ELMER PRESS

Case Report

J Hematol. 2021;10(5):221-227

Hemolytic Anemia Complicating COVID-19 Infection

Abeer N. AbouYabis[a, b], Grace Thompson Bell[a]

Abstract

Coronavirus disease 2019 (COVID-19) has been associated with a spectrum of reported hematological complications ranging from immune cytopenias to thromboembolic manifestations of coagulopathy. Moreover, there have been documented cases of hemolytic anemia associated with COVID-19 infection which have been mainly attributed to development of autoantibodies. We report a case of an African-American patient who presented with hemolytic anemia in the second week after his COVID-19 diagnosis. Throughout this report, we explore the potential immune and non-immune etiologies that contributed to the patient's hemolytic anemia in the setting of COVID-19 infection guided by a review of literature.

Keywords: Hemolytic anemia; COVID-19; Autoimmune hemolytic anemia; G6PD deficiency

Introduction

Coronavirus disease 2019 (COVID-19) infection is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) strain and has been associated with a wide spectrum of disease manifestations ranging from asymptomatic disease to a severe inflammatory cytokine storm affecting multiple organ systems. The most commonly reported hematological complications of COVID-19 infection have been cytopenia, coagulopathy and thromboembolic events [1-3].

We report here an African-American patient with hemolytic anemia in the setting of positive direct antiglobulin test (DAT) and within the timeframe of COVID-associated cytokine storm. Given the timeframe and setting, this could be labeled as COVID-19-associated autoimmune hemolytic anemia (AIHA) supported by the growing number of reported cases of AIHA presenting during SARS-CoV-2-induced hyper-inflammatory state (Table 1) [4-20]. However, a negative eluate along with delayed and suboptimal response to steroids triggered a search for another contributory mechanism for hemolysis. Given patient's ethnic background, a glucose-6-phosphate dehydrogenase (G6PD) level was ordered, and results confirmed deficiency which we think contributed significantly to patient's hemolysis. This report further investigates the potential mechanisms of hemolysis that can be associated with COVID-19 infection and is the first to raise the possibility of COVID-19 infection as an infectious trigger for hemolysis in patients with G6PD deficiency.

Case Report

A 54-year-old African-American man presented to the emergency department reporting a 103 °F temperature and 2-week history of worsening shortness of breath, cough, fatigue and nausea. He had tested negative for SARS-CoV-2 twice during those 2 weeks; however, 9 days prior to presentation, a third SARS-CoV-2 polymerase chain reaction (PCR) resulted positive. A positive SARS-CoV-2 PCR was confirmed upon admission. Three weeks prior to presentation, he had a tooth infection for which he took amoxicillin for 5 days. He had no history of anemia, drug allergies or blood transfusions.

On admission patient was afebrile, in no acute distress, hemodynamically stable with no significant findings on physical exam as summarized in Table 2.

A complete blood count (CBC) revealed hemoglobin (Hgb) of 6.7 g/dL, with leukocytosis and normal platelet count. Indirect antiglobulin test (IAT) was positive with no alloantibody identified. Lactate dehydrogenase (LDH) and total bilirubin were elevated while haptoglobin was low (Table 3). DAT on admission was weakly positive for complement C3 and negative immunoglobulin G (IgG). G6PD was later found to be decreased at 3.1 U/g of Hgb. Viral workup was negative except for COVID-19. Creatinine was elevated > 5 mg/dL on admission with workup suggestive of acute tubular necrosis secondary to COVID-19 that improved during hospitalization. Chest X-ray demonstrated bilateral airspace opacities consistent with SARS-CoV-2 infection. Ultrasound of the lower extremities performed due to right leg pain was positive for deep vein thrombosis and patient was started on anticoagulation. Other diagnostic findings are summarized in Table 4.

