Case Report
Volume 12:8, 2022

Clinical Case Reports

ISSN: 2165-7920 Open Access

Thrombotic Thrombocytopenic Purpura (TTP): A Rare Presentation in COVID-19

Jabir MP [1*], **Nikitha K**[1], **Ismail NA**[2]

[1]*Department of General Medicine, Aster MIMS Hospital, Kozhikode, Kerala, India*

[2]*Department of Nephrology, Aster MIMS Hospital, Kozhikode, Kerala, India*

Abstract

A 22-year-old female with no previous morbidities presented with acute onset neurological symptoms in the form of hemi sensory phenomenon. On evaluation she had fever and routine COVID-19 RT-PCR testing turned out to be positive. During the course of hospital stay she developed classical features of acquired TTP. Her ADAMTS 13 level was 36% of normal activity suggestive of direct viral mediated thrombotic microangiopathy. High vWF levels and low ADAMTS 13 activity is reported in COVID 19 Infection. In rare cases like ours this can mimic classical TTP.

Keywords: COVID-19 • Thrombotic thrombocytopenic purpura • Plasma exchange • ADAMTS13

Abbreviations: TTP: Thrombotic Thrombocytopenic Purpura; COVID 19: Coronavirus Disease 2019; ADAMTS13: A Disintegrin and Metalloproteinase with Thrombospondin Type 1 Motif, Member 13; vWF: von Willebrand Factor; HUS: Haemolytic Uremic Syndrome; RT-PCR: Real Time Reverse Transcriptase Polymerase Chain Reaction; MAHA: Macroangiopathic Haemolytic Anaemia; LDH: Lactate Dehydrogenase; ANA: Antinuclear Antibody; ELISA: Enzyme Linked Immunosorbent Assay; PLEX: Plasma Exchange; TMAL: Thrombotic Microangiopathy; SARS-CoV2: Severe Acute Respiratory Distress Coronavirus 2; HCQ: Hydroxychloroquine.

Introduction

TTP is a rare haematological disorder which can be Hereditary or Acquired. Hereditary TTP is a rare autosomal recessive disorder caused by ADAMTS 13 mutations that result in the absence or severe deficiency of the plasma metalloprotease ADAMTS 13. ADAMTS 13 deficiency is most frequently acquired *via* ADAMTS13 auto antibodies (iTTP). 50% of all iTTP are caused by clinical conditions like bacterial infections, SLE, Antiphospholipid syndrome, pregnancy, drugs, pancreatitis, HIV infection, cancers and organ transplantation. COVID-19 related thrombotic microangiopathy both TTP and a HUS have been described in literature. We report a case of TTP in a young female in the setting of COVID 19 infection.

Case Presentation

A 22-year-old previously healthy obese female presented with sudden weakness and numbness of the right side of her body. She also had slurring of speech and facial deviation which resolved in a few hours. She did not report fever, anosmia, and cardio respiratory or gastrointestinal symptoms. No recent exposure to drugs. Family history was negative. There was no history of any illness during childhood. On evaluation in the emergency room- TEMP 38'C. HR 100/min. BP 120/80 mmHg. RR 12/min. Pallor was noted. No lymph nodes or purpura were seen. Neurological examination showed power of 5/5 in all the limbs. No sensory, cranial nerve or cerebellar deficits. Rest of systems were normal on examination. In view of pandemic scenario, a nasopharyngeal swab was taken which tested positive for COVID-19 by RT-PCR. Laboratory investigations revealed anaemia, thrombocytopenia, unconjugated hyperbilirubinemia, and elevated reticulocyte count (18%) (T able 1).

Table 1: Etiological work-up.

