2 on RT-PCR in a sample from a bronchoalveolar lavage. His fevers completely resolved after a five-day course of remdesivir.

Key words: X-linked agammaglobulinemia, COVID-19

SARS-CoV-2 infection in an adolescent with X-linked agammaglobulinemia.

Introduction

There are limited data on patients, including children, with immunodeficiency and SARS-CoV-2 infection. Children with X-linked agammaglobulinemia have been found to have prolonged shedding of the virus [1]. The use of chest CT to identify typical changes in COVID -19 and bronchoalveolar lavage are important in the management of the illness in adults, especially when nasopharyngeal samples have tested negative [2]. We present a case of an adolescent with X-linked agammaglobulinemia who developed SARS-COV-2 infection requiring the use of both investigations to make the diagnosis and whose symptoms subsequently resolved with the use of a course of remdesivir.

Case Report

A 17 year old male with X-linked agammaglobulinemia (XLA) presented to our hospital with persistent fever four weeks after testing positive for SARS-CoV-2. He had been diagnosed with XLA in the first year of life and was on regular subcutaneous immunoglobulin (SCIG) with stable IgG levels. He had been well up to this point with no significant infections or chronic respiratory symptoms of note. He had tested positive in the community for SARS-COV-2 by RT-PCR on a nasopharyngeal sample four weeks prior to the current presentation. He was tested having developed a cough and fever, but his symptoms had spontaneously completely resolved within a week.

He presented to our hospital 18 days after his symptoms from COVID -19 had resolved due to a history of a new fever for 9 days and was admitted to hospital for evaluation and treatment. He had no cough, shortness of breath, malaise or lethargy. The fever was intermittent and he was well during the interfebrile period. His other observations were normal including oxygen saturation of 97% in air. On examination, his weight was 57.75kg (9^{th} – 25^{th} centile) and height 165.5cm (2^{nd} – 9^{th} centile), BMI was 20.22 kg/m^2 (50^{th} -75^{th} centile). He looked well and his general systemic examination did not reveal any abnormal findings including a normal respiratory examination.

Investigations are shown in Figure 1. Of note testing for SARS-COV-2 on nasopharyngeal swabs were negative on five occasions during the illness (also negative for other common respiratory viruses and bacteria e.g. pertussis, mycoplasma) and the only positive microbiology result was a urine culture taken at presentation which grew Klebsiella species. Chest X-ray was normal.

He was initially treated with two courses each of IV Ceftriaxone and oral Co-amoxiclav due to a suspected urinary tract infection in view of the positive urine culture. Subsequent urine cultures were negative. After the initial course of intravenous antibiotic, he became afebrile for 3 days but then the fever recurred. He was subsequently reviewed as a day case on several occasions as he was well and had no other symptoms besides fever. His CRP improved slightly (**Figure 1**) but the febrile episodes continued for 5 weeks. He also received

intravenous immunoglobulin (IVIG) (in place of his usual SCIG replacement) on two occasions while in hospital due to the family's reluctance to give SCIG at home whilst febrile.

Due to the ongoing fevers he had a HRCT chest done which showed ground glass patchy appearances in both lower lobes suggestive of COVID-19 pneumonia but no signs of bronchiectasis (**Figure 2**).

His did not show SARS-CoV-2 antibodies in serum. However, fluid taken from a bronchoalveolar lavage detected SARS-COV-2 using the BioFire FilmArray (we did not have a cycle threshold value).

He was given a five day course of IV Remdesivir; 200mg on day 1, 100mg on Days 2 – 5, became afebrile shortly after starting it, and his inflammatory markers normalised (Figure 1). He was discharged on completing the course of remdesivir and at 6 months follow up remains clinically well.

Discussion

In our immunocompromised patient, a past infection with SARS-COV-2 made us suspect the possibility of persistent infection despite testing negative on nasopharyngeal swabs on several occasions. HRCT chest showed typical findings of COVID pneumonia, despite a normal chest X-ray, and testing of bronchoalveolar fluid confirmed the presence of SARS-COV-2 virus in the lung.

