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THROMBOTIC THROMBOCYTOPENIC PURPURA PRESENTING AS A STROKE MIMIC

Medicine

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ABSTRACT

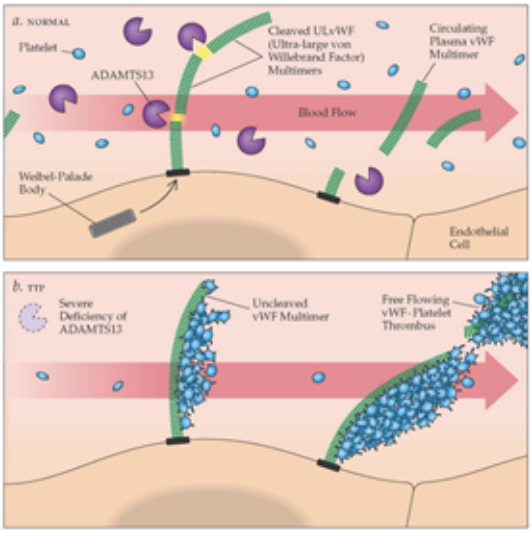
Thrombotic thrombocytopenic purpura (TTP) is an episodic microangiopathic coagulopathy characterized by profound thrombocytopenia and hemolytic anemia. Neurovascular complications, including stroke and TIA, occur commonly upon initial TTP presentation, and the underlying etiology of such neurologic manifestations is usually hinted by the concomitant hematologic abnormalities. These neurologic manifestations may present long before the hematological disturbances may manifest clinically and hence a high degree of suspicion is necessary for diagnosis. We present here such a case of TTP presenting with a Transient Ischemic Attack (TIA).

KEYWORDS

INTRODUCTION

Thrombotic micro angiopathy (TMA) describes a specific pathologic lesion in which abnormalities in the vessel wall of arterioles and capillaries lead to microvascular thrombosis. TMA is a pathologic diagnosis made by tissue biopsy. However, it is commonly inferred from the observation of micro angiopathic hemolytic anemia (MAHA) and thrombocytopenia in the appropriate clinical setting.

Eli Moschcowitz reported the first detailed description of TTP in 1924. The patient was a 16-year-old girl with fever, severe anemia, leukocytosis, petechiae, and hemiparesis. Her renal function was not impaired, but the urine contained albumin, hyaline casts, and granular casts. She became comatose and died 2 weeks after her first symptoms. At autopsy, hyaline thrombi were found diffusely in terminal arterioles and capillaries, particularly of the heart and kidney. For many years, patients with similar findings were said to have Moschcowitz disease. TTP can be acquired, due to an autoantibody inhibitor, or hereditary, due to inherited mutations in *ADAMTS13*. Acquired TTP was the first of the primary TMAs to be described and is perhaps the best understood of the TMAs pathophysiologically. TTP is unique among the primary TMAs for minimal abnormalities of kidney function, despite microthrombi observed throughout the kidney. TTP is caused by severely deficient activity of the ADAMTS13 (**A** **D**isintegrin **A**nd **M**etalloprotease with a **T**hrombo**S**pondin type 1 motif, member **13**) protease, clinically defined as an activity level <10 percent.



ADAMTS13 is a plasma protease that was initially defined by its function as a von Willebrand factor (VWF)-cleaving protease. It cleaves the ultralarge, string-like molecules of VWF that are synthesized by endothelial cells and secreted into the plasma but remain attached to the endothelial surface. This normal cleavage to smaller sized multimers prevents ultralarge multimers from accumulating, especially in areas of high shear stress. When protease activity is reduced, ultralarge VWF multimers accumulate on the endothelial surface, where platelets attach and accumulate leading to formation of small-vessel platelet-rich thrombi that cause thrombocytopenia, microangiopathic hemolytic anemia, and sometimes organ damage. Hence it is important to make a prompt diagnosis of TTP. In a resource poor country like India, ADAMTS13 activity levels are not readily available and if available there is significant delay in the report. The PLASMIC score has been devised to predict the likelihood of ADAMTS13 activity <10 percent in adults to help estimate the pretest probability and support the diagnosis of TTP. The score gives one point each for the following features:

- Platelet count <30,000/microL
- Hemolysis (defined by reticulocyte count >2.5 percent, undetectable haptoglobin, or indirect bilirubin >2 mg/dL)
- No active cancer
- No solid organ or stem cell transplant
- MCV <90 fL
- INR <1.5
- Creatin in e <2.0 mg/dL

PLASMIC score of 0 to 4 indicates low risk; 5 indicates intermediate risk; 6 to 7 indicates high risk of severe ADAMTS13 deficiency. With appropriate treatment, survival rates of up to 90 percent are possible.

