VOLUME - 11, ISSUE - 05, MAY - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Haematology

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP) - AN UPDATED REVIEW

Parmila Malik	Ph.D. Scholar, Department of Medical Laboratory Technology, NIMS College Of Paramedical Technology
Dr. Atul Khajuria*	Ph.D. Medical Microbiology, Professor & H.O.D., Department of Medical Laboratory Technology, NIMS College Of Paramedical Technology. *Corresponding Author
Dr. Mahendra Kumar Verma	Principal, NIMS College Of Paramedical Technology

ABSTRACT Thrombotic thrombocytopenic purpura is a microangiopathic hemolytic amenia characterized by fever, neurological dysfunction, renal dysfunction, thrombocytopenia, hemolytic anemia. TTP can be inherited or acquired, caused due to ADAMTS13 enzyme malfunctioning. As the condition is medical emergency timely treatment is essential and vital plasma exchange and chemotherapy are used to control the activities of the enzymes. The present article describes the causes, risk factors, diagnosis and standard treatment for the management of TTP.

KEYWORDS : ADAMTS 13 ENZYME,THROMBOTIC THROMBOCYTOPENIC PURPURA,

INTRODUCTION

Thrombotic thrombocytopenic purpura is a medical emergency and life threatening blood disorder. In TTP the blood clot in small blood vessels which limit the flow of blood leads to injury, ischemia and necrosis. The clot can form in brain, kidneys, heart. Platelets work by clotting mechanism, prevent bleeding. In TTP the increase clotting occurs utilizing the platelets and deficit of platelets lead to timy bruising and bleeding in tissue which are seen as purpura.[1]

TTP incidence is abrupt and persistant, the symptoms last for days to years, result as cerebrovascular accident.

EPIDEMIOLOGY

- TTP is adult disorder accur after 40years and in congenital form in children. The incidence rate is 1 in 13 million people depend on geographical location.
- The incidence is more common in women than in men at 2:1 ratio.
- 90% mortality are observed in patient without treatment.
- High risk of TTP is associated with Africans, American descents and pregnancy.[2]

PATHOLOGY

TTP is caused due to deficiency of ADAMTS13 enzyme caused by gene mutation or acquired by autoantibodies produced by spleen. ADAMTS13 is a plasma von willebrand factor cleaving protease, which cleaves the VWF ultra large to VWF sammler size multimer. When the cleavage is hampered the large VWF multimer accumulates on the endothelial surface cause platelets to aggregate forming thrombi. These thrombi cause the ischemia, leads to necrosis and organ failure. The thrombocytopenia results due to platelets consumptions during thrombus formation. Anemia is caused due to hemolysis and destruction of RBC's, these are morphologically disrupted RBC's are called schistocytes.[3,4]

CLINICAL FINDINGS OF TTP

- The cause of TTP can be congenital or inherited the symptoms starts appearing at birth a fine bruising under skin, petechiae small flat red spots, red purple yellowish brown spots indentified as purpura.
- The yellowish discoloration of skin, scleara are due to break down of RBC appears as jaundice, pallor skin.
- The patient's complaint of fatigue, tiredness, fever, dyspnea, tachycardia.
- The neurological symptoms include headache, aphasia, confusion, paralysis, paraparesis, seizures, irritability, disorientation and coma[5]
- Oliguria are seen due to TTP involvement in kidneys
- Nausea, vomiting, diarrhea, feeling sick are common identified symptoms.

ETIOLOGY FOR TTP

TTP is inherited and acquired, in both the cases the cause is due to fault in the genetic makeup which leads to deficiency of ADAMTS13 enzyme which function by controlling the blood clot mechanism.

In inherited cause the gene is passed from parent due to mutation the enzyme function improperly lead to inherited TTP, where as in acquired TTP the enzyme is functioning correctly, but due to certain diseases and its progress the antibodies are developed in the system that cause ADAMTS13 enzyme function improperly leads to acquired TTP.

The risk factors that cause TTP are age, medication, gender, race and medical procedure.

Adults are at risk of acquired TTP and newborn are at risk of inherited TTP.[6]

The chemotherapeutic drugs used for cancer treatment can cause TTP the drugs are ticlopidine, clopidogrel, cyclosporine.

The medical condition such as HIV infection, Lupus, cancer can cause acquired TTP. Obesity and pregnancy can also add for acquired TTP.[7,8]

Africans and Americans are at risk of TTP, women are more prone to TTP than men.

The medical procedures such as bone marrow transplantation, stem cell transplant are at risk of developing TTP.

DIAGNOSIS OF TTP

- The family history of TTP is essential as the condition is inherited.
- The medical, mediational, race are vital for the diagnosis of TTP.[9]
- The blood investigations aim to identify the underlying cause of the TTP the test such as ADAMTS13 assay is performed to check for enzyme and their activity. The lack of ADAMTS13 confirms the TTP. The plasmic score is

calculated to find presentation and prediction of ADAMTS13 activity.