A study by Patrucco et al [3], demonstrated that bronchoscopy helped detect SARS-COV-2 in 76% of adult patients despite at least two negative nasopharyngeal swabs. Those suspected to have SARS-COV-2 had a higher number of abnormalities noted on CT scan compared with those without infection. This study complements a case series [4] highlighting the usefulness of CT scanning and bronchoalveolar lavage in making the diagnosis of COVID-19 in patients when routine imaging (chest x-ray) and virology testing (nasopharyngeal swabs) are negative.

Several case reports of SARS-CoV-2 infection in adults with X-linked agammaglobulinemia have been published in the literature. An adult from the UK developed persistent SARS-COV-2 infection (or reinfection) and had negative SARS-CoV-2 antibodies [5]. Another small case series showed two adults with X-linked agammaglobulinemia and SARS-CoV-2 pneumonia improved after receiving experimental treatments (subsequently shown to not be effective for treatment for SARS-CoV-2) used early in the COVID pandemic along with immunoglobulin infusions [6,7]. On the other hand, one patient recovered with IV antibiotic and regular IVIG only [8]. Five patients with X-linked agammaglobulinemia have been reported to be infected with SARS-COV-2 virus and recovered after receiving convalescent plasma, one of whom, also received a course of remdesivir [10-14]. Three of them had CT chest findings suggestive COVID -19, however BAL was not performed as nasopharygeal swabs were positive for SARS – COV-2 [10,13,14]. Two more patients have been reported to demonstrate prolonged shedding of SARS-COV-2 virus ranging from 3 – 7 weeks, a feature seen commonly in patients with primary immunodeficiency [7,9,11,15]. Another case series reported 6 patients with X-linked agammaglobulinemia who had asymptomatic or mild SARS-CoV-2 infection and who promptly recovered without any

specific treatment [16]. Patients with X- linked agammaglobulinemia may have milder infection because of amelioration of the cytokine storm due to impaired IL-6, IL-12 and TNF – α production and STAT1/3 upregulation through the Toll -like receptor 9 (TLR9) pathway [16,17].

Another child with primary immunodeficiency with STAT 1 GOF on an immunomodulator as well as regular IVIG recovered with no additional treatment suggesting a possible role played by immunomodulatory drugs [9]. However, our patient continued to have fever despite receiving two doses of IVIG and only recovered after initiation of a course of Remdesivir. It is possible either or both of these interventions may have helped resolve his symptoms.

These cases demonstrate that patients with XLA may take a prolonged period to clear the virus and they can develop resurgence of symptoms after an initial improvement, although generally the infection seems to be relatively mild. If they are found to be negative for SARS-CoV-2 on nasopharyngeal swab but there is still a clinical concern SARS-CoV-2 infection may be present, consideration should be given to doing a chest CT scan and BAL. There is no clear evidence for treatment regimens but as with our case, immunoglobulin replacement should be optimised and consideration given to remdesivir in cases who are not improving or deteriorate.

Conclusion

We conclude that the identification of SARS-CoV-2 virus from bronchoalveolar lavage fluid as well as a diagnostic chest CT scan may be helpful to identify SARS-CoV-2 infection in symptomatic patients with X-linked agammaglobulinemia with negative nasopharyngeal swabs and a normal chest x-ray. Remdesivir may be an appropriate treatment for patients who do not improve or deteriorate.