CASE REPORT

A 42-year-old previously healthy, menstruating, right-handed obese female presented to Civil Hospital, Ahmedabad with sudden-onset right-sided upper limb weakness and slurring of speech. She had never experienced similar symptoms in the past. She had 2 children and no history of obstetric complications. She had denied tobacco, drug or alcohol abuse. She was not on any medications. She had no family history of any cardiovascular, neurological or hematological conditions. She was apprehensive but alert and conscious with intact orientation. Her general examination was unremarkable. Her neurological examination was significant for right hand grip weakness, right elbow and wrist power grade of 2 and right sided subtle lower facial weakness. Her NIH Stroke Scale (NIHSS) Score was 3. Her blood count showed leukocytes 13.6 × 10^3 cells/mm^3, hemoglobin 6.3 g/dL, hematocrit 19.8%, platelets 14 × 10^3 cells/mm^3, schistocytes in peripheral blood smear, MCV 89 fL, total bilirubin 3.1 mg/dL, indirect

bilirubin 2.46 mg/dL, INR 1.09, Corrected Reticulocyte count 8.39%, Lactate Dehydrogenase (LDH) 1693 U/L and glycosylated haemoglobin A1c 5.4%. Her urinalysis showed pus cells 1+, isomorphic red blood cells 3+, protein 2+, bacteria 4+ and no pathological casts. She had an elevated erythrocyte sedimentation rate of 85 mm/h. Her serum liver enzymes, electrolytes, creatinine, blood glucose, D-dimer, fibrinogen, thyroid-stimulating hormone, lipid panel, antinuclear antibody, C3, C4, antiphospholipid antibodies, anti-β2 glycoprotein antibodies, homocysteine, direct antiglobulin tests (DAT) were within normal limits. Her chest x-ray was normal, ECG showed sinus rhythm, transthoracic echocardiogram & carotid doppler showed no abnormalities. Bacterial blood cultures, HIV, dengue and hepatitis serologies were negative. Her initial head CT and CT angiogram were unremarkable. MRI of the brain showed no abnormality. PLASMIC Score was 7.

In view of the clinical setting and the above reports and an unavailability of ADAMTS13 activity levels, a provisional diagnosis of acquired TTP was considered and patient was treated with daily cycles of Plasma Exchange (PEX). There was rapid improvement in her neurological status with complete resolution of limb & facial paresis and dysarthria with NIHSS Score 0, following the first cycle of PEX. Daily PEX was continued for 6 more days along with appropriate antibiotics & supportive treatment to achieve a target LDH <250 U/L & platelet count >100 x 10^3 cells/mm^3. After 7 cycles of PEX her blood count showed hemoglobin 9.4 g/dL, leukocytes 9.6 x 10^3 cells/mm^3, platelets 182 x 10^3 cells/mm^3, absence of schistocytes, LDH 241 U/L, corrected Reticulocyte count 1.2% and normal liver function tests and urinalysis.

The patient was put on lifestyle and dietary modifications. At 6-month follow-up, patient has not suffered any symptoms and has had 15 kg weight loss, platelet count of 352 x 10^3 cells/mm^3 and normal LDH and Reticulocyte levels.

DISCUSSION/CONCLUSION

TTP is relatively uncommon before age 20 years, with a peak incidence between ages 30 and 50 years. Across many reports the female-to-male ratio averages approximately 2:1, but female preponderance is more pronounced below age 50 years and the ratio approaches equality above age 60 years. Other risk factors for TTP include African ancestry and obesity. Women have a tendency to present during late pregnancy or peripartum. The presentation of the above patient particularly shows that it is essential to have a high degree of clinical suspicion for prompt diagnosis of TTP. The diagnosis of TTP should be entertained for any patient with microangiopathic hemolytic anemia and thrombocytopenia, without evidence for disseminated intravascular coagulation. However, making a diagnosis of TTP can be a challenge and a wide differential diagnosis often must be considered. TTP is a medical emergency that is almost always fatal if appropriate treatment is not initiated promptly. However, the absence of ADAMTS13 alone may not by itself produce TTP. Often, an additional inflammatory trigger (such as infection, surgery, pancreatitis, or pregnancy) is required to initiate clinical TTP. This may be mediated by human neutrophil peptides that inhibit cleavage of von Willebrand factor by ADAMTS13.

The above patient presented with Transient Ischemic Attack, microangiopathic hemolytic anemia and thrombocytopenia along with Urinary Tract Infection (UTI). This can be considered Acquired TTP which was probably precipitated by the underlying UTI. Prompt treatment with PEX led to rapid resolution of the neurological & hematological abnormalities and the patient has not suffered a relapse since.

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Nil.

CONFLICT OF INTEREST

There are no conflicts of interest.

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