

Clinical course of COVID-19 among immunocompromised children: a clinical case series

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SUMMARY

Infection with SARS-CoV-2 represents a great source of concern and a new threat for immunocompromised patients. Limited studies are available on COVID-19 in immunocompromised children. This case series aimed to evaluate the clinical and laboratory characteristics, management and outcomes of COVID-19 in five children immunocompromised due to different underlying conditions. All had mild symptoms or were asymptomatic at presentation. All had a benign course of illness. No changes or delays in their treatment regimens occurred, and none experienced a relapse of the original disease, developed severe COVID-19 or died. However, these cases showed a prolonged duration of virus shedding. This report suggests that immunocompromised paediatric patients may not be at a higher risk of developing severe COVID-19. However, further studies are required to elaborate on the pathogenesis of COVID-19 in this vulnerable group.

low threshold of admitting to our centre all children with an altered immune status presenting with suspected or confirmed COVID-19. Accordingly, these patients were admitted for further observation and management. Apparently, immunocompromised children with no other major comorbidities infected with SARS-CoV-2 are not at a higher risk of developing severe respiratory distress or pneumonia than are other healthy children. None of our patients had a relapse of their original disease, developed severe COVID-19 or died. Moreover, our patients continued to receive their life-saving medications or chemotherapy during this outbreak.

CASE PRESENTATION

This clinical case series describes five children immunocompromised due to different underlying conditions. The clinical and laboratory findings, treatment and outcomes for the described patients are listed below (table 1).

BACKGROUND

As of 21 June 2020, more than 8.79 million SARS-CoV-2 infections and >464 thousand deaths worldwide have been confirmed.¹ Immunocompromised children, whether due to immunodeficiency or being on immunosuppressants medications such as steroids or biological therapies, are at a higher risk of severe viral infections. Infection with SARS-CoV-2 causes much concern and fear among these children and their caregivers.² However, as reports on SARS-CoV-2 infection in immunocompromised children are still scarce, there is an urgent need to share experience and knowledge about this virus and how it can affect vulnerable groups. The purpose of this case series is to share our knowledge and preliminary experience in the management of immunocompromised children infected with SARS-CoV-2. We describe the clinical course and outcome of COVID-19 in five children with altered immune responses. The patients recovered without complications from the infection, with no relapse of their original disease.

To our knowledge, this is the first clinical case series describing the details of the clinical course and outcomes of COVID-19 in children with an immunocompromised or immunosuppressed status. We present five paediatric patients immunocompromised due to different underlying diseases. They presented either with mild symptoms or were identified via contact screening. The diagnosis of COVID-19 was confirmed by real-time reverse-transcriptase PCR assays. As the UAE began to see COVID-19 cases in early January 2020, we had a

Case 1

The patient was a 12-year-old Asian boy with common variable immunodeficiency and stable bronchiectasis on regular Immunoglobulin infusions every 4 weeks. His last infusion was 18 days before presenting to the emergency department (ED). On admission, he had a low-grade fever (38.1°C) and cough for 3 days. He had no breathlessness or another constitutional symptom. His father was hospitalised with acute COVID-19. His general examination was within normal limits and maintained adequate oxygen saturation on room air. On investigation (table 1), he had mild neutrophilia, lymphopaenia and a rise in C-reactive protein (CRP). Routine electrolytes, renal function and liver function tests were within normal ranges. Chest X-ray (CXR) showed no new lung lesions. He was admitted for further observation and quarantine. He was started on hydroxychloroquine alone for 7 days based on initial emerging evidence of its potential effectiveness.³ Blood and sputum cultures were negative. He received his intravenous immunoglobulin (IVIG) dose as scheduled without delay. No complications were reported with IVIG therapy. His CoV-PCR test became negative after 24 days. He remained clinically well, haemodynamically stable and on room air throughout his hospital stay.

Case 2

This patient was a 3-year-old middle-eastern girl diagnosed with extrarenal rhabdoid tumour for 1 year. She received surgical resection of a left paraspinal cervicothoracic rhabdoid tumour in



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Table 1 Summary of the five cases

Case	Age (years)	Sex	Cause of immunodeficiency	Laboratory findings							Radiology findings	COVID-19 serology
				WBC (/μL)	ANC (per μL)	ALC (/μL)	CRP (mg/L)	Ferritin (μg/L)	LDH (IU/L)	D-dimer (μg/mL)		
				Reference range								
				5.5–15.5	1.8–7.7	1.5–7	≤5.00	10–118	135–225	≤0.50		
1	12	Male	Common variable immunodeficiency, on IVIG q4 weeks	13	10.67↑	1.34↓	11↑	Not done	196	0.46	No new changes in lungs	Not available
2	3	Female	Extrarenal rhabdoid tumour, on chemotherapy	2.2↓	0.62↓	0.61↓	3	1701↑	376↑	1.09↑	No new changes in lungs	Not available
3	12	Female	Hereditary pyruvate kinase deficiency status post-splenectomy	18.4↑	10.56↑	2.86	8↑	1466↑	194	0.54↑	Clear lung fields	Not done
4	12	Male	Steroid-dependent nephrotic syndrome, on prednisolone	9.1	9.55↑	2.62	2	24	1190↑	0.28	Clear lung fields	Not done
5	9	Female	Systemic lupus erythematosus, on prednisolone and mycophenolate mofetil	9.1	5.28	2.52	1.5	Not done	296↑	0.41	No new changes in lungs	SARS-CoV-2 IgA: Positive SARS-CoV-2 IgG: Positive

