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LETTER TO THE EDITOR

Severe warm autoimmune hemolytic anemia in COVID-19 managed with least incompatible RBC product and glucocorticoids

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Dear Editor,

Warm autoimmune hemolytic anemia (AIHA) is a rare autoimmune disorder mediated by autoantibodies that are active at normal body temperature. It is commonly associated with underlying conditions, such as viral infections, autoimmune disorders, lymphoproliferative diseases [1]. Recently, a few case reports found association between warm AIHA and COVID-19 [2–4]. Here we present a case of a new onset warm AIHA in a COVID-19 patient.

An 84-year-old Caucasian man with a past medical history of hypercholesterinemia who developed dry cough, mild shortness of breath, and fever 13 days prior to the presentation. Three days after onset, he was tested positive for SARS-CoV-2. The patient was hypoxic upon arrival to the hospital, requiring 4 L/min of supplemental oxygen. Physical exam revealed scleral icterus. Laboratory work was significant for severe anemia (hemoglobin 4.4 g/dL) and indirect bilirubinemia (2.3 mg/dL). Further analysis showed lactate dehydrogenase of 1253 U/L, haptoglobin <10 mg/dL, and reticulocyte count of 120×10^9/L. Peripheral smear identified numerous nucleated RBCs and microspherocytes. CT scan of the chest, abdomen, and pelvis did not show any occult hemorrhage but revealed diffuse patchy bilateral groundglass opacities within the lungs. The patient was found to have positive direct Coombs test with anti-K antibodies and IgG pan-agglutinins. He received packed RBCs that were type-specific, K-negative, and "least incompatible" based on cross-match. The diagnosis of warm AIHA secondary to COVID-19 was made. Convalescent plasma therapy, remdesivir, and dexamethasone were initiated. In the first 24 h, he received 5 units of packed RBCs and remained stable, with hypoxia and dyspnea improving significantly on the second day. He was discharged with prednisone taper dose. His hemoglobin has been stable for 12 weeks since discharge.

Recognizing warm AIHA in COVID-19 is important to avoid delay in treatment. To our best knowledge, there have been 20 AIHA cases reported in COVID-19. Warm AIHA was found in only seven cases (Table 1) [2–6]. The mean age is 63.3 years old. On average, it takes 8 days from the first COVID-19 symptom to the development of warm AIHA. Anemia-related symptoms are common. Physical exam may show jaundice. The mean hemoglobin is 5.7. In addition to low hemoglobin, laboratory evaluation may be notable for increased reticulocyte count, elevated lactate dehydrogenase, low haptoglobin, indirect bilirubinemia, and spherocytosis/microspherocytosis. Diagnosis is made based on the presence of hemolytic anemia mediated by warm antibodies. Due to the presence of pan-reacting autoantibodies, identifying cross-matched blood products may not be possible. If severe anemia is present, clinicians should contact blood bank immediately for type-specific, "least incompatible" blood products. Warm AIHA is often treated with glucocorticoids in addition to transfusion. Rituximab can be considered based on the severity of the anemia and response to the steroid therapy [1]. Since glucocorticoids are also used in moderate to severe COVID-19 cases, it is reasonable to treat COVID-19-associated warm AIHA with glucocorticoids [7].

In summary, warm AIHA is a rare but severe complication of COVID-19. Recognizing the necessity to initiate transfusion with "least incompatible" blood products is curial. Glucocorticoids can be used to treat COVID-19 patients with warm AIHA.

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Table 1 Summary of the COVID-19-associated warm AIHA in the literature. *HTN* hypertension, *CKD* chronic kidney disease, *CLL* chronic lymphocytic leukemia, *MGUS* monoclonal gammopathy of undetermined significance, *HLD* hyperlipidemia, *DM* diabetes mellitus, *CM* cardiomyopathy, *COPD* chronic obstructive pulmonary disease, *ITP* idiopathic thrombocytopenic purpura, *C* complement, *?* insufficient data

	Age	Gender	Comorbidity	Hgb (g/dL)	LDH (U/L)	Haptoglobin (g/L)	Antibody class	Optimal temperature	Day between the onset of COVID-19 and AIHA	Treatment	Response
Hindilerden et al. [2]	56	M	HTN	4.3	2529	11.5	IgG, C3d	Warm	4	Steroids, IVIG	Improving
Lazarian et al. [3]	61	M	HTN, CKD, CLL	6	1000	<10	IgG, C3d	Warm	13	Steroids	Unknown
	89	F	HTN, CKD, MGUS	8.4	598	<10	IgG, C3d	Warm	7	Steroids	Unknown
	75	M	DM, HLD, CM, COPD, CLL	7.1	2000	<10	IgG	Warm	6	Transfusion only	Unknown
	61	M	DM	7	1800	<10	IgG	Warm	9	Steroids, Rituximab	Unknown
Wahlster et al. [4]	17	M	ITP	2.5	1280	?	IgG, C3	Warm	4	Steroids	Improving
Our case	84	M	HLD	4.4	1253	<10	IgG, anti-K	Warm	13	Steroids	Improving

Availability of data and material The data that support the findings of this study are available on request from the corresponding author, Tien-Chan Hsieh.

Code availability (software application or custom code) Not applicable

Authors' contributions Tien-Chan Hsieh conceived the presented idea and drafted the manuscript. Both authors contributed to the final manuscript.

Declarations

Conflict of interest None to declare

Ethics approval Not required

Consent to participate Not required

Consent for publication Not required

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