

COVID-19 IN A PATIENT WITH X-LINKED AGAMMAGLOBULINEMIA: A CASE REPORT

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ABSTRACT

X-linked agammaglobulinemia (XLA), characterized by a profound deficiency of B lymphocytes, is caused by mutations in the gene encoding Bruton tyrosine kinase (Btk). XLA patients have a susceptibility to viral infections. In this report, we present a 45-year-old man with known XLA, with about a 2-week history of fever, chills, diarrhea and vomiting. He was diagnosed with COVID-19 infection, which was confirmed by a real-time reverse-transcriptase-polymerase chain reaction. The antiviral drugs, antibiotics, and interferon-beta were administered to him. Unfortunately, the patient passed away after 5 days. During an epidemic of infectious diseases, the best strategy to overcome the potential challenges of treating XLA may be prevention. Early detection of biomarkers such as D-dimer and IL-6 might be more helpful for initiating more aggressive therapy and decreasing the duration of illness in these patients.

Keywords: primary immunodeficiency disorders, X-linked agammaglobulinemia, COVID-19.



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INTRODUCTION

Primary immunodeficiency disorders (PIDs) are the group of immune deficiencies described by poor function in some elements of the immune system. These patients are at higher risk of several infections such as severe recurrent respiratory and gastrointestinal infections [1]. X-linked agammaglobulinemia (XLA) is one form of PIDs that is a result of gene defects in xq22 chromosomal location and a decrease in B-cell progenitor kinase (BTK) production [2]. It has been shown that males are affected by XLA much more commonly than females [3]. XLA is manifested by the partial or complete absence of gamma globulins including antibodies in the bloodstream which are vital for protecting against infections. The thymus gland is normal, but peripheral lymphoid tissues are typically absent. B cells and plasma cells are rare despite the normal numbers of pre-B cells in the bone marrow. They have significant problems with bacterial infections; they also have severe difficulty with persistent, disseminated echovirus infections, especially in the central nervous system.

XLA patients have a susceptibility to other viral infections, which can cause lethal infections [4]. Norovirus infection of the gut is another problematic viral infection in XLA cases [5]. Until now, the occurrence of coronavirus infection in patients with PIDs has not been studied. However, it is supposed that bacterial superinfections are more likely to occur following the coronavirus infection, which leads to a worse prognosis.

During the current novel coronavirus epidemic, one concerning problem about immunodeficient patients would be the higher risk of getting COVID-19 infection. Here, we present a patient with XLA who became infected with COVID-19.

CASE REPORT

A 45-year-old man with known XLA, that was diagnosed 6 years ago, had a 16-day history of fever, chills, diarrhea, vomiting and progressive dyspnea when he was admitted to our hospital. His medical history included XLA, cirrhosis and portal hypertension-induced esophageal varices, which led to band ligation 2 years earlier. His drug history was negligible except monthly intravenous immunoglobulin (IVIG) infusion therapy. High-resolution computed tomography (HRCT) was performed which was indicative of COVID-19 because the signs and symptoms were compatible with COVID-19 in the epidemic conditions of this infection. Patchy ground-glass opacity (GGO) consolidations were present in the lower lobes of both lungs accompanied by the reversed halo sign, which was indicative of viral pneumonia in general, and COVID-19 infection specifically (Figure1). The bronchiectatic changes were also observed in the posterior basal segment of the left lung which might be explained by his history of recurrent respiratory tract infections (RTIs) due to the underlying disease.

Despite receiving hydroxychloroquine and azithromycin combination therapy for 6 days in an outpatient setting, his

dyspnea got worse; thus he was admitted to hospital. At the admission, he had hypoxemia (the blood oxygen saturation of 82% while breathing the room air) with a body temperature of 38.7°C, blood pressure of 110/75 mm Hg, heart rate of 86 beats per minute, respiratory rate of 24 breaths per minute, and bilateral normal lung respiratory sounds (Table1).

