

Atypical manifestations of coronavirus disease 2019 (COVID-19)–associated autoimmune thrombotic thrombocytopenic purpura

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Abstract

Patients with coronavirus disease 2019 (COVID-19) infection can have various abnormal hematologic parameters. This report illustrates a case with unusual presentation of COVID-19–associated thrombotic thrombocytopenic purpura, in which the patient did not develop any typical respiratory signs or symptoms.

KEYWORDS

COVID-19, Thrombotic, Thrombocytopenic, Purpura

1 | CASE REPORT

A 47-year-old woman sought medical attention after 1 week of progressive fatigue, scleral icterus, and dark urine. She had no fever, cough, or shortness of breath. She had no history of HIV, cancer, autoimmune disease, recent infection, diarrhea, or new medication/supplements. In addition, she had no history of out-of-state travel. On examination at the time of admission, she had mild scleral icterus, normal spleen size, no evidence of petechiae or purpura, and a normal neurological examination. Laboratory tests revealed a white blood cell count of 4.8 K/ μ L, hemoglobin level of 11.5 g/dL, and platelet count of 8 K/ μ L. She was admitted and tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by nasopharyngeal swab via reverse transcription polymerase chain reaction (RT-PCR). Additional laboratory values were as follows: total bilirubin, 1.7 mg/dL; creatinine, 0.87 mg/dL; lactate dehydrogenase (LDH), 708 U/L; reticulocytes, 1.22%; haptoglobin, <9 mg/dL; prothrombin time, 13.1; and partial thromboplastin time (PTT), 26.6. mg/dL; fibrinogen, 389 mg/dL; and C-reactive protein, 0.1 mg/dL. D-dimer was elevated at 3.9 μ g/mL. Normal values for test results are given in Table 1. A direct antiglobulin test (DAT) was negative. The results of a urine pregnancy test were negative. She had extensive negative workup for nonimmune

hemolytic anemia that included paroxysmal nocturnal hemoglobinuria, hemoglobin electrophoresis, Epstein-Barr virus, HIV, cytomegalovirus, hepatitis B, hepatitis C, parvovirus, and deficiencies of copper, ceruloplasmin, glucose-6-phosphate dehydrogenase, and B12. Peripheral smear showed no evidence of schistocytes per high-powered field. She was started on intravenous immunoglobulin G (IgG) and dexamethasone for presumed COVID-19–associated immune thrombocytopenia purpura (ITP).

On hospital day 5, the patient had a transient episode of aphasia together with a low-grade fever of 100.6°F. Laboratories showed a white blood cell count of 13.4 K/ μ L, hemoglobin of 6.7 g/dL, and platelet count of 17 K/ μ L. Her creatinine level remained normal. LDH was 788 U/L. Reticulocyte percentage was elevated at 9.24% with undetectable haptoglobin. Head computed tomography (CT), CT angiography, and brain magnetic resonance imaging (MRI) with/without gadolinium were unremarkable. Repeat DAT was positive for both IgG and C3d. She had another extensive negative workup for her new immune-mediated hemolytic anemia, which included lupus, vasculitis, and other autoimmune diseases. Because her laboratory test results were consistent with autoimmune hemolytic anemia (AIHA) at this point, her neurological status was attributed to COVID-19 infection itself.¹ Rituximab was added for presumed COVID-19–associated AIHA.

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TABLE 1 Laboratory data

Variable	Reference range	On admission	Day 5	Day 17	Day 29
White cell count (K/ μ L)	3.7-11.1	4.8	13.4	10.3	9
Hemoglobin (g/dl)	11.5-15.0	11.5	6.7	7	7.6
Platelet count (K/ μ L)	140-400	8	17	14	171
Reticulocyte %	0.47-2.40	1.22	9.24	17.91	11.25
Schistocytes	None	None	1+	1+	None
Total bilirubin (mg/dL)	0.2-1.2	1.7	1.4	2.0	0.3
LDH (U/L)	\leq 270	708	788	2229	206
Haptoglobin (mg/dL)	30-220	<9	<9		
Direct antiglobulin test (DAT)	Negative	Negative	Positive for IgG and C3d		
PT (seconds)	11.7-14.3	13.1	14.3	15.6	13.6
PTT (seconds)	23.8-36.1	26.6	22.8	24.7	24
D-dimer (μ g/mL)	<0.49	>3.9	>4	>4	
Fibrinogen (mg/dL)	209-504	389	289	268	252
Creatinine (mg/dL)	\leq 1.11	0.81	0.84	1	0.64
CRP (mg/dL)	\leq 0.9	0.1	0.1	1.4	
Ferritin (ng/mL)	22-291		455	354	

On hospital day 17, the patient's blood counts showed minimal improvement. She also had a witnessed prolonged seizure, resulting in aphasia, right hemiparesis, and encephalopathy. Repeat contrast-enhanced brain MRI was unremarkable. Subsequent ADAMTS-13 activity sent earlier showed a level of <5% (reference range \geq 61%) and anti-ADAMTS-13 inhibitor of 63 U/mL. Total plasma exchange (TPE) and caplacizumab were promptly initiated. By the third consecutive day of TPE, the patient had an excellent response to treatment: Her platelet count was >150 K/ μ L, and her neurological status was markedly improved. She was discharged home on day 34 with normalized blood counts and significant improvement in neurological deficits.

2 | DISCUSSION

Infectious diseases, especially viral infections, are known to trigger autoimmune diseases, mainly via molecular mimicry. Although a causal link between SARS-CoV-2 and autoimmune diseases has not been firmly established, there are increasing reports of the onset of autoimmune disorders in the setting of COVID-19 infection. ITP, AIHA, and autoimmune thrombotic thrombocytopenic purpura (TTP) have been reported following the onset of severe COVID-19 symptoms.²⁻⁶ The unique features of this case include a lack of preceding respiratory signs or symptoms typical of COVID-19, and the

autoimmune hematologic findings were the only manifestations of COVID-19 infection.

Potential explanations for this patient's unique hematologic presentations include the following: (1) She may have had a hyperimmune response to SARS-CoV-2 infection, triggering autoantibodies to platelets, red blood cells, and ADAMTS-13. (2) Her presentation may be a manifestation of a novel autoimmune complex associated with COVID-19. (3) She may have had an atypical manifestation of COVID-19-associated TTP, namely Evans syndrome (ITP and AIHA) followed by TTP. To the authors' knowledge, there is only one case report in the medical literature of non-COVID-19-related Evans syndrome followed by TTP, which was quickly fatal.⁷ (4) Finally, COVID-19 might have triggered two parallel autoimmune processes concurrently, namely Evans syndrome and TTP.

A high index of suspicion and prompt initiation of therapy for atypical COVID-19-associated TTP is critical for successful recovery and prevention of end-organ damage and death. This case illustrates the need to be vigilant for immune-mediated hematologic complications associated with COVID-19, even in the absence of typical respiratory symptoms.

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CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest.

AUTHOR CONTRIBUTIONS

LL: wrote the paper, reviewed the literature, and evaluated the patient clinically. G.H: revised the manuscript and evaluated the patient clinically. D.C and J.S: took care of the patient. All authors: have read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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