CASE REPORT

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COVID-19 INFECTION IN A LEUKEMIC CHILD

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ABSTRACT

The newly emerged SARS-CoV-2 Betacoronavirus strain has infected more than one million people worldwide. The COVID-19 infection in children was reported to be less severe compared to adults. At this point, there were limited data available to describe the effect of COVID-19 infection in immunocompromised children. We reported a case of SARS-CoV-2 infection in an immunocompromised child with a delayed virus clearance. The report signifies the variability in the severity of SARS-CoV-2 infection in immunocompromised children together with a prolonged period of viral clearance.

Keywords: COVID-19, SARS-CoV-2, Immunocompromised
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Introduction

Globally, approximately two percent of those affected by COVID-19 were children, with less severe disease course compared to adults [1]. However, the prevalence varies, ranging between one and five percent in different countries [2]. Even within the same countries, the proportion of children with COVID-19 differs. For instance, in Sabah, the most affected state in Malaysia, a total of 3030 children younger than twelve years old were affected with COVID-19 by 20th November 2020. This number accounts for more than forty percent of the state's total cases [3]. Global data on the effect of COVID-19 infection on immunocompromised children were scarce. This scarcity is possibly due to the small number of positive cases and the majority of asymptomatic children were left unscreened. Worldwide, there are more than twenty-five published case series and reports on COVID-19 in children with malignancies; however, there is no reported case from Malaysia. We report a case of a leukemic patient who contracted a COVID-19 infection presented with delayed viral clearance.

Case report

We reported a 27-month-old boy; a known B-cell Acute Lymphoblastic Leukemia case commenced chemotherapy in late 2019. He was in remission but had to postpone his chemotherapy due to post-induction chemotherapy neutropenia. He stayed with his mother, two siblings and their extended family members. He was screened for COVID-19 infection after revealing that he had contact with his two extended family members who were positive for COVID-19. They had travelled interstate to a wedding function (nine days before his rescheduled chemotherapy) and subsequently developed a cough and sore throat without fever. Social distancing was not practiced

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among the household members. He was transferred to a COVID-19 designated hospital for quarantine and observation but remained asymptomatic during his 16 days of hospital stay.

His chest radiograph showed minimal consolidative changes. Figure 1 shows the chest radiograph of the patient. Full blood counts on admission showed a white cell count of $12 \times 10^9/L$, a neutrophil count of $4.9 \times 10^9/L$, a lymphocyte count of $4.24 \times 10^9/L$ and platelet counts of $337 \times 10^9/L$. Renal and liver function tests were within the expected value for age. C-reactive protein was twice negative. SARS-CoV-2 RT-PCR was repeated on day 10th, 13th and 16th of admission. His last naso- and oropharyngeal swab on day sixteen were negative and he was discharged well to continue for another one week of home quarantine. The patient completed his home quarantine period asymptotically and chemotherapy was commenced after that.

Figure 1. Chest radiograph taken at day one of admission.

His mother accompanied him throughout the admission because his father was away working in another state. She has to leave her 5-month-old breastfed baby at home. The current restriction of movement order limited their movement. Lack of information and the uncertainty over the child's outcome has caused a lot of distress to the mother. However with the great help and support from other family members, the family could cope well with the stressful situation.

Discussion

In the epidemiological study from China, ninety percent of the SARS-CoV-2 infected children had mild to moderate symptoms [4]. Younger children, less than 5-year-old, were more likely to develop a complication [4]. Majority of symptomatic children with COVID-19 presented with upper respiratory symptomatology [1]. There is lack of data on COVID-19 infection in immunocompromised children. However, the outcome can be predicted based on the effect of other Human Coronavirus (HCoV) infection on immunocompromised children. In a retrospective study, both immunocompromised and immunocompetent children with HCoV infection presented similarly, mainly with fever, cough and sore throat [5]. The severity was identical even with different strains of HCoV [1,5]. However, immunocompromised children were more likely to develop severe pneumonia than immunocompetent children [5].

Morbidity and mortality in the patients with COVID-19 are thought to be due to hyper-inflammatory state such as cytokine storm syndrome [6]. In a meta-analysis that compared the level of various laboratory inflammatory markers and severity of COVID-19 infection, it was found that patients with the severe disease have a significantly higher level of inflammatory markers such as CRP, ESR, Ferritin, Interleukin-2 (IL-2), IL-4, IL-6 and IL-10 [7]. It is thought that immature and inadequate functioning of ACE-2 receptor which reduced the SARS-CoV-2 virus affinity to the receptor, higher level of antibody against respiratory viruses, the cross-protection of childhood immunisation program and the lack of coronavirus-specific memory cells have led to reducing direct cell-mediated attack and inflammation on alveoli and other organs [4, 8].

In contrast to the reported case of COVID-19 positive leukemic child by Chen et al., our patient was asymptomatic throughout the disease course. The reported child developed a high-grade fever, which progressed into pneumonia, requiring intensive care unit (ICU) admission [9]. The severe neutropenia, high level of IL-6 and IL-10 and concomitant influenza A infection might have contributed to more severe disease in the reported child [7]. In our reported patient, the recent chemotherapy received might have reduced the innate and adaptive immune

responses and blunted the exaggerated inflammatory responses usually seen in an immunocompetent patient with COVID-19 infection. The repeatedly normal level of CRP supported this blunted response [7]. However, due to limited facility to measure the level of humoral marker such as interleukin (IL) 6 and IL-10, we were unable to ascertain the correlation between the severity of symptoms and the level of inflammatory markers in our patient. Similarly, during the SARS-CoV outbreak in 2002/2003, immunocompromised children who underwent organ transplants had a good outcome. There was also no documented severe COVID-19 pneumonia among paediatric liver transplant patients in Italy [10].

There is limited data on the effect of COVID-19 on children with primary immunodeficiency, which permits comparison between the primary and secondary causes of immunodeficiencies [11]. Earlier study hypothesised that there is an inverse relationship between the severity of immunodeficiencies and the complication of COVID-19 infection [11]. Humoral protein deficiencies such as deficiency in type 1 interferon due to mutation in genes coding for Toll-like receptor 3 (TLR3), Interferon Regulatory Factor 7 (IRF7) and others were found in more than 3 percent patients with life-threatening COVID-19 infection [12]. The duration of viral clearance in immunocompromised patients, both primary and secondary, seems to be longer than in immunocompetent people [6]. For instance, in a case series of COVID-19 in patients with primary immunodeficiencies, the viral clearance period lasted between one to four weeks [11, 13]. Usually, the viral clearance is achieved by day 10 of illness [14]. Our patient has shown a more prolonged viral shedding and clearance period as positive RT-PCR test turned negative only after 23 days from the first day of contact with the index case. This finding was similar to the previous case report of an immunocompromised child where the SARS-CoV-2 nucleic acid test remained positive even after 21 days of fever [9].

The high psychological distress among people quarantined during an infection outbreak has been established in a recent review article. The psychological impacts include post-traumatic stress, depression, anxiety and social detachment. The long duration of quarantine (more than ten days), fear of infection, especially among women

with young children and limited information were the main stressors during the quarantine period [15]. However, no published data looked explicitly at the distress level of affected patients and their families during the COVID-19 outbreak.

In conclusion, although the SARS-CoV-2 infection in our immunocompromised child was mild, delayed viral clearance was seen. As this is only a case report, further evidence on the pathogenesis and outcome of SARS-CoV-2 infection on immunocompromised children is required before any conclusion can be made.

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