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Case Report: COVID 19 infection induced Autoimmune Hemolytic Anemia

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ABSTRACT

SARS-CoV 2 was designated a pandemic by WHO on March of 2019. There have been over 120 million confirmed cases of COVID-19 globally with greater than 4 million hospitalizations in the US alone. These cases can range from asymptomatic disease to multi-organ dysfunction resulting in death. The spectrums of complications stemming from COVID-19 are much broader and can include other autoimmune disorders. Here we present a case of a woman who developed autoimmune hemolytic anemia from COVID-19 infection and was successfully treated with high dose corticosteroids.

Keywords: COVID 19, autoimmune hemolytic anemia, Cold agglutinin disease, corticosteroids

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INTRODUCTION

Coronaviruses are enveloped positive-stranded RNA viruses that infect animals and humans, albeit rarely [1]. SARS-CoV 2 was designated a pandemic by WHO on March of 2019 [1]. Since the first reports of cases from Wuhan, China in late 2019, there have been over 120 million confirmed cases of COVID-19 globally with greater than 4 million hospitalizations in the US alone [2]. CDC estimates that 80 percent of people present with asymptomatic disease or with mild pneumonia, approximately 14 percent with severe disease characterized by dyspnea and hypoxia, and about 5 percent have critical illness involving respiratory failure and multi-organ dysfunction [2]. The spectrums of complications stemming from COVID-19 are much broader and can include autoimmune disorders. Here we present a case of a woman who developed autoimmune hemolytic anemia from COVID-19 infection where its pathophysiology is still a mystery at this time.

CASE REPORT

A 57-year-old female presented with a 2-week history of generalized weakness associated with dyspnea on exertion. The patient reported that she thought she might have contracted COVID due to exposure from sick family members approximately 1 month ago. Review of system was otherwise negative except for subjective chills and lethargy. She had a medical history of hypothyroidism, obesity, and is a current 1ppd smoker.

Patient was hemodynamically stable at the time of admission. Physical examination was significant for obesity, pale complexion, and scleral icterus. Her initial lab work was significant for anemia with Hemoglobin of 5.0 with normal MCV, elevated Total bilirubin of 2.5, and indirect bilirubin of 2.0 (Table 1). A guaiac-based fecal occult blood test was negative. Additionally, lab work was performed which showed negative ANA, negative anti-phospholipid Antibodies, low haptoglobin, elevated lactic acid dehydrogenase, elevated reticulocyte index and positive (C3d) direct Coomb's test with positive cold reactive antibody titers (Table 1 and 2). Her Influenza test and RSV were negative but her SARS-COVID-2 RNA (RT-PCR) test was positive. Additionally, her acute phase reactant titers were elevated (Table 1) and her HIV/Hepatitis panel was negative (Table 2). However, her Chest X-ray was normal (Figure 1).

Table 1: shows the values of the blood tests and other laboratory results.

Data values	Serum Value
Hemoglobin (g/dL)	5.0
Total Bilirubin (mg/dL)	2.5
Indirect Bilirubin (mg/dL)	2.0
LDH (unit/L)	563
Ferritin (ng/ml)	449
International Normalized Ratio (INR)	1.01
Reticulocyte Index	2.6
Haptoglobin (mg/dL)	<20

Table 2: shows the test results for further investigations performed in this patient.

Data values	Test Results
Hepatitis Panel	Negative
HIV panel	Negative
Anti-phospholipid Antibodies	Negative
ANA	Negative
RSV	Negative
Influenza A and B	Negative
Mycoplasma	Negative
COVID 19	Positive
Direct Antiglobulin Test	C3d Antibody Positive
Cold Reactive Antibody Titer	>1:120