Patient received one unit of packed red blood cells (PRBCs) on admission and subsequent daily transfusions with no significant improvement in Hgb. Prednisone 1 mg/kg was also started on admission. On day 3, his DAT became positive for IgG (2+) and complement C3 (3+). Eluate was non-

Manuscript submitted August 9, 2021, accepted September 17, 2021
Published online October 5, 2021

[a]Department of Hematology and Oncology, Emory University, Atlanta, GA, USA
[b]Corresponding Author: Abeer N. AbouYabis, Department of Hematology and Oncology, Emory University School of Medicine, 550 Peachtree St NE, MOT Suite 1075, Rm 1001, Atlanta, GA 30308, USA.
Email: abeer.n.abouyabis@emory.edu

doi: https://doi.org/10.14740/jh906

Table 1. Literature Review of Autoimmune Hemolytic Anemia Associated With COVID-19

References	No. of patients	Age	Median Hgb at diagnosis (g/dL)	AIHA type	Day of onset[a]	Underlying disease likely contributing	Treatment type	Time to remission and/or stabilization of Hgb
Campos-Cabrera et al [4]	2 F	35 and 58	NA	Warm IgG + C3d	D+1	None	Prednisone	NA
Capes et al [5]	1 M	62	6.9	Positive C3b	D+16	Questionable[b]	Transfusion support only (8 units over 1 week)	NA
Chiare et al [6]	1 F	86	8.3	Positive IgG	D+49	None	Steroids	D+13
Hindilerden et al [7]	1 M	56	4.3	Positive IgG + C3d	D+4	None	IVIG then steroids	D+12 transfusion independent; D+14 Hgb 8.4; D+17 Hgb > 10.7
Hseih et al (2021) [8]	1 M	84	4.4	Positive IgG + anti-Kell	D+10-13	None	Transfusion + steroids	NA
Huda et al (2021) [9]	1 M	54	9	Positive IgG	D+8	None	Prednisone	NA
Jacobs and Eichbaum [10]	1 F	33	1.3	Positive IgG + C3; possibly mixed AIHA	D-2	None	Steroids + rituximab + tocilizumab	D+10
Jawed et al [11]	1 M	About 50	7.9 to 10.7[c]	Positive C3d (did not specify if cold or warm)	NA[d]	None	NA	D+21
Lazarian et al [12]	7 (3 F, 4 M) + 1 with Hx of AIHA	> 60	7	4 with warm (2 IgG only, 2 IgG + C3d); 3 with cold (2 C3d only, 1 C3 + IgG)	Median + D9 (range 4 - 13)	5 (CLL, MZL, MGUS)	Five treated with steroids; two treated with rituximab	NA
Li et al (2020) [13]	1 M	39	6	DAT 3+ (did not specify if IgG or complement)	D+10[e]	None	IVIG only: patient had gastrointestinal bleed due to ITP treated with IVIG	D+28 (Hgb 7 after IVIG, Hgb 11 four weeks post discharge)
Liput et al [14]	1 F	33	6.5, nadir 6.2-transfused	Positive IgG + C3	D+1[f]	None	Prednisone	Not reported[g]
Lopez et al [15]	1 F	46	9.7	Warm (positive IgG + C3)	D-3	Congenital TCP	Prednisone after IVIG	D+15[h]
Patil et al [16]	1 F	51	5.1	Positive C3d; cold agglutinin titer 80	D+1	None	Solumedrol for respiratory deterioration	D+14 (Hgb 11)
Raghuwanshi [17]	1 M	45	6.9	Cold agglutinin	D+1	None	NA	NA
Ramos-Ruperto et al (2021) [18]	3 (1 M, 2 F)	54, 72,76	6.5 - 8	2 with positive IgG; one only C3	Unknown D+1	One with CLL None	Steroids Steroids + plasma exchange	
Woldie et al [19]	1 M	24	7.5, nadir = 5.8	Positive IgG + C3	D+1	History of AIHA[i]	Prednisone + cyclophosphamide	D+13
Zagorski et al [20]	1 F	46	5.3	Positive IgG + C3d	D+1	History of ITP in pregnancy (unlikely contributing)	Died before treatment	NA