CBC	Haemoglobin	6 g/dL
	Total count	15,000 cells / cu.mm
	Platelet count	13,000 cells/ cu.mm
	MCV	88.3 fL
Hemolysis work-up	Direct Coomb's test	Negative
	Indirect Coomb's test	Negative
	LDH	3918 U/L

***Address for Correspondence:** Dr. Jabir MP, Department of General Medicine, Aster MIMS Hospital, Kozhikode, Kerala, India; Tel: +91 9496357213; E-mail: jabir.mp@asterhospital.com*

Received: 03-Jan-2022, Manuscript No. JCCR-22-001-PreQc-22; **Editor assigned:**07-Jan-2022, PreQC No. JCCR-22-001-PreQc-22; **Reviewed:** 27-Jan-2022, QC No. JCCR-22-001-PreQc; **Revised:** 11-Aug-2022, Manuscript No. JCCR-22-001-PreQc-22; **Published**: 18-Aug-2022, DOI: 10.37421/2165-7920.2022.12.1523.

	Reticulocyte count	18 %
	Total bilirubin	4.5 mg/dL
	Direct bilirubin	0.7 mg/dL
Renal function	Urine microscopy	Albumin 1+, RBC 50 cells/hpf
	Urea	20 mg/dL
	Creatinine	0.6 mg/dL
Coagulation profile	D-dimer	6262 ng/mL
	PT-INR	1.05
	aPTT	26.2 seconds
	Fibrinogen	399 mg/dL
Serology	ESR	62 mm 1st hour
	CRP	23.2 mg/L
	ANA (EIA)	Negative
	Phospholipid antibody IgM	Negative
	Serum C3, C4	Normal
	HIV 1 and 2	Non-reactive
	HCV	Non-reactive
	HBsAg	Non-reactive
Infection work-up	Ferritin	1081 ng/mL
	Procalcitonin	0.06 ng/mL
	Blood c/s	Sterile
Malignancy work-up	Bone marrow study	Normal
Imaging	Chest X-Ray	Normal
	MRI Brain and MRV	Normal
ADAMTS 13		36% of normal activity (low)

Peripheral smear showed normocytic anaemia, thrombocytopenia and schistocytes (12%) consistent with Microangiopathic Haemolytic Anaemia (MAHA). Coagulation parameters like fibrinogen, PT-INR and APTT were normal. LDH and D-Dimer were markedly elevated. Direct and indirect coomb's tests were negative. Serum C3 and C4 were normal. Troponin was normal. ANA by ELISA and antiphospholipid antibody IgM were negative. Automated blood cultures were sterile. Serology testing for HIV, Hep B, Hep C and Dengue viruses were negative. Rapid malarial antigen was negative. Urinalysis revealed trace albuminuria and microhaematuria. Renal function was normal. Liver function showed mild elevation of SGOT. Bone marrow examination was consistent with peripheral platelet destruction. Radiological investigations revealed a normal chest X-ray. MRI and MRV Brain were normal. ADAMTS 13 testing revealed 36% of normal activity. Inhibitor assay was not available. A diagnosis of TTP was made and she was started on IV Methyl prednisone and Plasma exchange. She received daily plasma exchanges of 2-2.5 litres with replacement by fresh frozen plasma. She had only minimal symptoms of COVID 19. After 3 sessions of PLEX, her haematological parameters started improving. Her neurological symptoms also improved. Rituximab was not given in view of COVID 19. She showed good response and achieved remission and discharged on Oral prednisone. COVID 19 antigen was negative at Day 10. She has not shown any signs of relapse after discharge.

Results and Discussion

TTP (Thrombotic Thrombocytopenic Purpura) can be hereditary or acquired, characterized by deficiency of ADAMTS 13, a polymer which degrades the multimers of von Willebrand factor. ADAMTS 13 deficiency is most frequently acquired *via* ADAMTS13 auto antibodies, but rarely inherited *via* mutations of the ADAMTS 13 gene. Hereditary TTP usually presents in childhood and has a relapsing tendency. The first episode of TTP mostly occurs during adulthood (90% of all TTP cases). In 50% of the cases another clinical condition could trigger the onset of TTP. The well described triggers are bacterial infections, SLE, pregnancy, drugs, HIV Infection and organ transplantation. In 50% cases the trigger remains `idiopathic`.