Demographics, clinical and laboratory findings of the five paediatric patients with COVID-19.

ALC, absolute lymphocyte count; ANC, absolute neutrophil count; CRP, C-reactive protein; IVIG, intravenous immunoglobulin; LDH, lactate dehydrogenase; WBC, white blood cells.

March 2020 and was deemed to carry an overall poor prognosis. She was on both chemotherapy (ARST 0431 protocol) and radiotherapy. As she visited the infusion centre for chemotherapy infusion, she received intravenous irinotecan. On the same day, she was screened for SARS-CoV-2, with a positive test. Elective admission was arranged immediately for further observation. She was totally asymptomatic. No index case was identified. Vitals were all within normal ranges including normal oxygen saturation at room air, as was her general examination. On investigation, she had leucopaenia with lymphopaenia and neutropaenia (table 1). She had significantly elevated ferritin (1701 μg/L) and high lactate dehydrogenase (LDH) (376 IU/L) levels. D-dimer was elevated. She had normal routine electrolytes and renal function tests. Her CXR showed no new changes. Following a multi-disciplinary team discussion including oncology and infectious disease specialists, she was started on antiviral medications, both hydroxychloroquine and favipiravir, due to severe presentation of myelosuppression. She was asymptomatic and remained well during her hospitalisation. The CoV-PCR test continued to be positive on hospital day 4 and hospital day 7. She did not deteriorate clinically; she did not develop fever, and no supplemental oxygen was needed. She did not require a higher level of care. Her CoV-PCR test became negative after 12 days. She survived the viral infection. We did not stop any of her medications, and she received chemotherapy as per the protocol. While hospitalised, the girl was accompanied by her mother who was regularly screened for SARS-CoV-2, with a repeatedly negative test.

Case 3

The patient was a 12-year-old middle-eastern girl known to have hereditary pyruvate kinase deficiency status postsplenectomy. She received red blood cell (RBC) transfusion almost every 3–4 months. She was adherent to her antimicrobial prophylaxis and regularly followed the postsplenectomy vaccination protocol. She presented to the ED with low-grade fever, pallor and worsening jaundice with a duration of 1 day. Her mother was infected with SARS-CoV-2. On admission, her temperature was 37°C, she had tachycardia with a heart rate of 98 bpm. She had no signs of respiratory distress and maintained normal oxygen saturation

on room air. Laboratory findings (table 1) revealed leucocytosis with neutrophilia, a mild increase in CRP, acute haemolysis with low haemoglobin (67 g/L) and a high reticulocyte count (54%). The ferritin level was also significantly increased (1466 μg/L). She was admitted, received a packed RBC transfusion and was started empirically on ceftriaxone. No antiviral therapy was given based on relatively preserved current cellular immunity. She stayed haemodynamically stable, and on room air during her hospitalisation, with no deterioration in clinical status. Her blood, urine and sputum cultures were negative. She was discharged with a positive CoV-PCR test, which became negative after 20 days. Repeat Complete Blood Count (CBC) prior to discharge revealed haemoglobin of 116 g/L.

Case 4

The patient was a 12-year-old Asian boy known to have steroid-dependent nephrotic syndrome and was on daily prednisolone. He was known to have frequent hospital visits due to his chronic illness. He complained of fever, chills and cough of a 3-day duration. The boy's parents had COVID-19. Clinical examination revealed a temperature of 38°C, mild tachycardia, normal respiratory rate with no evidence of hypoxemia at room air when presenting to the ED. On examination, his chest was clear by auscultation, with no signs of respiratory distress or dehydration. His CoV-PCR test was positive. On investigation (table 1), no significant laboratory findings except for a high LDH level were noted and CXR showed clear lung fields. He was treated empirically with intravenous ceftriaxone and received 7 days of hydroxychloroquine. He continued to receive his daily steroid doses. His blood and urine cultures came negative. Additionally, he had a negative respiratory viral panel (RVP) and sputum culture. During his stay, no new symptoms developed and continued on room air throughout. No relapse of the nephrotic syndrome was observed. He was regularly assessed by the nephrology team. His CoV-PCR test became negative after 10 days. It is undetermined whether he acquired the SAR-CoV-2 infection from his parents or during his repeated visits to the hospital.

