Autoimmune Hemolytic Anemia; A Late Presentation of Post COVID-19 Syndrome

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Abstract:

Introduction and case report: The coronavirus disease 2019 (COVID-19) is a severe respiratory disease with a spectrum of clinical presentation and complications. Warm autoimmune hemolytic anemia (WAIHA) is increasingly recognized in patients with COVID-19 either as an initial presentation or shortly after the infection.

Case description: We report a 36-year-old male with clinical and laboratory findings consistent with (WAIHA). Medical history is significant for COVİD-19 infection three months before patient presentation. He was initially resistant to steroids but had substantial improvement following rituximab initiation with a complete recovery thereafter.

Conclusion: WAIHA is a frequent association with COVİD-19 infection that either diagnosed concurrently or as late complications. Serial assessment of CBC parameters and hemolysis markers post COVID-19 infections warranted for early detection and prompt treatment.

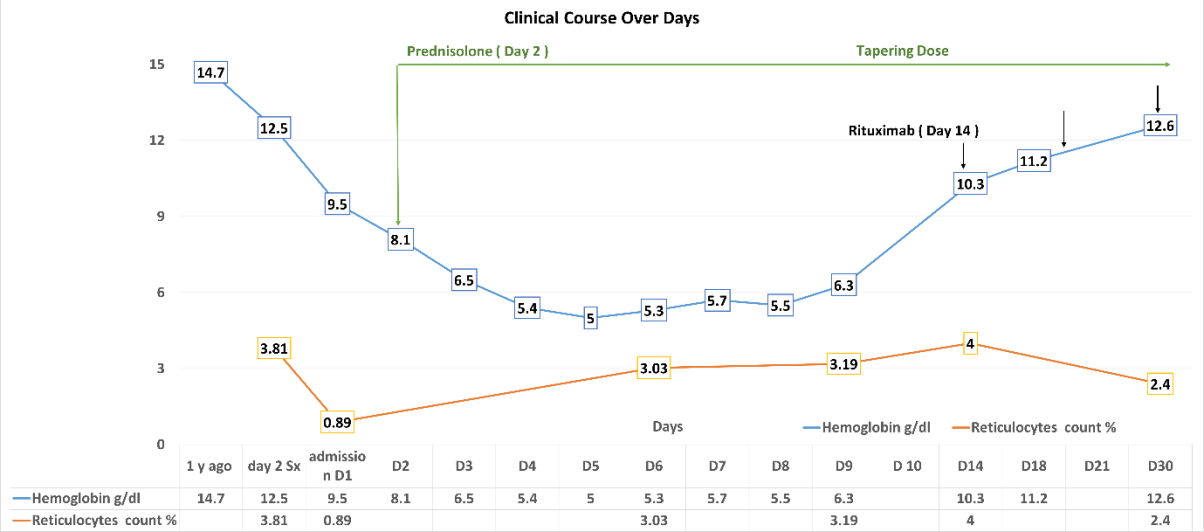
Introduction and case report:

The coronavirus disease 2019 (COVID-19) is a severe respiratory disease caused by the novel severe acute respiratory syndrome coronavirus2 (SARS-CoV-2) that emerged in December 2019. [(1)] Individuals with the mild form of the disease have an efficient immune system controlling and eliminating the virus. On the other hand, individuals with a severe form of disease experience intense immune responses that may result in multiple organ pathology. Therefore, patients may develop acute kidney injury, coagulopathy, cerebrovascular events, and septic shock. [(2,3)]

We report a case of warm autoimmune hemolytic anemia (WAIHA) three-month post mild COVİD-19 infection that did not required hospitalization and was treated conservatively. A 36-year-old male presented with a one-week history of anemia symptoms in the form of fatigue, tiredness, and shortness of breath, along with back pain and tea-colored urine. His past medical history is negative for recent ingestion of fava beans or medications. Further, no family history suggestive of congenital hemolytic anemia.

Clinical examination revealed a tachycardia at 105/min and marked jaundice in the sclera. Investigations revealed normocytic anemia with a hemoglobin of 9.5 g/L, thrombocytopenia with a platelet count of 121 X 10^9/L.Additionally; there is reticulocytosis, indirect hyperbilirubinemia, and normal Liver enzymes with no DIC evidence. Peripheral smear revealed spherocytes, polychromasia, with a few RBC fragments but no agglutination or red blood cell clumping could be seen. Both direct and indirect Coombs tests were positive. He is tested negative for HIV, hepatitis B and C during recent employment assessment.

Cross-sectional imaging of the body with contrast was normal. The clinical and laboratory findings were consistent with IgG WAIHA. He initially started on prednisone 1 mg/kg escalated to 1 g methylprednisolone for three consecutive days. However, due to lack of response and further deterioration in hemoglobin level, weekly Rituximab in four divided doses was added to the treatment protocol. On day 10, the patient has a significant resolution of the clinical symptoms discharged from the hospital following the second dose of Rituximab. He had an excellent response to treatment in the form of substantial improvement in hemoglobin level and regression of hemolysis parameters, as illustrated in Figure 1.



	1 y ago	day 2 Sx	admission D1	D2	D3	D4	D5	D6	D7	D8	D9	D 10	D14	D18	D21	D30
Hemoglobin g/dl	14.7	12.5	9.5	8.1	6.5	5.4	5	5.3	5.7	5.5	6.3		10.3	11.2		12.6
Reticulocytes count %		3.81	0.89					3.03			3.19		4			2.4

Figure 1: illustration of the clinical course of the disease from the time of diagnosis until complete recovery.

Discussion:

Warm autoimmune hemolytic anemia is an acquired heterogeneous hemolytic disorder caused by the host's immune system acting against its own red cell antigens. WAIHA can be idiopathic in around 45% of the cases. Secondary causes of WAIHA include autoimmune disease, lymphoproliferative disorders, miscellaneous causes, including infections and drugs. [4,5] Glucocorticoids are considered the first-line treatment for WAIHA. While splenectomy is historically the treatment of choice in refractory cases, Rituximab increasingly superseded it. [6]

Several reports indicate that COVID-19 has been associated with several autoimmune phenomena. WAIHA has been increasingly recognized in patients with COVID-19 as an initial presentation or shortly after the infection. The clinical course of WAIHA related COVID-19 may range from a quiescent course where no treatment is needed to a refractory course requiring more than one line of treatment. [7,8] Unlike previous reports, our patient presented with features of WAIHA as a late presentation for COVID-19. Moreover, he was resistant to the steroid's pulse dose that mandate initiation of monoclonal antibody medication in the form of Rituximab, similar to one previously described report.[9,10]

The result from this report reflects the importance of serial follow-up of CBC parameters and hemolysis markers post COVID-19 infections. Additionally, WAIHA post COVID-19 infection might be more resistant to standard treatment that warrants the second treatment line, such as Rituximab. However, a time frame of at least six months following rituximab infusion is needed before vaccination becomes effective.[11] This raises the question of whether refractory cases of WAIHA should be treated differently in the COVID-19 infection era while awaiting coronavirus vaccination.

In conclusion, WAIHA is a frequently reported complication in patients with COVID-19 disease with a broad spectrum of clinical course and variable response to treatment.

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