*Case Report*

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# Case Report of TTP, A Diagnosis Worth Consideration in Patients with Coagulation Disorders

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**Abstract**

Thrombotic thrombocytopenic purpura (TTP) refers to the disorder of widespread microvascular thrombosis involving the capillaries and arterioles of the brain and other organs.

The incidence of TTP is about 4-5 cases per million people per year.

TTP has long been recognized as a complex and life-threatening disease. Without treatment, TTP undertakes a rapid course of deterioration. Plasma exchange or infusion is the mainstay of treatment for TTP.

In recent years, our understanding of the basic biochemistry of the VWF-ADAMTS13 axis has provided valuable insights into the pathogenesis of TTP, as well as the investigation and development of new therapeutic strategies. Although the mortality associated with TTP has been appreciably reduced, much yet remains to be learned to more effectively treat and better understand this disease.

The authors take the opportunity to present the case report of a young female with varied signs and symptoms,diagnosed as TTP. The rapidly progressive and fatal course of the acute illness explains the need for considering TTP as a probable diagnosis in ED in a patient with fever with purpura and thrombocytopenia.

**Keywords:** TTP; Adamts-13; VWF; Coagulopathy.

## Introduction

Thrombotic Thrombocytopenic Purpura is a rare autoimmune blood disorder that is considered a true medical emergency. TTP is diagnosed at a rate of 4 to 5 in 1 million people per year. Potentially fatal complications can result from internal blood clotting with damage to critical organs such as the brain, heart and kidneys.

The cause of TTP continues to evade us. What is known is that blood becomes "sticky" and forms clots in blood vessels throughout the body which are made up of platelets. Vital blood flow to the body's organs is restricted, placing the organs at risk for damage due to a lack of oxygen and nutrients from the blood.

Moreover, since platelets are being used to form numerous blood clots, their availability to perform their normal function, which is to seal injury sites to prevent excess bleeding, is compromised. Therefore life threatening bleeding may occur.

Research has shown that in some cases the ADAMTS 13 enzyme is deficient. This finding can be used to explain blood clotting; however, while ADAMTS 13 enzyme deficiency is found in congenital TTP cases, this is not always true in adult TTP. So we know that there is more to the recipe for TTP and a need for further research is required.

In its full-blown form, the disease consists of the pentad of microangiopathic hemolytic anemia, thrombocytopenic purpura, neurologic abnormalities, fever, and renal disease.

In the last 15 years there has been a marked increase in the understanding of the pathogenesis of TTP. It is now recognized that congenital and acute acquired TTP are due to a deficiency of

von Willebrand factor (VWF) cleaving protein, also

known as ADAMTS13. In the absence of ADAMTS13, ultra large multimers of VWF (ULVWF) released from endothelium are not cleaved appropriately, and cause spontaneous platelet aggregates in conditions of high shear, such as in the microvasculature of the brain, heart and kidneys. Congenital TTP is due to an inherited deficiency of ADAMTS13, but acquired immune TTP is due to the reduction of ADAMTS13 by autoantibodies directed against ADAMTS13. Other clinical forms of thrombotic microangiopathy (TMA) occur in the absence of severe deficiency. Diagnosis can be difficult, as there is clinical overlap with haemolytic uraemic syndrome (HUS), autoimmune disease and a spectrum of pregnancy-related problems.

**Case Report**

48year old female brought to ER with complaints of fever with bodyache and rashes on right side, abdominal discomfort and vomitings. Outside CBC showed platelet count of 15000 per cmm with no active bleed from any site. Patient had blood pressure of 90/60mmHg with no significant findings on primary and secondary survey except rashes over right side of the body.

Patient was managed symptomatically in ED and fever panel inclding CBC, LFT, RFT, CXR, Dengue NS1Ag, blood culture were sent which intially revealed a normal study.

Patient was later shifted to ICU in view of low platelet count and reduced BP. After two days of hospital stay she developed an episode of hematuria with severe bleeding PR and sudden drop of hemoglobin from 11.3 to 8.7mg/dl. LFT revealed S. Bil levels of 1.7 with indirect bilirubin of 1.1, retic count 2.5 and raised LDH with deranged coagulation profile.

The peripheral smear confirmed the presence of schistocytes.

Inspite of intensive care and symptomatic management the patient's clinical status kept worsening. She overnight had an episode of GTCS for which she was started on anticonvulsants and neuroimaging was done which came out to be normal. Considering the patient's sympyomatic profile and based upon investigations results a provisional diagnosis of TTP/HUS was made. The need for plasmapheresis was considered and ADAMTS-13 test was sent. The patient received two cycles of plasmapheresis over a course of four days along with high dose of corticosteroids. Meanwhile ADAMTS-13 reports showed positive study confirming the diagnosis of TTP. Inspite of receiving intensive care, the patient's clinical status kept detoriating with multi system involvement. The patient was unable to maintain vital signs, was started on ionotropic support with maintainence hemodialysis and mechanical ventilation. The patient went into cardiopulmonary arrest, resuscitation was started as per ACLS protocol but could not be revived despite of best resuscitative measures.

**Discussion**

Without treatment, TTP undertakes a rapid course of deterioration and death in most cases. Plasma exchange or infusion is the mainstay of treatment for TTP. Although quite effective, plasma therapy has defied many efforts to understand why it leads to remission of TTP.

Advances in recent years have transformed TTP from an intriguing mystery to a disease mostly explicable on the deficiency of a newly discovered metalloprotease, ADAMTS13. It leads to the appreciation that the spectrum of TTP presentation is much more variable than previously believed. Like monogenetic diseases, the phenotypic severity of TTP is affected by multiple epistatic genes and environmental modifiers.

Following the esoteric discovery that normal plasma contains a VWF cleaving protease, the past decade has witnessed the most exciting advances in the history of TTP. However, many challenges lie ahead. Development of sensitive and reliable ADAMTS13 assays with rapid turnaround time will greatly improve the management of TTP. The courses of both hereditary and acquired TTP and the nature of modifiers of TTP phenotype in patients with the disease require further delineation.

Systemic studies are needed to define the role of immunosuppressive therapies in acquired TTP. The development of recombinant ADAMTS13 proteins may obviate the use of fresh frozen plasma.

Bioengineered ADAMTS13 that is non-suppressible by TTP antibodies may circumvent the difficulties that recombinant ADAMTS13 replacement therapies may encounter in patients with acquired TTP.

Basic research to elucidate the interaction between VWF and ADAMTS13 and the molecular mechanisms of ADAMTS13 inhibitors may provide new directions

toward improving the diagnosis and management of TTP.

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