[a]Day of onset of AIHA from day of COVID diagnosis. +D1 defined as occurring on the day of COVID diagnosis. [b]Oropharyngeal squamous cell CA on chemo-radiation; positive mycoplasma IgM: NEG PCR. [c]Exact date of diagnosis not specified; Hgb ranged from 10.7 to 7.9 during hospitalization. [d]Date of COVID test not specified; coryzal symptoms started 2 weeks prior to COVID diagnosis. [e]COVID diagnosis with thrombocytopenia was D+7 after respiratory symptoms started. AIHA occurred D+10 after COVID diagnosis (D+17 from onset of symptoms). [f]Asymptomatic COVID infection diagnosed same day as AIHA. [g]Hgb = 8.1 on D6; Hgb = 12.6 at 7 weeks. [h]Patient discharged on day 8; Hgb was 11g/dL 7 days after discharge. [i]Prior history of AIHA, 3 years before COVID maintained on daily prednisone 20 mg. AIHA: autoimmune hemolytic anemia; IVIG: intravenous immunoglobulins; Hgb: hemoglobin; Hx: history; CLL: chronic lymphocytic leukemia; MZL: marginal zone lymphoma; MGUS: monoclonal gammopathy of unknown significance; TCP: thrombocytopenia; ITP: immune thrombocytopenic purpura; NA: not available.

Table 2. Vital Signs and Physical Exam Findings

Vital signs	Findings
Temperature	36.6 °C
Blood pressure	160/82 mm Hg
Heart rate	84 beats per minute
Respiratory rate	18 breaths per minute
Oxygen saturation	96% on room air
Physical exam	Anicteric sclera, no palpable lymphadenopathy or splenomegaly. Rectal exam guaiac negative.

reactive. Patient was switched to dexamethasone 40 mg orally daily for 4 days on day 5 as Hgb continued to be below 7 g/dL with daily transfusions. Hgb trend in response to steroid treatment is depicted in Figure 1. Rituximab was not given in setting of COVID-19 infection. When Hgb dropped again to lower than 7 g/dL after initial improvement on dexamethasone, prednisone 60 mg daily was restarted. Hgb increased to 9.3 g/dL and patient became transfusion-independent. Patient was discharged on day 14 of admission and continued prednisone taper outpatient over 2 weeks with stabilization of Hgb at 8.5

Table 3. Laboratory Findings

Laboratory test	Result	Reference range (if applicable)
Hemoglobin	6.7 g/dL	12.9 - 16.1
Mean corpuscular volume	82 fL	79.0 - 92.2
White blood cell count	18,000/µL, 70% neutrophils	4,200 - 9,100
Platelet count	389,000/µL	150,000 - 400,000
Lactate dehydrogenase	2,569 U/L	140 - 271
Haptoglobin	4 mg/dL	32 - 197
Total bilirubin	2.7 mg/dL	0.3 - 1.9
Direct	0.84 mg/dL	≤ 0.18
Indirect	1.86 mg/dL	0.1 - 1.0
Absolute reticulocyte count	71,000/µL	26,000 - 95,000
Indirect antiglobulin test	Positive, no alloantibody identified	-
Direct antiglobulin test		-
On admission	Positive, negative IgG and weakly positive complement C3	
On day 3 of hospitalization	Positive, positive IgG (2+) and positive complement C3 (3+)	
Eluate	Non-reactive	-
Cold agglutinins titer	< 1:32	-
Iron	83 µg/dL	50 - 212
Ferritin	1,076 ng/mL	24 - 336
Vitamin B12	> 2,800 pg/mL	180 - 914
Folate	> 20 ng/mL	≥ 5.9
G6PD	2.2 - 5.0 U/g Hgb	7.9 - 16.3
C-reactive protein	117 mg/L	≤ 10.0
Fibrinogen	787 mg/dL	200 - 393
D-dimer	> 5,000 ng/mL	≤ 574
Creatinine		0.70 - 1.30
On admission	5.56 mg/dL	
On day 45	1.15 mg/dL	
Serum protein electrophoresis	Negative	

G6PD: glucose-6-phosphate dehydrogenase; IgG: immunoglobulin G; Hgb: hemoglobin.