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Figure

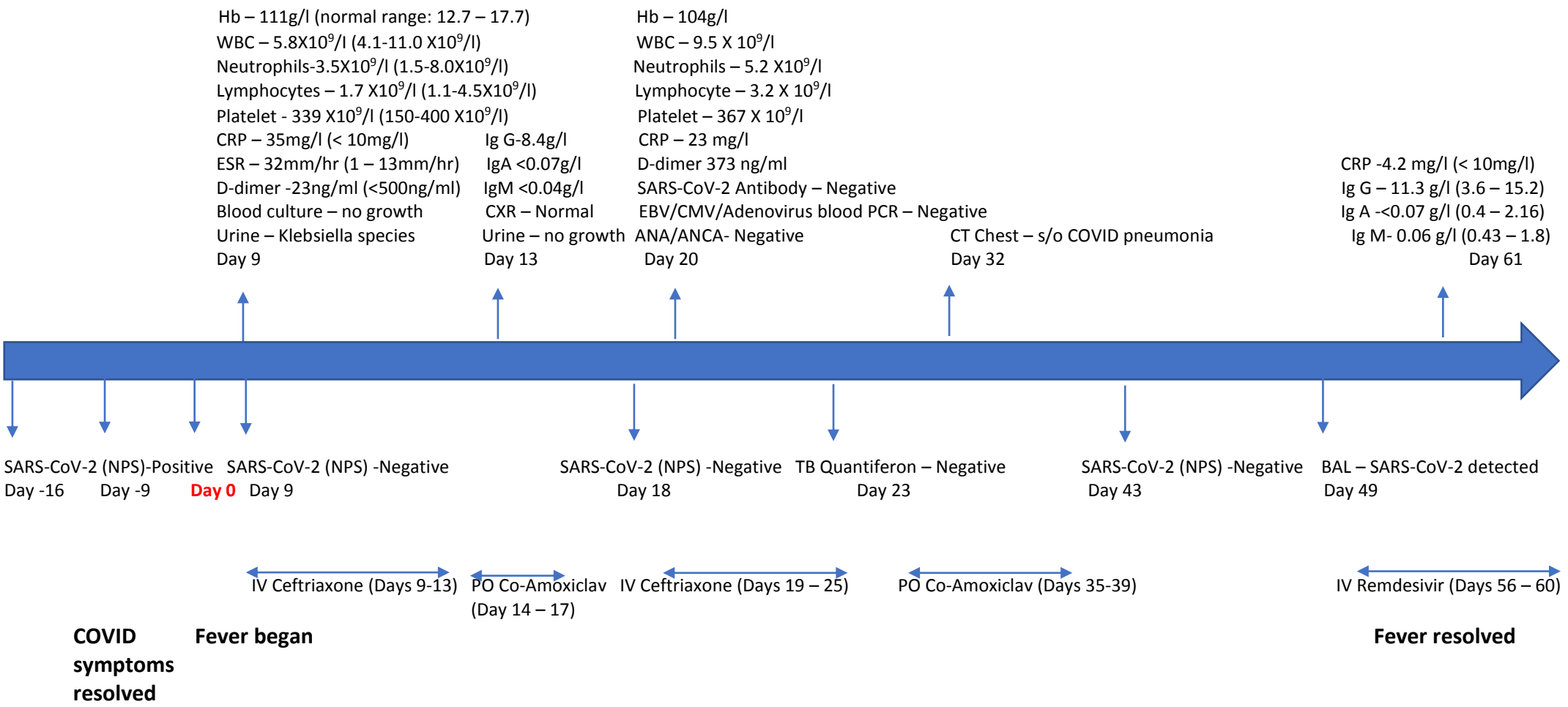

FIGURE 1: Timeline for investigations and treatments

Key: NPS = Nasopharyngeal Swab
CXR = Chest X-ray
BAL = Bronchoalveolar lavage
CRP = C-Reactive Protein
ESR = Erythrocyte Sedimentation Rate
CMV = Cytomegalovirus
ANA = Antinuclear Antibody
ANCA = Antineutrophil Cytoplasmic Antibodies

Figure

Figure 2: Chest CT showing subpleural patchy ground glass opacification, predominantly affecting the lower lobes. No bronchiectasis seen.