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A Rare Presentation of COVID-19 Associated Thrombotic Thrombocytopenic Purpura; Therapeutic Challenges

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Abstract Since COVID-19 has been declared a global pandemic, variable clinical presentations have been reported, most commonly with respiratory symptoms and less commonly gastrointestinal or neurological symptoms. Hematologic disorders in the form of thrombotic microangiopathies (TMA) such as immune thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), and microangiopathic hemolytic anemia (MAHA) were also linked to the COVID-19 positive population. Many studies have proposed several possible theories, including viral-mediated, endothelial related, immune triggered, and consumptive mechanisms. In most of the literature, the severity of the disease is associated with more severe thrombocytopenia, with lower levels being associated with higher mortality. We herein report a case of a patient who tested positive for COVID-19 and went on to develop severe thrombocytopenia. Workup of the thrombocytopenia revealed that he had developed acquired Thrombotic thrombocytopenic purpura (TTP). Our case report highlights the need for early recognition, prompt diagnosis, and the subsequent initiation of urgent treatment.

Keywords: *COVID-19, TTP*

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1. Introduction

Thrombocytopenia is a common manifestation of various infectious diseases; viruses were found to be the most common pathogens that induce thrombocytopenia, as well as bacteria followed by fungi [1]. Thrombocytopenia was found in 5 - 41.7% of COVID-19 positive patients [2]. TTP is a potential fatal clinical syndrome caused by autoantibodies against VWF cleaving Metalloprotease ADAMTS13 with severe deficiency of ADAMTS13 activity <10 IU/dl to support the diagnosis of TTP if a patient presents with a thrombotic microangiopathic hemolytic anemia [3]. Up to date, the pieces of literature associating COVID-19 with acquired TTP are scanty; thus, we sought to report this case to shed light on the possible correlation as the rapid identification and treatment of this entity is crucial to prevent any unwanted morbidity and mortality.

2. Case Presentation

A 49-year-old African American male with a past medical history notable for hypertension and hyperlipidemia presents to the ED with rectal bleeding and hematuria lasting for a few days. He was found to have COVID-19, but he did not endorse any respiratory symptoms at the time of presentation. Laboratory works up was ordered and showed: hemoglobin of 8 g/dl, platelet count of 25 Thousand/mL, normal renal function, LDH 619 U/L. His most recent labs a few years ago were within the normal range. No abnormalities were found during the physical exam other than left lower quadrant abdominal tenderness. CT abdomen and pelvis were unremarkable. He was presumed to have ITP related to COVID-19 infection, but TTP was also on the differential diagnosis list. The patient's hematuria and rectal bleeding were resolved, and he was stable for discharge with a plan of outpatient follow up. He was discharged on steroids and recommended to follow up in one week, but he was lost. After three weeks, the patient re-presented to the ED with vomiting and confusion. His labs showed hemoglobin 6.4 g/dl, platelet 12 Thousand/mL, Cr 4.45 mg/dl, LDH 1959U/L, reticulocyte count 9.5%, haptoglobin <8 mg/dl, with peripheral blood smear demonstrating an increased number of schistocytes with associated nucleated red blood cells (nRBCs) and

left myeloid shift was noted which was consistent with microangiopathic destruction of RBCs (Figure 1). ADAMTS13 was sent in the patient's first admission but resulted after the patient had been discharged, the value was <5%, consistent with TTP. Other viral markers, including HCV-AB, HBsAg, HBc IgM, were unremarkable. A dialysis catheter was placed, and urgent plasmapheresis started. The patient's encephalopathy improved after the first plasmapheresis. He received six rounds of plasmapheresis. The complete blood count (CBC), LDH, and haptoglobin have been regularly rechecked throughout his hospital stay and showed significant improvement after plasmapheresis (Table 1).

