

Cold Agglutinin Anemia Induced by COVID-19

International Journal of Cardiology and Cardiovascular Disorder

Case Report

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Submitted : 26 Feb 2021 ; Published : 18 Mar 2021

Abstract

Background: SARS-CoV-2, also known as COVID-19, is the most significant pandemic of the past century. The associated thromboembolic phenomenon and multi-system organ failure due to the severe inflammatory reaction driven by the toxic cytokine release syndrome results in fatal consequences leading to death. We describe a patient with a history of this viral illness who later developed cold agglutinin anemia.

Case: A 50-year-old obese African-American male was admitted and treated for new-onset diabetes mellitus type II with ketoacidosis. The past medical history included hypertension, dyslipidemia, heart failure with recovered ejection fraction, chronic kidney disease stage 3, pancreatitis, cocaine dependence, alcohol misuse and former smoking. The admission was during the COVID-19 pandemic, but he tested negative for the SARS-CoV-2 rRT PCR. He denied fever, malaise, abdominal or musculoskeletal discomfort. There was no recent travel or sick contacts. Furthermore, he denied active tobacco or recent alcohol use or recreational drugs.

The patient was subsequently re-admitted due to acute numbness and weakness of the left arm, acute cerebrovascular accident was ruled out and SARS-CoV-2 rRT PCR was negative. Urine toxicology revealed recent cannabis use. The patient was found to have a drop in hemoglobin from 12.0 to 10.7 g/dl with the presence of cold agglutinin which was absent during the previous admission and has persisted for the past eight months. The SARS-CoV-2 IgG/IgM antibodies were reactive.

Conclusion: In summary, transient autoimmune agglutinins have been reported in COVID-19 patients. Our patient has an exceptional experience of persistent cold agglutinin anemia after the viral infection.

Keywords: COVID-19; Anemia; Cold Agglutinin.

Introduction

The SARS-CoV-2, also known as COVID-19, has impacted our countries in different ways, but there is no doubt about the challenges represented to the medical community in terms of approaching, treatment and following of patients affected with this lethal virus, being the most significant pandemic of the past century, it has been associated multiple complications, from thromboembolic phenomenon, encephalitis to multi-system organ failure [1].

The mechanism of this viral entity would be based in a severe inflammatory reaction driven by the toxic cytokine release syndrome resulting in fatal consequences leading to death. In patients who survived this infection, multiple sequelae have been reported, but since this is a new virus, its consequences

are still to be unveiled; We describe a patient with a history of this viral illness who later developed persistent cold agglutinin anemia after a mild disease.

Case

The patient is a 50-year-old obese African-American male who was admitted and treated for new-onset diabetes mellitus type II and ketoacidosis. The past medical history included hypertension, dyslipidemia, heart failure with recovered ejection fraction, chronic kidney disease stage 3, pancreatitis, cocaine dependence, alcohol misuse and former smoking. The admission was during the COVID-19 pandemic, but he tested negative for the SARS-CoV-2 rRT PCR. He denied fever, malaise, abdominal or musculoskeletal discomfort. There was

no recent travel or sick contacts. Furthermore, he denied active tobacco or recent alcohol use or recreational drugs.

The patient was subsequently re-admitted due to acute numbness and weakness of the left arm, acute cerebrovascular accident was ruled out and SARS-CoV-2 rRT PCR was negative. Urine toxicology revealed recent cannabis use. The patient was found to have a drop in hemoglobin from 12.0 to 10.7 g/dl with the presence of cold agglutinin which was absent during the previous admission and has persisted for the past eight months. The SARS-CoV-2 IgG/IgM antibodies were reactive.

Discussion

The SARS-CoV-2 which is responsible for the disease COVID-19, has infected over 84 million people and has caused more than 1,835,000 deaths worldwide, it is known to cause significant pulmonary disease, leading to acute respiratory distress syndrome (ARDS) but clinicians have seen many extra pulmonary manifestations of COVID-19 [2].

The main mechanisms playing a role in the pathophysiology of multi-organ injury include direct viral toxicity, endothelial cell damage, thrombo-inflammatory reaction, dysregulation of the immune response, and also affects on the renin-angiotensin-aldosterone system (RAAS) [3]. Autoimmune hemolytic anemia (AHA) is a rare manifestation of COVID-19 characterized by autoantibodies to patient's own red blood cells (RBCs); it is divided into cold or warm based on thermal reactivity of the autoantibodies [4].

The cold agglutinins are IgM antibodies that recognize RBC antigens typically "I" and "i" on the RBC surface when below normal core body temperature [5]. Cold Agglutinin disease (CAD) is a rare form of AHA, the primary form is common however secondary is rarer and is seen in the setting of infections like *Mycoplasma pneumoniae*, Epstein Barr Virus (EBV) and Cytomegalovirus [6].

Key clinical features include cold induced symptoms like acrocyanosis, livedo reticularis or Raynaud's phenomenon along with extravascular hemolysis ranging from mild, compensated hemolysis to severe anemia requiring blood transfusion. Patients with cold agglutinin syndrome present with laboratory evidence of hemolysis (high LDH and bilirubin with low haptoglobin) and a positive direct coombs test [7]. The diagnosis of cold agglutinin mediated hemolytic anemia is made when a patient has evidence of autoimmune hemolytic anemia (AIHA), positive direct coombs test, and positive CAD antibodies [8].

In this case, the patient was admitted due to new-onset diabetes mellitus type II with multiple comorbidities [9] who tested negative for SARS CoV-2 rRT PCR but subsequent readmission due to acute numbness and weakness of left arm, revealed drop in hemoglobin with presence of cold agglutinin and the SARS Cov-2 IgG/IgM Antibodies were reactive [10].

Different data have described similar cases, however in cases reported were related to transient cold agglutinins or cold agglutinin associated with severe COVID-19 [11].

Conclusion

The transient autoimmune agglutinins have been reported in COVID-19 patients, our case report demonstrates the association of COVID with cold agglutinin hemolytic anemia and represents an exceptional experience of persistent cold agglutinin anemia after a mild viral infection.

Grant support

None

Disclosures

None of the authors report any conflicts of interest

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