COVID-19 and COVID Vaccination has been reported to cause thrombocytopenia and macro thrombosis [1]. Thrombotic microangiopathy involving the lungs and kidneys are also described. The SARS-CoV 2 causes endothelial injury by binding to the ACE-2 receptors expressed in the vascular endothelial cells. Generation of auto antibodies to ADAMTS 13 leads to TTP [2]. The other potential mechanisms suggested are elevated vWF factor and low ADAMTS 13 activity. Both have been reported to predict development of TMA in COVID 19 [3].

As of April 2021, varying presentations ranging from 'Classical TTP' to 'TTP like illness of COVID 19' numbering less than 20 cases have been reported in literature. Two Case reports with clinical features consistent with TTP in the setting of COVID-19 infection have been reported [4]. ADAMTS 13 levels were not available in both those cases. However, very low ADAMTS 13 activity and positive Inhibitor leading to i TTP has been reported [2]. COVID 19 infection triggered autoimmune haemolytic anaemia and iTTP [5]. A case series from Iran reported 4 patients with classical clinical and haematological parameters consistent with classical TTP during COVID 19 infection [6]. COVID 19 infection has also been reported to trigger anti phospholipid antibodies leading to thrombosis and thrombocytopenia. COVID 19 infection has been reported to cause high von Willebrand Factor (vWF) levels with low ADAMTS 13 activity which may lead to the development of thrombotic microangiopathy [3].

In our case female gender, obesity and COVID 19 were the only risk factors for TTP. Clinical and haematological parameters features were classical of TTP. ADAMTS 13 activity, being 36% of normal raises the question whether this is mechanistically more like 'TTP like illness of COVID 19' rather than acquired iTTP where ADAMTS 13 activity is <10%. An increased incidence of young stroke in COVID 19 has been reported. Possible mechanisms being hypercoagulable state from systemic inflammation, cytokine storm and direct viral-induced endothelial damage leading to cerebral arterial and venous thrombosis [3]. TTP should be considered in young individual with COVID 19 and neurological symptoms.

Conclusion

COVID-19 infection is emerging as strong risk factor for the development of thrombotic microangiopathy. 'COVID 19 induced TTP' is likely a spectrum ranging from Classical iTTP (<10% ADAMTS 13 activity and antibodies to ADAMTS 13 in plasma) to COVID 19 induced TTP (direct endothelial damage leading to high vWF/ADAMTS 13 ratio). Plasma exchanges and steroids have shown anecdotal benefit in all case series. Role of Rituximab remains unclear. Neurological and haematological parameters have shown sustained improvement with lower reported relapse rate than classical immune TTP suggesting a strong causative role for the COVID-19.

References

1. Ohba, Norio and Yasushi Isashiki. "Clinical and Genetic Features of Choroideremia." *Japanese J Ophthalmol* 44 (2000): 317.
2. Hart, Nadav J, Yosef Koronyo, Keith L. Black and Maya Koronyo-Hamaoui. "Ocular Indicators of Alzheimer's: Exploring Disease in the Retina." *Acta Neuropathol* 132 (2016): 767-787.
3. Pidro, Ajla, Mirko Ratkovic, Melisa Ahmedbegovic Pjano and Alma Biscevic. "A Case Study of Choroideremia and Choroideremia Carrier." *Med Arch* 73 (2019): 61.
4. McLaren, Terri L., John N. De Roach, Hannah Montgomery and Ling Hoffmann, et al. "Genetic Analysis of Choroideremia Families in the Australian Population." *Clin Exp Ophthalmol* 43 (2015):727-734.
5. Zinkernagel, Martin S. and Robert E. MacLaren. "Recent Advances and Future Prospects in Choroideremia." *Clin Ophthalmol* 2015 (9): 2195-2200.
6. Kim, Seon Hee and Hae Young Lee. "A Case of Choroideremia with Recurrent Anterior Uveitis ." *Korean J Ophthalmol* 17 (2003): 55-62.

How to cite this article: Jabir, MP, Nikitha K and Ismail NA. Thrombotic Thrombocytopenic Purpura (TTP): A Rare Presentation in COVID-19." *Clin Case Rep* 12 (2022) : 1523.