Case Report

ANNALS OF MEDICINE & SURGERY

OPEN

Autoimmune hemolytic anemia associated with COVID-19 infection: a rare case report

Eman Shhada, MD[a], Lava Abdullah, MD[b,*], Nour Abduljalil, MD[c], Ghazal Gharib, MD[c], Dima Barhoom, MD[c], Sawssan Ali, MD[d]

Introduction: Coronavirus disease 2019 (COVID-19) is an illness due to severe acute respiratory syndrome, symptoms and severity of disease varies from patient to patient, autoimmune hemolytic anemia (AIHA) in children with COVID-19 is rare.
Case presentation: A 12-year-old female presented with fever, headache, myalgia, and hematuria. At admission, she was hemodynamically stable, severe anemia was present, and severe acute respiratory syndrome coronavirus 2 infection was confirmed by RT-PCR. The diagnosis of AIHA was confirmed and treated.
Discussion: There are few reports of patients with AIHA and COVID-19. However, the majority of patients in these reports also have autoantibodies and other underlying conditions known to be associated with the development of AIHA.
Conclusion: In this current pandemic, it should be taken into account that previously healthy children with severe acute respiratory syndrome coronavirus 2 infection have been found to have severe hemolytic anemia in the absence of COVID-19.

Keywords: autoimmune hemolytic anemia, children, COVID-19, SARS-Cov-2

Introduction

Coronavirus disease 2019 (COVID-19) is an illness due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The signs and symptoms of COVID-19 illness vary from patient to patient. The most common clinical symptoms are fever, fatigue, cough, phlegm, anorexia, phlegm, shortness of breath, sore throat, headache, confusion, hemoptysis, and chest tightness, nausea, vomiting, diarrhea, and gastrointestinal complications. Similar signs and symptoms of COVID-19 include: although seen in children like adults, these symptoms are generally milder than in adult patients[1].

Over 3 million SARS-CoV-2 cases at the end of April 2020 were reported worldwide, relatively sudden occurrences in children with severe hyperinflammation disorders with multisystem involvement are international null alarm[2].

As of 12 April 2023, there are 762 791 152 confirmed cases of COVID-19 worldwide, including 6 897 025 deaths[3].

HIGHLIGHTS

- Coronavirus disease 2019 is an illness due to severe acute respiratory syndrome.
- Autoimmune hemolytic anemia is a heterogeneous disease entity associated with increased destruction or clearance of red blood cells by antierythrocyte antibodies.
- This paper suggests that severe acute respiratory syndrome coronavirus 2 can induce autoimmune hemolytic anemia in children.

Hemolytic anemia occurs when RBCs are targeted by anti-RBC membrane autoantibodies (Auto-Abs), resulting in autoimmune hemolytic anemia (AIHA), depending on the temperature at which Auto-Abs bind optimally to RBCs. AIHA is classified as warm type mediated by IgG and C3d or cold type mediated by IgM.

SARS-CoV-2 infection may lead to hemolytic anemia directly through cytopathic injury or indirectly through induction of auto-Abs[4].

However, few cases of pediatric SARS-CoV-2-associated AIHA have been reported to date[5].

A total of 26 cases of AIHA associated with COVID-19 infection have been reported according to AbouYabis[6].

This case report was conducted in accordance with the Surgical CAse REport (SCARE) criteria[7].

Case presentation

A12-year-old female was admitted to our hospital with a complaint of a 2-weeks period of pallor, fatigue, fever, headache, and myalgia and a 2-day duration of high-colored urine after a 2-week duration of respiratory infection. The patient was treated upper respiratory infection with improvement until she was

[a]Department of Pediatrics, Children's Damascus University Hospital, Damascus University, [b]Department of Obstetrics and Gynecology, Police Hospital, Damascus, [c]Pediatrics Department and [d]Pulmonary Pediatrics Department, Children's Damascus University Hospital, Syria

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Al-Mazzah, Damascus, Syria. Tel: +963 997 769 874. E-mail: Lava7abdullah@gmail.com (L. Abdullah).

Annals of Medicine & Surgery (2023) 85:3604–3606

Received 29 March 2023; Accepted 15 April 2023

Published online 3 May 2023

http://dx.doi.org/10.1097/MS9.0000000000000742

developed hematuria, so she was referred to our hospital for a detailed evaluation.

At admission, she was pale, febrile, and hemodynamically stable with the following vital signs: temperature, 38.7°C; blood pressure, 110/65 mmHg; heart rate, 120 beats/minute; respiratory rate, 20 min; and oxygen saturation, 99% at room air. She had no clubbing, cyanosis, lymphadenopathy, edema, arthritis, or rash.