Table 4. Diagnostic Findings

Diagnostic test	Findings
Peripheral blood smear	Few echinocytes, rare schistocytes (1 - 2 per high powered field), large platelets with few platelet clumps; no significant agglutination. No immature white blood cells, frequent bands.
Chest X-ray	Bilateral airspace opacities consistent with SARS-CoV-2 infection
CT chest of abdomen and pelvis	No acute findings, negative for splenomegaly, hepatomegaly or lymphadenopathy
Renal studies	
Urinalysis	Large blood but only 3 RBCs
Urine microscopy	Muddy brown casts
Renal ultrasound	No hydronephrosis - 10.7 cm, 11.1 cm kidney size
Bone marrow biopsy and aspiration	Mildly hypo-cellular marrow (20-30%) with no dysplasia or abnormal hematolymphoid cell populations

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; RBC: red blood cell.

g/dL. DAT became negative 4 weeks after initial diagnosis of AIHA. Patient was re-admitted 3 weeks after discharge with multifocal pneumonia and treated with antibacterial agents. His Hgb remained 8 - 8.5 g/dL during his second hospitalization with negative DAT and no evidence of hemolysis. In the outpatient setting, his Hgb continued to fluctuate between 8.5 and 10.5 g/dL with no obvious underlying cause of persistent anemia. A bone marrow biopsy was done and revealed mildly hypocellular marrow (20-30%) with no dysplasia or abnormal hematolymphoid cell populations.

Review of literature

We conducted a computerized literature research to identify publications on AIHA in adult COVID-19 patients using PubMed, Google Scholar and EMBASE from January 1, 2020 to July 31, 2021. The following keywords were used: autoimmune hemolysis, autoimmune hemolytic anemia, COVID-19 and SARS-CoV-2. The references of studies or reports were checked to confirm positive DAT (direct Coombs) as well as positive COVID test upon diagnosis of AIHA.

A total of 26 cases of AIHA associated with COVID-19 infection have been reported to date (Table 1). Both warm and cold autoantibodies have been implicated in COVID-19-associated AIHA.

Time of onset of autoimmune hemolysis was variable; however, most cases were diagnosed in the first 2 weeks of infection. Only one case was reported after 7 weeks of COVID-19 diagnosis [6]. Five reported cases had underlying hematologic malignancy that could have contributed to the development of AIHA [12].

The majority of patients were treated with steroids, only three received rituximab [10, 14] and three received intra-