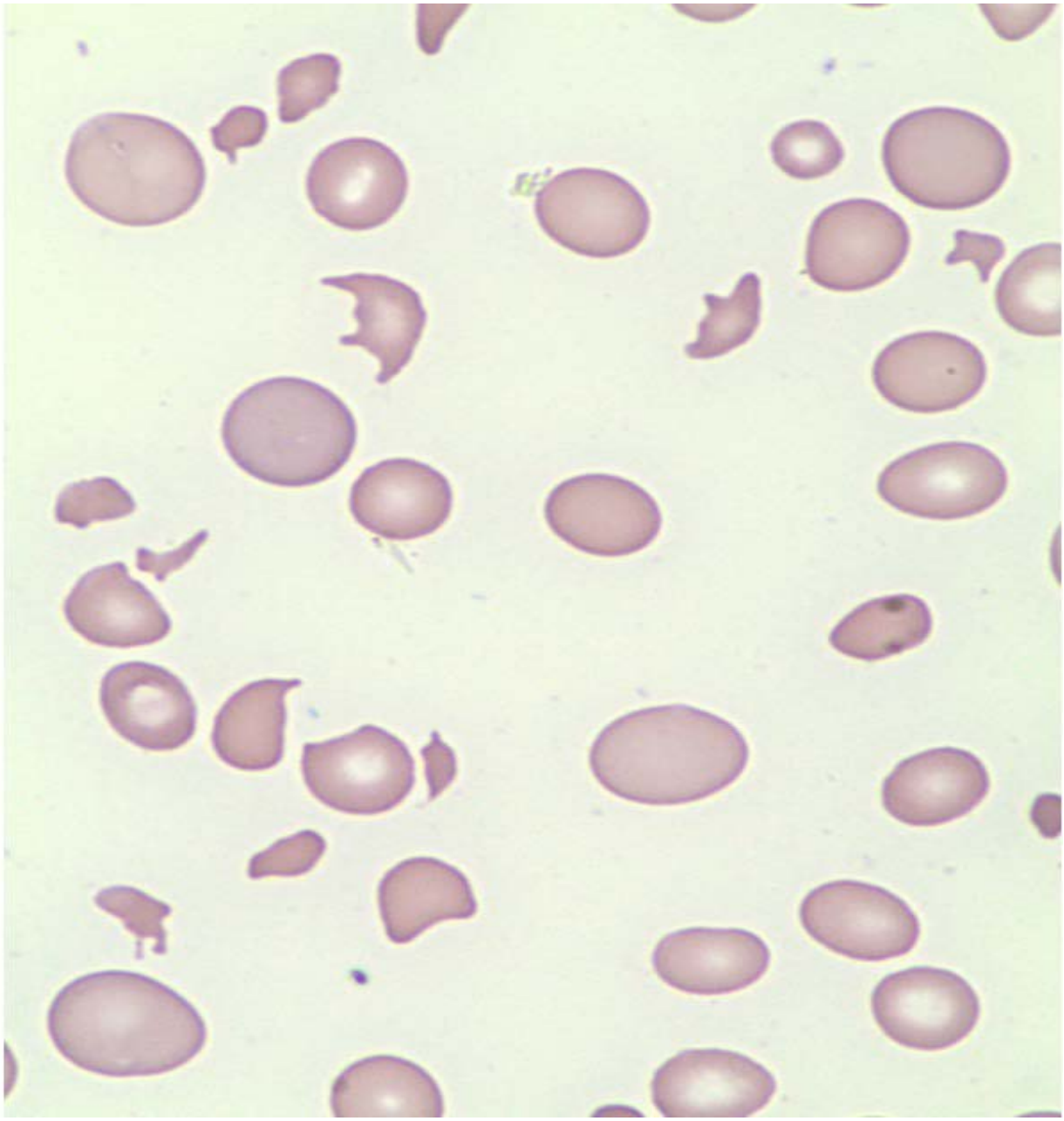

Figure 1. Peripheral blood smear with schistocytes, higher magnification

Table 1. Laboratory findings of the patient on each day of hospital admission

Hospital days	Hemoglobin (g/dl)	Platelets count (Thousand/µL)	Lactate dehydrogenase (U/L)	Haptoglobin (mg/dl)
Day 1	6.4	12	1959	<8
Day 2	7.1	17	880	-
Day 3	7.4	19	596	74
Day 4	7.4	58	419	-
Day 6	7.8	112	341	29
Day 7	8	159	-	-
Day 8	8.8	225	228	63
Day 9	8	246	257	-

3. Discussion

TTP is a relatively rare yet is a severe and serious complication of thrombotic microangiopathy that was first described in literature back in 1924 by Dr. Eli Moschcowitz [4]. TTP can be congenital and familial due to mutations to ADAMST13, idiopathic, or acquired due to commonly; infections, medications, pregnancy, malignancy, vasculitides, etc. [5]. Multiple viruses, especially RNA viruses, were found to play a role as a trigger factor for microangiopathic hemolytic anemia and subsequently TTP by different mechanisms proposed such as direct endothelial damage with subsequent release of VWF, autoantibodies against ADAMTS13, immune destruction of the platelets, direct Bone Marrow invasion, or increased consumption during thrombus formation. [1,3,5,6,7]. TTP is a medical emergency that requires close attention from clinicians as mortality can reach as high as 80-90% If left untreated; however, with the treatment, the overall mortality can be reduced to 20-30 % [6]. TTP diagnosis can be made based on the reduced activity of ADAMTS13 (<10 IU/dL) in addition to evidence of MAHA (Schistocytes, elevated LDH, decrease hemoglobin, decrease haptoglobin) in a patient with or without symptoms or signs of multi-organ damage favor the diagnosis of TTP [3,6,8].

4. Conclusion

TTP can be triggered by viruses that may include COVID-19 as in our patient after excluding other possible triggering causes. Plasma transfusion or exchange appears to be the most effective treatment for TTP patients in the setting of COVID-19. As we continue to learn about the COVID-19 pandemic, its manifestations, and pathophysiology, our case serves as an example of how severely this virus can present.

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