Cutaneous stigmata of chronic liver disease were not present. The respiratory, cardiovascular, gastrointestinal, and central nervous systems were normal on examination. No other abnormalities were found in the physical examination. Results of blood tests showed decreased hemoglobin (5.4 g/dl), hematocrit (18.8%), mean corpuscular volume (82 fl), haptoglobin (<7.38 µmol/l) associating reticulocytosis (5%). Erythrocyte sedimentation rate 34 mm /h, C-reactive protein = 0,2 mg /l Increased lactate dehydrogenase (458 U/l) and hyperbilirubinemia (3.5 mg/dl) with indirect predominance (2.25 mg/dl), serum aspartate aminotransferase comparatively higher than serum alanine aminotransferase.

Platelets and leukocytes counts, serum electrolytes and renal function levels, and serum irons were within normal range. Ferritin (148.6 ng/ml) was normal. A direct Coombs test was performed with a positive result (positive immunoglobulin G and C3 and negative C4).

Family, medical, and drug histories were unremarkable,

Due to the pandemic situation, and the personal history of respiratory infection, SARS-COV-2 infection was confirmed by RT-PCR of the nasopharyngeal swab, and she was treated with antipyretics.

Hypochromia, some polychromatic macrocytes, anisocytosis, red cell fragmentation with moderate numbers of micro-spherocytes and nucleated red cell compatible with hemolytic anemia features were detected at the peripheral blood smear [Fig. 1].

Urine analysis showed dark urine with a positive hemoglobin.

The chest radiography was unremarkable [Fig. 2].

AIHA was diagnosed and the treatment with methylprednisolone pulses (30 mg/kg daily) was given for the first 72 h. Afterward, the maintenance dose of prednisolone 1 mg/kg daily was administered. Two weeks later, hemolysis was reduced, and hemoglobin value increased to 8.2 g/dl without the need for blood transfusions. After 2 months, at follow-up the patient, the laboratory tests showed that the hemoglobin and reticulocyte levels were be normalized slowly, with a negative Coombs value, with improvement the vitality, and general condition.

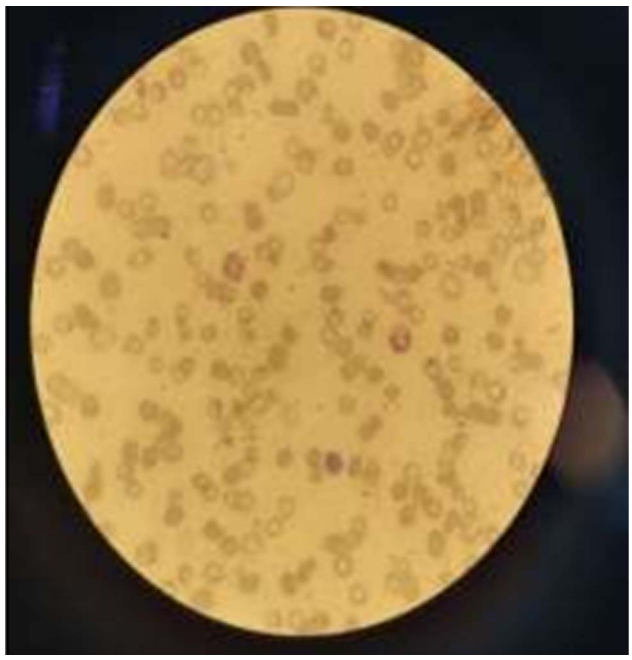

Figure 1. Peripheral blood smear: hypochromia, some polychromatic macrocytes, anisocytosis, red cell fragmentation with moderate numbers of microspherocytes, and nucleated red cells compatible with hemolytic anemia features.

Discussion

AIHA is a heterogeneous disease entity associated with increased destruction or clearance of red blood cells by antierythrocyte antibodies. This destruction can occur at:

Intravascular space due to complement-mediated hemolysis or extravascular space primarily due to antibody and complement-mediated phagocytosis or removal of red blood cells[8,9].

AIHA can be primary or secondary, depending on the presence of an underlying disease or condition that promotes dysregulation of the immune system[10].

AIHA is a rare disease that occurs in 1–3 cases per 100 000 people annually[11].

AIHA is a rare but complex disease with variable symptoms and variable clinical severity.