Table1. Examined parameters of patient infected with COVID-19

Parameter	Value
Body temperature	38.7°C
Blood pressure (mm Hg)	110/75
Heart rate (beats per minute)	86
Respiratory rate (breaths per minute)	24
White blood cell count, $\times 10^9/L$	3100
Lymphocyte count, $\times 10^9/L$	600
Platelet count, $\times 10^9/L$	122000
Haemoglobin (g/L)	11.6
Erythrocyte sedimentation (mm/h)	50
C-reactive protein (mg/L)	60
Procalcitonin (ng/mL)	0.12
Interleukin-6 (pg/mL)	56
Pro B-type natriuretic peptide (pg/mL)	661
D-dimer (ng/mL)	368

Laboratory tests showed the white blood cell count (WBCs) per microliter ($3.100 \times 10^9/L$) and 20% lymphocytes; hemoglobin, 11.6 gm/dL; platelet (PLT), 122000 per microliter. The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and procalcitonin levels were 50 mm/h, 60 mg/L, and 0.12 ng/mL, respectively.

Interleukin-6 (IL-6), pro B-type natriuretic peptide (pro-BNP) and D-dimer levels were 56 pg/mL, 661pg/mL, and 368 ng/mL, respectively. The liver and kidney function tests, electrolytes, and cardiac enzyme levels were within the normal range. He had positive RT-PCR results for COVID-19. Kaletra (lopinavir/ritonavir) two 200 mg tablets twice daily, azithromycin 500 mg PO daily, meropenem 1 g IV q8hr, and vancomycin 1 gram q12hr were administered. He de-escalated within 48 hours. Despite using the reservoir bags, his oxygen saturation (SpO_2) did not increase and his dyspnea continued. Therefore, interferon-beta was administered to him. Unfortunately, the patient passed away after 5 days.



Figure 1. CT scan performs GGOs in both lungs accompanied by the reversed halo sign and bronchiectatic changes were observed in the posterior basal segment of the left lung.



DISCUSSION

X-linked agammaglobulinemia (XLA), characterized by a profound deficiency of B lymphocytes, is caused by mutations in the gene encoding Bruton tyrosine kinase (Btk). This group of patients has a susceptibility to several types of infections [6].

Any types of immunosuppression such as humoral or cellular immune responses are risk factors for occurrence, severity, and poor prognosis of COVID-19. It is important to note, that a delayed diagnosis of infection in these patients due to the unspecific symptoms or radiographic patterns, and the poor innate immune defense in immunosuppressed individuals against respiratory infections, could generally lead to the low cure rate [7]. During an epidemic of infectious diseases, the best strategy to overcome the potential challenges of treating these patients may be prevention [8]. To achieve these goals, it is necessary for these patients to receive IVIG replacement monthly to defend more properly against the novel virus [9]. Also, the hospital infection control policies should be in place with the strictest precautions to isolate the patients with, or at risk of acquiring COVID-19 and the patients themselves should be advised to rigidly perform hand hygiene and other standard and respiratory precautions to prevent getting the infection.

Although, radiographic features in this patient were similar to immunocompetent patients, there was no delay in the diagnosis. Moreover, high levels of the prognostic factors such as D-dimer and IL-6 would be associated with worse outcomes, more critical condition, and non-response to the standard therapy; perhaps, earlier checking of these biomarkers might be more helpful for initiating more aggressive therapy and decreasing the duration of illness in these cases. Some studies reported that IFN β 1 might account for a safe treatment against COVID-19 in the early stages of the disease. Also, in vitro studies propose that COVID-19 could be more sensitive to IFN-I than other coronaviruses [10, 11]. Probably, the use of interferon in our patient in addition to the antiretroviral therapy and antibiotics could improve his

prognosis. But our patient was admitted in the early phase of this epidemic event of COVID-19 and in that period in beta formulations were not suggested in the studies and treatment protocols of COVID-19.

In conclusion, clinicians should pay attention to XLA patients who have a susceptibility to viral infections such as COVID-19 and earlier checking of some biomarkers might be more helpful for initiating the treatment and decreasing the duration of infection in these patients.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national) and the Helsinki Declaration of 1975, as revised in 2013. Voluntary written and informed consent was obtained prior to enrollment in the study.

COMPETING INTERESTS

There are no conflicts of interest.

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