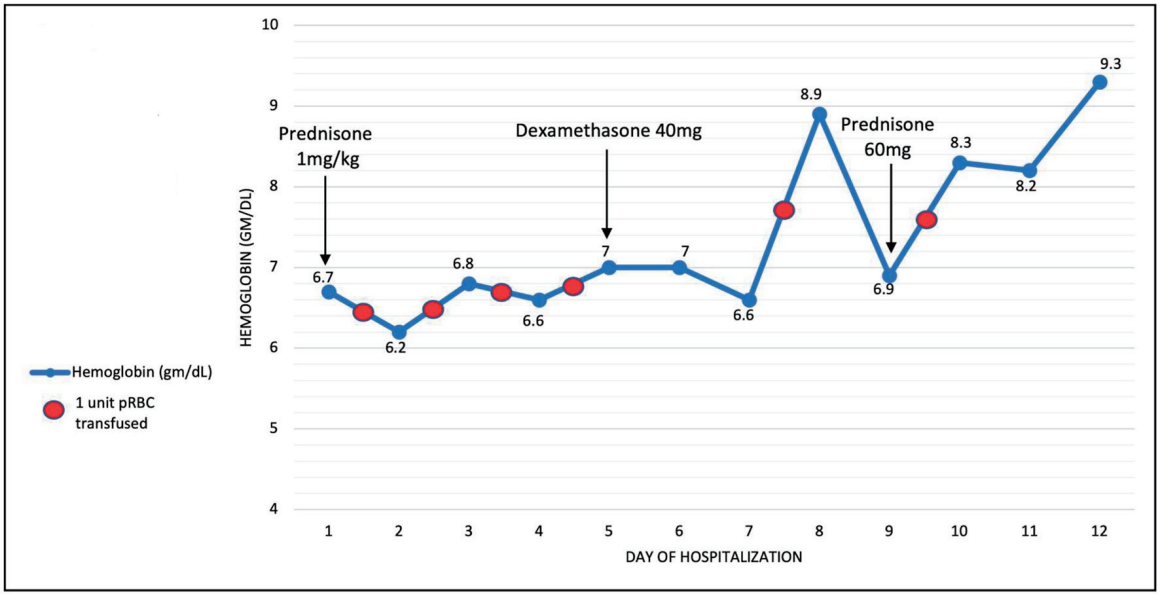

Figure 1. Hemoglobin throughout hospitalization. Arrows indicate start date of medications. Red circles indicate blood transfusion.

venous immunoglobulins [7, 13, 15]. There has not been a consistent definition of remission among different reports and most patients did not have follow-up beyond discharge. However, from available data, it can be concluded that most patients achieved Hgb ≥ 8 g/dL within 14 days of diagnosis (Table 1).

To date, there are no reported cases of G6PD deficiency-associated hemolysis complicating COVID-19 infection.

Discussion

We report a case of hemolytic anemia presenting 9 days after positive SARS-CoV-2 PCR test and coinciding with worsening respiratory symptoms and increased inflammatory markers. We propose that the patient's hemolysis has both immune and non-immune components. Immune-mediated hemolysis is supported by the positive DAT and lack of response to transfusions. Patient's G6PD deficiency likely played an additional role in the severity of anemia, suboptimal response to steroids and delayed remission.

Drug-induced immune hemolytic anemia was first considered given the weakly positive complement-only DAT and later non-reactive eluate. The possible culprit was the amoxicillin which the patient took within 2 weeks prior to admission. However, this does not explain patient's worsening symptoms, continued hemolysis requiring transfusion, and increase in the strength of DAT positivity (2+ IgG and 3+C3) 3 days after admission and more than 1 week after stopping amoxicillin.

Since the patient's immune-mediated hemolysis coincided with worsening COVID-19 symptoms within the timeframe compatible with COVID-associated cytokine storm, SARS-CoV-2-mediated immune hemolysis became high on the differential. There is a growing number of reported cases of AIHA in the setting of COVID infection presenting during SARS-CoV-2-induced hyper-inflammatory state (Table 1). The exact mechanism of AIHA in the setting of COVID-19 infection remains unknown. One proposed mechanism is that the SARS-CoV-2 cytokine-rich inflammatory environment causes alteration in antigen presentation creating cryptic antigens [21]. Those cryptic antigens stimulate T lymphocytes which in turn activates autoreactive B lymphocytes to produce antibodies against those antigens [21-23]. These antibodies then coat the red blood cells (RBCs) causing the positive DAT in around 44-46% of COVID-19 patients [21, 24]. The importance of the COVID-induced inflammatory milieu in exposing cryptic antigens was further emphasized by demonstrating that the DAT can be "transmitted" to allogeneic RBCs that have been in contact with the plasma of DAT-positive COVID-19 patients [21, 23]. In their study, Brochier et al reported a negative eluate among all of the 99 hospitalized COVID-19 patients who had a positive DAT [21], a finding similar to that of our patient. The number of COVID-19 patients with positive DAT who would eventually develop clinically significant hemolysis remains unknown. Since reporting on AIHA in the setting of COVID-19 has been limited to few case reports, it is not clear if other factors would contribute to the development and severity of hemolysis in those COVID-19 patients with positive DAT.