The most common form of AIHA is caused by warm autoantibodies that react with autoantigens on RBC membranes at 37

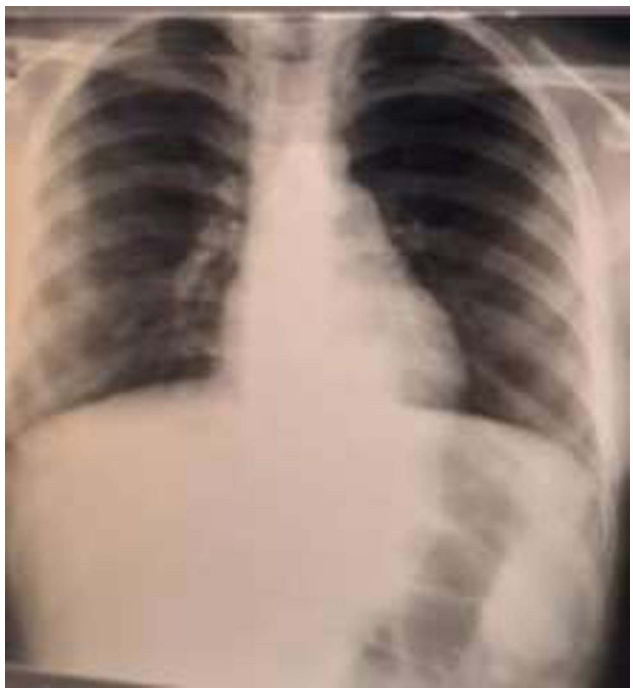

Figure 2. Unremarkable chest radiography.

°C. Warm autoantibodies accounts for 70–80% of all cases of AIHA in adults and 50% of AIHA in children[12].

There is little evidence in the literature regarding patients with COVID-19 and AIHA. Therefore, the relationship between these diseases is unknown[8].

There are few reports of patients with AIHA and COVID-19. But the majority of patients in these reports also have Auto-Abs and other underlying conditions known to be associated with the development of AIHA.

This paper reports a unique case of AIHA in a child with COVID-19 who have no underlying autoimmune, neoplastic, or lymphoproliferative disease typically induce AIHA.

Conclusion

AIHA associated with COVID-19 is a rare combination, this paper suggests that SARS-CoV-2 can induce AIHA in children. In this current pandemic, the finding of severe hemolytic anemia without any presentation of COVID-19 in a previously healthy child, SARS-CoV-2 infection should be considered.

Ethical approval

Ethical approval was obtained from the research ethical committee in Damascus University.

Consent

Written informed consent was obtained from the patient's parents for publishing the case report and all the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

No funding

Author contribution

E.S., L.A., N.A., G.G., D.B., S.A.: all the authors contributed in diagnosis and management the case, performing literature search, writing the paper, and approved.

Conflicts of interest disclosure

No conflict of interest.

Research registration unique identifying number (UIN)

NA.

Guarantor

Lava Abdullah.

Provenance and peer review

Not commissioned, externally peer reviewed.

References

[1] Majumder J, Minko T. Recent developments on therapeutic and diagnostic approaches for COVID-19. AAPS J 2021;23:14.
[2] Hoste L, Van Paemel R, Haerynck F. Multisystem inflammatory syndrome in children related to COVID-19: a systematic review. Eur J Pediatr 2021;180:2019–34.
[3] WHO. Coronavirus (COVID-19) Dashboard afhcwi, Accessed 12 April 2023.
[4] Al-Kuraishy HM, Al-Gareeb AI, Kaushik A, *et al*. Hemolytic anemia in COVID-19. Ann Hematol 2022;101:1887–95.
[5] Vega Hernández P, Borges Rivas Y, Ortega Sánchez E, *et al*. Autoimmune hemolytic anemia in a pediatric patient with severe acute respiratory syndrome coronavirus 2 infection. Pediatr Infect Dis J 2020;39:e288.
[6] AbouYabis AN, Bell GT. Hemolytic anemia complicating COVID-19 infection. J Hematol 2021;10:221.
[7] Agha RA, Franchi T, Sohrabi C, *et al*. The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines. Int J Surg 2020;84:226–30.
[8] Jacobs J, Eichbaum Q. COVID-19 associated with severe autoimmune hemolytic anemia. Transfusion 2021;61:635–40.
[9] Hill A, Hill QA. Autoimmune hemolytic anemia. Hematol Am Soc Hematol Ed Prog 2018;2018:382–9.
[10] Hill QA, Hill A, Berentsen S. Defining autoimmune hemolytic anemia: a systematic review of the terminology used for diagnosis and treatment. Blood Adv 2019;3:1897–906.
[11] Kalfa TA. Warm antibody autoimmune hemolytic anemia. Hematol Am Soc Hematol Ed Prog 2016;2016:690–7.
[12] Gehrs BC, Friedberg RC. Autoimmune hemolytic anemia. Am J Hematol 2002;69:258–71.