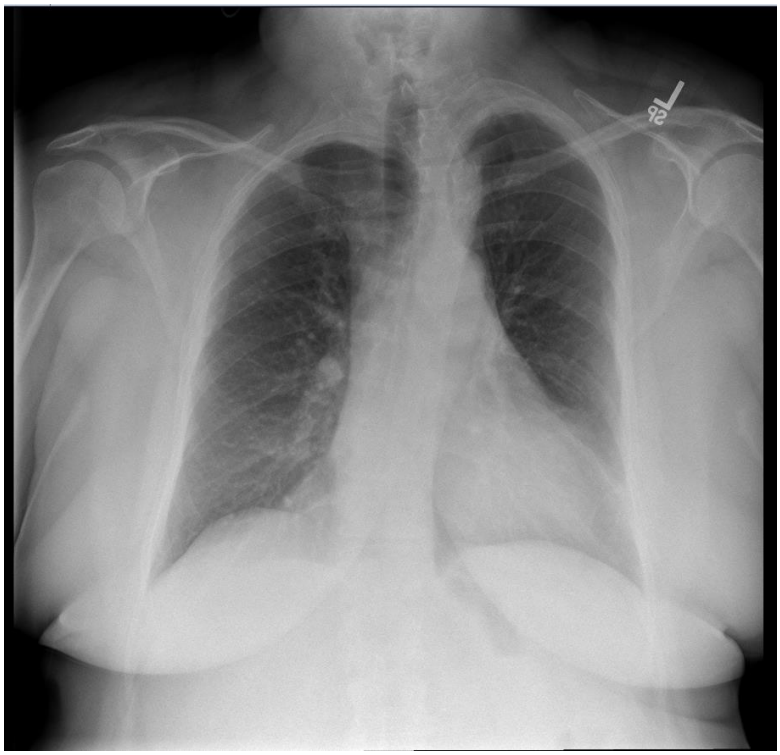

Figure 1: shows normal Chest X-ray.

Patient received 2 units PRBC and 1mg/kg prednisone daily was started. Her subsequent hemoglobin level stabilized was 7.6. Patient remained hemodynamically stable and was discharged home on the same dose of prednisone. Patient followed up with our outpatient clinic. Her hemoglobin level was 10.2 and 12.6 at the time of her 2-week and 4-week visits respectively. Patient is currently on the tapering prednisone dosage as her hemoglobin has responded well.

DISCUSSION

Autoimmune hemolytic anemia (AIHA) is an uncommon yet acquired disorder, which is caused by the host's immune system attacking its own red blood cells [3]. The typical incidence rate is

approximately around 1 out 100000/year with a mortality rate of ~11% [3]. Approximately 50% of the cases are idiopathic, 20% is due to lymphoproliferative disorders and 20% is due to infection/tumors/medications.

AIHA cases are divided into warm, cold, paroxysmal nocturnal hemoglobinuria, or mix types and are diagnosed by presences of specific anti-erythrocytes antibodies via DAT (Direct antiglobulin test). In warm AIHA, DAT is positive with mostly IgG antibodies plus/minus C3d (complement) antibodies [3]. Cold AIHA is caused by IgM Antibodies that are mostly active at low temperatures. DAT is characteristically positive for only Anti-C3d antibodies and rarely for IgM (inactive at room temperature). Once C3d Ab is positive, Antibody titers are assessed. Cold AIHA is diagnosed with a positive DAT, clinical findings, and high cold reactive antibody titers (>1:64 at 4° C) [4]. In our patient, her DAT was positive for C3d with negative IgG. A subsequent test showed positive cold reactive antibody titers (>1:120), which confirmed the diagnosis of Cold AIHA. Since all of her infectious disease workup was negative except for a COVID test, it is safe to endorse the diagnosis of COVID-induced Cold AIHA.

The overall treatment for Cold agglutinin disease is still not evidence-based, as there are no controlled clinical trials up to this date but the first line of therapy is Rituximab based on general recommendations [3], [4]. However, we successfully used corticosteroids as the primary and only treatment in the setting of COVID diagnosis. A review of PubMed showed multiple case reports of COVID-induced AIHA resolved with the use of corticosteroids such as our patient [5], [6], [7].

The underlying pathophysiology of this phenomenon is not known yet. However, Angileri et al have proposed that COVID 19 viral spike protein and Ankrin 1 (Erythrocyte protein membrane that provides a primary connection between membrane skeleton and plasma membrane) share immunogenic antigenic epitope leading to cytokine surge triggering cascade of hemolytic anemia [8]. Furthermore, research is needed to establish the connection between COVID 19 and AIHA.

CONCLUSION

There are limited numbers of case reports showing COVID 19 infection induced autoimmune hemolytic anemia, which have ranged from mild to moderate disease such as in our patient to severe cases leading to death. The association between these two entities is not fully established yet and more research is required to determine the underlying pathophysiology.

CONFLICT OF INTEREST

There are no conflicts of interest in publishing this case report.

AUTHOR'S CONTRIBUTIONS

Waheed Abdul – Primary author → drafted the case report and wrote the case report and the discussion section and discussion session.

Kavita Krishnakant – Secondary author → obtained references and wrote the abstract section and introduction section

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