The patient we are reporting here has G6PD deficiency which we believe contributed to his worsening hemolysis and prolonged anemia. Our patient was treated with amoxicillin 2 weeks prior to presentation. Amoxicillin-induced hemolysis in G6PD-deficient patients has been reported [25]. However, a positive DAT and hemolysis that developed more than 7 days after the last dose of amoxicillin make it an unlikely culprit. On the other hand, there have been several pieces of evidence suggesting that G6PD deficiency may increase susceptibility to, and severity of illness associated with COVID-19 infection [26, 27]. RBC destruction in otherwise asymptomatic patients with G6PD deficiency can be triggered by certain infectious agents and medications where decreased production of G6PD results in deficient levels of nicotinamide adenine dinucleotide phosphate and reduced glutathione, causing oxidative stress and RBC destruction. COVID-19 infection could be among those infectious triggers for hemolysis in patients with G6PD deficiency. In light of growing evidence that African-American patients are disproportionately affected by severe COVID-19 infection and given increased prevalence of G6PD deficiency among African-American patients, further studies are needed to determine whether a positive correlation exists between G6PD deficiency and COVID-19 with respect to increased susceptibility to infection and severity of illness [26-28].

Conclusion

Hemolytic anemia in the setting of SARS-CoV-2 appears multifactorial. The exact mechanism of autoimmune hemolysis in COVID-19 infection requires further elucidation. G6PD deficiency is another factor that requires additional consideration especially in patients who belong to ethnic groups where G6PD deficiency is prevalent and demonstrate hemolysis in the setting of acute COVID-19 infection.

Acknowledgments

The authors would like to express sincere gratitude to Dr. Christine Kempton for reviewing the manuscript and to the patient for giving permission to share his case.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Consent was obtained from the patient.

Author Contributions

All authors contributed to the editing of the manuscript. ANA wrote the manuscript. GTB made the accompanying tables and figure. All authors read and approved the final manuscript.

Data Availability

The data that support the findings of this study are available from the electronic medical records of the patient. Data are available from the authors upon reasonable request and with permission of the patient.