Case 5

This patient was a 9-year-old Asian girl known to have systemic lupus erythematosus (SLE) controlled by prednisolone and mycophenolate mofetil. She was identified as having SARS-CoV-2 infection as part of the contact screening programme. All her family members were infected with SARS-CoV-2. She was asymptomatic, and her general examination was normal with normal respiratory rate and no evidence of hypoxaemia. Laboratory findings (table 1) showed high LDH levels and no other remarkable findings. She had a normal full blood count, no rise in CRP, no derangement in coagulation profile. Her CXR revealed no new changes. She was hospitalised for quarantine with the family and for further observation due to her immunocompromised status. Her rheumatologist was involved in the care from the time of admission. During her stay, she remained asymptomatic and on room air. The patient received hydroxychloroquine for 7 days in addition to her daily immunosuppressant medications, with no resulting complications or flare of SLE. Her CoV-PCR test became negative after 9 days. Her SARS-CoV-2 serology was positive.

OUTCOME AND FOLLOW-UP

The five patients had an uneventful course of illness, and all recovered without any sequelae.

DISCUSSION

Children appear to experience a milder form of COVID-19 than do healthy adults.^{4–6} Reports from the most affected countries indicate that COVID-19 in the paediatric population is different from that in adults and has a favourable clinical course and outcome.^{4,5} Various theories exist with regard to the reason for mild COVID-19 in children. One theory is related to the difference in expression of ACE2 receptor, which is necessary for SARS-CoV-2 binding and infection.⁶ Another interesting theory is linked to ACE2 gene polymorphism and genetic predisposition towards increased susceptibility to SARS-CoV-2 infection.⁷

In our case series, the five patients had a benign clinical course of COVID-19 and fully recovered despite their variable immunocompromised status and underlying pathology. None had a significant inflammatory disease, and none progressed to respiratory distress or developed pneumonia. None had a relapse of the original disease, developed severe COVID-19 or died. Our findings are in line with the reported observations from studies in adult populations with immune dysregulation. For example, a clinical series describing the clinical course of the disease in patients with chronic arthritis on immunosuppressive therapies indicated that none developed signs of SARS or died.⁸ Another case series from Spain describing adult patients with HIV infection who contracted COVID-19 reported no deaths.⁹ We believe the benign course of COVID-19 in immunocompromised children can be attributed to the fact that the host immune response seems to be the key driver of lung tissue damage during infection or to the relative resistance in children due to the lower distribution and maturation of viral receptors, namely the ACE2 receptor.^{6,10} Gralinski *et al*¹¹ confirmed that COVID-19 is an immune-driven disease. It includes activation of the complement system, the release of inflammatory cytokines and chemokines, and immune cell tissue infiltration, resulting in a pathological outcome. Moreover, innate immune factors seem to play a fundamental role in defining the severity of COVID-19.^{11,12} Hence, it is possible that immune suppression or immune dysregulation may reduce SARS-CoV-2

pathogenesis, which explains why our five immunocompromised paediatric patients did not have severe COVID-19. Furthermore, immunodeficiency without other comorbidities may not be a major risk factor for poor prognosis. Wang *et al*¹³ reported obesity, cardiopulmonary chronic disease, diabetes, renal diseases, advanced age and male sex as the main risk factors for poor prognosis.

In contrast, it has been suggested that immunodeficient children may have prolonged viral shedding and potentially be contagious for longer duration, as per experience from other respiratory viral infections.¹⁴ This concern is still valid and requires further studies to investigate it. Our patients continued to shed the virus for an average of 2 weeks. However, in the setting of mild COVID-19 presentation as in cases 2, 4 and 5, they received their immunosuppressant medications and continued their treatment regimens as planned, without delays. Immunosuppressant medications were well tolerated and with favourable outcome.

It is extremely important to protect immunocompromised children, especially with the current challenges that the healthcare system is facing worldwide. Data on the clinical findings and outcomes of immunocompromised children infected with SARS-CoV-2 are still scarce, and recommendations continue to be elusive. However, we believe that sharing experiences can contribute positively to the cumulative knowledge about emerging COVID-19, especially among the most vulnerable groups. We hope that this article contributes to future clinical practice and analysis of COVID-19 pathogenesis and that it offers insight for novel interventions. In general, we hope that this paper provides a sense of reassurance and support for this group of patients and their families.

Learning points

- Immunocompromised children are unlikely to be at a higher risk of developing severe COVID-19. Thus, the paediatrician could provide reasonable reassurance to this vulnerable group of patients and their caregivers.
- Immune suppression seems to be a protective factor against severe COVID-19. This can provide researchers with further insight into SARS-CoV-2 pathogenesis or novel interventions.
- Immunosuppressive therapies are likely tolerated in the setting of mild COVID-19 in children, preventing relapse and morbidity from underlying conditions.

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