COVID-19 and Cold Agglutinin Hemolytic Anemia

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TH Open 2020;4:e175–e177.

Abstract

Novel coronavirus disease 2019 (COVID-19) has spread throughout the world and has infected close to 4 million people. It commonly presents with fever, cough, and fatigue. Due to the high inflammatory response, it is suggested that the coagulation cascade is enhanced causing thrombotic events for many patients. We describe a patient with clinical features of cerebrovascular accident, as well as documented blood clots in bilateral upper extremities. Labs revealed the presence of cold agglutinin hemolytic anemia. The association between cold agglutinin autoimmune hemolytic anemia and thrombotic events in COVID-19 patients has not been well investigated. The patient unfortunately passed away within 48 hours after admission. This case stresses the importance of considering a full workup to diagnose autoimmune hemolytic anemia (AIHA) in COVID-19 patients with thromboses and possible implications for management.

Keywords
► viral infection
► thrombosis
► autoantibodies

Introduction

Starting in November, 2019, novel coronavirus disease 2019 (COVID-19) emerged in Wuhan, China, and by March of 2020, spread worldwide. Currently, there are over 3,800,000 cases with 268,000 deaths.¹ Patients present with fever, cough, myalgias, and fatigue.² Anosmia and ageusia have also been found to be common symptoms.³ As COVID-19 emerged, many patients also presented with coagulation disorders.⁴ It is presumed that the high levels of inflammation throughout the body cause excessive activation of the coagulation cascade. Hospitals have been using anticoagulation aggressively to mitigate the catastrophic thrombotic events. Even with this approach, a high number of patients with COVID-19 develop life-threatening thrombotic complications.⁵

Although many COVID-19 patients present with coagulopathy, the relationship between COVID-19 and autoimmune hemolytic anemia (AIHA) causing thrombosis has not been well investigated. Hemolytic anemia presents with anemia, elevated lactate dehydrogenase (LD) and bilirubin, and decreased haptoglobin.⁶

Case Report

This case discusses a patient with no history of autoimmune disease presenting with COVID-19 who quickly deteriorated and ultimately passed away due to thrombotic complications. Tests later revealed cold agglutinin hemolytic anemia.

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There is evidence that cold agglutinin syndrome has also been seen in COVID-19 patients. Diagnosis of cold agglutinin mediated hemolytic anemia is made when a patient has evidence of AIHA, positive direct coombs test, and positive cold agglutinin titer.

In this case, the patient did not have a complete evaluation for underlying hematologic malignancy. Antiphospholipid antibodies were negative. While it is likely that the cause of this patient’s cold agglutinin was COVID-19 infection, this cannot be definitive without a full workup. Another publication describes similar case presentations in which an underlying B-cell lymphoma was identified.

No systematic studies have been performed to determine optimal treatment for cold agglutinin syndrome, due to its rarity. The primary goal is to treat the underlying infection or malignancy. Case reports have reported using corticosteroids to treat M. pneumoniae associated cold agglutinin syndrome. However, less is known on how to treat patients with severe, life-threatening hemolytic anemia with cold agglutinins. Plasmapheresis and intravenous immunoglobulin have been used in the setting of fulminant hemolytic anemia due to cold agglutinin disease and could have been considered in this case. Unfortunately, the cold agglutinin test did not result until after the patient’s death. It may have been beneficial to empirically treat this critically ill patient with multiple signs of cold agglutinin AIHA. In particular, the patient was noted to have clotted blood in all initial laboratory draws.

Conclusion
When a patient presents with thrombosis, it’s important to consider an underlying hemolytic disease. One may want to complete a full work up for AIHA and consider beginning treatment depending on the acuity of the condition.

Conflict of Interest
None declared.

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