References

1. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. Blood. 2020;135(23):2033-2040.
2. Klok FA, Kruip M, van der Meer NJM, Arbous MS, Gommers D, Kant KM, Kaptein FHJ, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145-147.
3. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-1069.
4. Campos-Cabrera G, Mendez-Garcia E, Mora-Torres M, et al. Autoimmune hemolytic anemia as initial presentation of COVID-19 infection. Blood. 2020;136(Supplement1):8.
5. Capes A, Bailly S, Hantson P, Gerard L, Laterre PF. COVID-19 infection associated with autoimmune hemolytic anemia. Ann Hematol. 2020;99(7):1679-1680.
6. Pelle MC, Tassone B, Ricchio M, Mazzitelli M, Davoli C, Procopio G, Cancelliere A, et al. Late-onset myocardial infarction and autoimmune haemolytic anaemia in a COVID-19 patient without respiratory symptoms, concomitant with a paradoxical increase in inflammatory markers: a case report. J Med Case Rep. 2020;14(1):246.
7. Hindilerden F, Yonal-Hindilerden I, Akar E, Yesilbag Z, Kart-Yasar K. Severe autoimmune hemolytic anemia in COVID-19 infection, safely treated with steroids. Mediterr J Hematol Infect Dis. 2020;12(1):e2020053.
8. Hsieh TC, Sostin O. Severe warm autoimmune hemolytic anemia in COVID-19 managed with least incompatible RBC product and glucocorticoids. Ann Hematol. 2021.
9. Huda Z, Jahangir A, Sahra S, Rafay Khan Niazi M, Anwar S, Glaser A, Jahangir A. A case of COVID-19-associated autoimmune hemolytic anemia with hyperferritinemia in an immunocompetent host. Cureus. 2021;13(6):e16078.
10. Jacobs J, Eichbaum Q. COVID-19 associated with severe autoimmune hemolytic anemia. Transfusion. 2021;61(2):635-640.
11. Jawed M, Hart E, Saeed M. Haemolytic anaemia: a consequence of COVID-19. BMJ Case Rep. 2020; 13(12):e238118.
12. Lazarian G, Quinquenel A, Bellal M, et al. Autoimmune hemolytic anemia associated with COVID-19 infection. Br J Haematol. 2020;190(1):29-31.
13. Li M, Nguyen CB, Yeung Z, Sanchez K, Rosen D, Bushan S. Evans syndrome in a patient with COVID-19. Br J Haematol. 2020;190(2):e59-e61.
14. Liput JR, Jordan K, Patadia R, Kander E. Warm autoimmune hemolytic anemia associated with asymptomatic SARS-CoV-2 infection. Cureus. 2021;13(3):e14101.
15. Lopez C, Kim J, Pandey A, Huang T, DeLoughery TG. Simultaneous onset of COVID-19 and autoimmune haemolytic anaemia. Br J Haematol. 2020;190(1):31-32.
16. Patil NR, Herc ES, Girgis M. Cold agglutinin disease and autoimmune hemolytic anemia with pulmonary embolism as a presentation of COVID-19 infection. Hematol Oncol Stem Cell Ther. 2020.
17. Raghuwanshi B. Serological blood group discrepancy and cold agglutinin autoimmune hemolytic anemia associated with novel coronavirus. Cureus. 2020;12(11):e11495.
18. Ramos-Ruperto L, Garcia-Perez E, Hernandez-Maraver D, Kerguelen-Fuentes A, Viejo-Llorente A, Robles-Marhuenda A, Busca-Arenzana C. A 3-case series of autoimmune haemolytic anaemia and COVID-19: is plasma exchange an alternative? SN Compr Clin Med. 2021;3:1420-1423.
19. Woldie IL, Brown IG, Nwadiaro NF, Patel A, Jarrar M, Quint E, Khokhotva V, et al. Autoimmune hemolytic anemia in a 24-year-old patient with COVID-19 complicated by secondary cryptococcemia and acute necrotizing encephalitis: a case report and review of literature. J Med Cases. 2020;11(11):362-365.
20. Zagorski E, Pawar T, Rahimian S, Forman D. Cold agglutinin autoimmune haemolytic anaemia associated with novel coronavirus (COVID-19). Br J Haematol. 2020;190(4):e183-e184.
21. Brochier A, Cabo J, Guerrieri C, et al. Autoimmune hemolytic anemia in COVID-19 patients, the "transmissible" direct Coombs test. J Hematol and Clin Research. 2021;5:004-008.
22. Fagiolo E, Toriani-Terenzi C. Mechanisms of immunological tolerance loss versus erythrocyte self-antigens and autoimmune hemolytic anemia. Autoimmunity. 2003;36(4):199-204.
23. Prasad S, Starck SR, Shastri N. Presentation of cryptic peptides by MHC class I is enhanced by inflammatory stimuli. J Immunol. 2016;197(8):2981-2991.
24. Berzuini A, Bianco C, Paccapelo C, Bertolini F, Gregato G, Cattaneo A, Erba E, et al. Red cell-bound antibodies and transfusion requirements in hospitalized patients with COVID-19. Blood. 2020;136(6):766-768.
25. Blanquicett CJ, Raavi T, Robert SM. A severe episode of hemolytic anemia after amoxicillin exposure in a G6PD deficient patient. Arch Clin Med Case Rep. 2019;3(3):104-112.
26. Vick DJ. Glucose-6-phosphate dehydrogenase deficiency and COVID-19 infection. Mayo Clin Proc.

2020;95(8):1803-1804.
27. Wu YH, Tseng CP, Cheng ML, Ho HY, Shih SR, Chiu DT. Glucose-6-phosphate dehydrogenase deficiency enhances human coronavirus 229E infection. J Infect Dis. 2008;197(6):812-816.
28. Gold JAW, Wong KK, Szablewski CM, Patel PR, Rossow J, da Silva J, Natarajan P, et al. Characteristics and clinical outcomes of adult patients hospitalized with COVID-19 - Georgia, March 2020. MMWR Morb Mortal Wkly Rep. 2020;69(18):545-550.