- Bilirubin level test shows high levels of bilirubin as the RBC's breakdown increases due to anemia or other medical conditions.
- A routine blood smear is performed for morphology of RBC's which shows broken or torn RBC's.
- Complete blood count and bone marrow examination gives complete picture of the blood and its components.
- To rule out the medical cause of the diseases certain specific test are performed such as Coombs's test to determine the cause of hemolytic anemia, kidney function test and urine routine for creatinine, BUN and for presence of RBCs in urine. Lactate dehydrogenase (LDH) test specifies the tissue breakdown and blood clot caused due to TTP.[10,11]

TREATMENT OF TTP

TTP is life threating and medical emergency blood disorder and rapid effective treatment is essential to save life. Plasma treatment is the choice for the TTP, in plasma treatment the plasma form health donor is transfused through machine which removes the antibodies that damage the ADAMTS13 enzyme function. Platetet transfusion can also help to better the patient condition. This is called plasmapheresis in which plasma is transfused. In contrast to this plasma infusion is used in treatment of inherited TTP, through intravenous infusion health donor plasma is infused which replace the missing faulty ADAMTS13 enzyme.[12]

Corticosteroids such as prednisone which slow the process of antibodies forming in acquired TTP. The other drugs used in management of TTP are rituximab, vincristine, cyclophosphamide and cyclosporine A when underlying cause is due to cancer.[14]

Surgical management of TTP includes splenectomy. Spleen is principle organ that produces antibodies to misfunction ADAMTS13 enzyme hence removing of spleen can slow the process of developing TTP.[13]

Guidelines for the treatment of TTP given by International society on thrombosis and hemostasis.

1. Initial treatment is done by strong corticosteroids and with therapeutic plasma exchange.
2. For patients with first acute incidence, rituximab, corticosteroid and plasma exchange are recommended.
3. For patients with relapsing TTP, plasma exchange, corticosteroid and rituximab for initial treatment with additional caplacizumab.
4. Patients with TTP and remission with low plasma ADAMTS13 activity, rituximab recommended for prophylaxis.
5. Expected mother with decreased plasma ADAMTS13 activity, plasma infusion products are recommended.[15]

CONCLUSION

TTP demands the right time treatment, early treatment with plasma exchange and steroids decreases the mortality, the longer the patient is avoided with the treatment greater the adverse outcomes. The patient without treatment has 90% mortality rate, hence before the adverse outcomes skillful treatment should be initiated which demise the occurrence of coronary thrombosis, stroke, myocardial infarction and sudden death.

REFERENCES

1. Tanner L, Müller MM. [Blood Transfusion: a Guide to Clinical Decision Making]. Anasthesiol Intensivmed Notfallmed Schmerzther. 2019 Mar;54(3):194-205.
2. Coppo P, Cuker A, George JN. Thrombotic thrombocytopenic purpura: Toward targeted therapy and precision medicine. Res Pract Thromb Haemost. 2019 Jan;3(1):26-37.
3. Wiernek SL, Jiang B, Gustafson GM, Dai X. Cardiac implications of thrombotic thrombocytopenic purpura. World J Cardiol. 2018 Dec 26;10(12):254-266.
4. Cox EC. Thrombotic thrombocytopenic purpura: report of three additional cases and a short review of the literature. J S C Med Assoc. 1966 Dec;62(12):465-70.
5. Bell WR, Braine HG, Ness PM, Kickler TS. Improved survival in thrombotic thrombocytopenic purpura-hemolytic uremic syndrome. Clinical experience in 108 patients. N Engl J Med. 1991 Aug 08;325(6):398-403.
6. Gavriilaki E, Anagnostopoulos A, Mastellos DC. Complement in Thrombotic Microangiopathies: Unraveling Ariadne's Thread Into the Labyrinth of Complement Therapeutics. Front Immunol. 2019;10:337.
7. Amin Asnafi A, Jalali MT, Pezeshki SMS, Jaseb K, Saki N. The Association Between Human Leukocyte Antigens and ITP, TTP, and HIT. J Pediatr Hematol Oncol. 2019 Mar;41(2):81-86.
8. van Dorland HA, Taleghani MM, Sakai K, Friedman KD, George JN, Hrachovinova I, Knöbl PN, von Krogh AS, Schneppenheim R, Aebi-Huber I, Bütikofer L, Largiadèr CR, Cermakova Z, Kokame K, Miyata T, Yagi H, Terrell DR, Vesely SK, Matsumoto M, Lämmle B, Fujimura Y, Kremer Hovinga JA., Hereditary TTP Registry. The International Hereditary Thrombotic Thrombocytopenic Purpura Registry: key findings at enrollment until 2017. Haematologica. 2019 Oct;104(10):2107-2115.
9. Swart L, Schapkaitz E, Mahlangu JN. Thrombotic thrombocytopenic purpura: A 5-year tertiary care centre experience. J Clin Apher. 2019 Feb;34(1):44-50.
10. Terrell DR, Vesely SK, Kremer Hovinga JA, Lämmle B, George JN. Different disparities of gender and race among the thrombotic thrombocytopenic purpura and hemolytic-uremic syndromes. Am J Hematol. 2010 Nov;85(11):844-7.
11. Shelat SG, Ai J, Zheng XL. Molecular biology of ADAMTS13 and diagnostic utility of ADAMTS13 proteolytic activity and inhibitor assays. Semin Thromb Hemost. 2005 Dec;31(6):659-72.
12. Zander CB, Cao W, Zheng XL. ADAMTS13 and von Willebrand factor interactions. Curr Opin Hematol. 2015 Sep;22(5):452-9.
13. Chiasakul T, Cuker A. Clinical and laboratory diagnosis of TTP: an integrated approach. Hematology Am Soc Hematol Educ Program. 2018 Nov 30;2018(1):530-538.
14. Dane K, Chaturvedi S. Beyond plasma exchange: novel therapies for thrombotic thrombocytopenic purpura. Hematology Am Soc Hematol Educ Program. 2018 Nov 30;2018(1):539-547.