

A Case of Thrombotic Thrombocytopenic Purpura

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Abstract: Thrombotic thrombocytopenic purpura (TTP) can develop at any age, in newborns and in the elderly over 90 years of age, with a median age of 35 years. The onset of the disease is often rapid, with acute outbreaks common and failure to diagnose and treat patients early results in high mortality rates. By analyzing the clinical manifestations and laboratory findings of a patient with TTP in the First Affiliated Hospital of Jinan University, the clinical characteristics of this disease were clarified to help medical workers deepen their understanding of this disease in their follow-up work.

Keywords: TTP; Microvascular Hemolytic Anemia; Platelet; ADAMTS13; Case Report.

1. Introduction

Thrombotic thrombocytopenic purpura (TTP) is a rare, thrombotic microangiopathy characterized by systemic platelet thrombosis, organ ischemia, very severe thrombocytopenia, and often red blood cell destruction. Its clinical features include fever, thrombocytopenia, neuropsychiatric symptoms, hemolytic anemia, and renal involvement, and this pentad is present in 88%-98% of patients. It is mainly due to a deficiency in vascular hemophilic factor cleaving enzyme (ADAMTS13) activity[1]. In healthy individuals, this cleaving enzyme, when present, can promptly shear the vWF multimer released by endothelial cells, whereas when ADAMTS13 activity is deficient in TTP patients, this product cannot be sheared in a timely manner and continues to spontaneously bind platelets, which further leads to thrombosis in the microvasculature, which in turn leads to microangiopathic hemolysis, ischemia and hypoxia of the respective organs, as well as dysfunction. Therefore, based on the differences in ADAMTS13 deficiency mechanisms, TTP is subdivided into congenital TTP (cTTP) and immunologic TTP (iTTP)[2]. Since TTP is a chronic disease, but often presents with acute attacks and a more severe course, rapid diagnosis is crucial to help reduce patient mortality as well as to avoid further blows to tissues and organs and to improve patients' quality of life in the long term. However, the low incidence of TTP and its diverse clinical manifestations pose a challenge for clinicians to make a definitive diagnosis in the first instance. For this reason, the author will be Jinan University Affiliated Hospital No. 1 recently admitted a case of thrombotic thrombocytopenic purpura patients for clinical analysis, so that the front-line medical personnel can be more intuitive feel the characteristics of the disease.

2. Case presentation

The patient, 62 years old, was admitted to the emergency department of the Fifth Affiliated Hospital of Southern Medical University on 2023-08-11 with dizziness and fever[3], and was immediately examined in the emergency department for blood routine, biochemistry, and cranial CT. Subsequently, the routine blood test showed that the white blood cells were $17.6 \times 10^9/L$, red blood cells were $2.79 \times 10^{12}/L$, hemoglobin was 86 g/L, platelets were $14 \times 10^9/L$,

biochemistry showed that the albumin was 35 g/L, creatinine was 145 $\mu\text{mol/L}$, uric acid was 796 $\mu\text{mol/L}$, and the cranial CT showed that there was cerebral leukoencephalopathy and cerebral atrophy. The patient was admitted to the department of neurology for consideration of neurologic-related diseases, and was given nutritional nerves and dizziness-relieving treatment. After the treatment of nutritional nerves and stopping dizziness, the patient felt that he still had dizziness and discomfort, so he requested to be discharged from the hospital on his own. he was admitted to the Emergency Department of the First Affiliated Hospital of Jinan University on 2023-08-12. On entering the hospital, the patient presented with an acute face, irritable state, bilateral pupils of equal size and roundness, sensitive to light reflexes, with large hemorrhagic spots and petechiae scattered over the whole body, blood crusts visible in the oral cavity, and moist rale audible at the bottom of the lungs, physiological reflexes were normal, pathological reflexes were not elicited. Blood test: white blood cells $15.34 \times 10^9/L$, red blood cells $2.64 \times 10^{12}/L$, hemoglobin 80 g/L, platelets $12 \times 10^9/L$. Biochemistry: lactic acid 6.15 mmol/L, creatinine 184 $\mu\text{mol/L}$, glomerular filtration rate 33ml/min/1.7m², alanine aminotransferase 24 U/L, glutamic oxal transaminase 1440U/L, total bilirubin 118.9 $\mu\text{mol/L}$, conjugated bilirubin 15.8 $\mu\text{mol/L}$, unconjugated bilirubin 102.1 $\mu\text{mol/L}$. Urine routine suggests protein 1 g/L, latent blood 150REY /uL. Urgent head CT suggests leukoaraiosis, cerebral atherosclerosis, and then transferred to the Hematology internal medicine hospitalization. The patient was dizziness, agitation with fever and other symptoms, and the whole body can be seen scattered petechial hemorrhage ecchymosis, bilirubin, creatinine, plasma lactic acid is elevated, according to the monist diagnostic thinking, all the signs indicate that the patient may have coagulation, fibrinolytic mechanism of the abnormality of microvascular circulation disorders, leading to inadequate perfusion of the tissues, organs, resulting in the emergence of a number of tissues and organs hypoxia, ischemic injury. In addition, the patient's unconjugated bilirubin was elevated along with a persistent decrease in platelets and hemoglobin, which was highly suspicious of thrombotic thrombocytopenic purpura. Immediately, the coagulation, rheumatism, ADAMTS13 activity test and other tests were supplemented. Among them, the coagulation test showed: fibrinogen degradation product: 34.75ug/ml, D-dimer: 10170 ng/ml. The rheumatism set

suggested: anti-nuclear antibody 116 IU/ml, anti-SS-A52 antibody positive (+). ADAMTS13 activity test reported: inhibitory antibody for ADAMTS13 activity (+), ADAMTS13 activity 0.86%[4]. Bone marrow aspiration shows: bone marrow film: bone marrow nucleated cell proliferation is obviously active, granulocyte-red ratio = 0.52:1, red lineage proliferation is active, the proportion is increased, the classification is predominantly medium-late juvenile red, megakaryocytes are increased in the whole film, platelets are rare. Blood smear: erythrocytes were unequal in size, broken erythrocytes were easily seen, and platelets were rare. The patient had very low platelets and co-infections, with a high risk of death, and was transferred to ICU intensive care after communication, considering the need for plasma exchange and subsequent continuous renal replacement therapy. After consultation with the hematology department, the patient was recommended to receive plasma exchange, continuous renal replacement therapy, and glucocorticoid and gammaglobulin, and the rest of the treatment included anti-infective therapy and component blood transfusion after symptomatic relief. After treatment, the patient was discharged from the hospital with improved symptoms, and after discharge, he continued to apply glucocorticoids regularly, as well as clopidogrel and atorvastatin antiplatelet lipid-modulating therapy.

3. Discussion

The patient started with dizziness and fever, accompanied by a decrease in platelets and a persistent decrease in hemoglobin, with marked elevations in lactate, lactate dehydrogenase, creatinine, and unconjugated bilirubin. Meanwhile, Subcutaneous petechiae visible throughout the body. Unfortunately, the initial diagnosis was not considered to be multiple tissue and organ damage due to TTP and treat the symptoms with neurology, which causes the patient's symptoms to worsen. In fact, TTP should be suspected first in all patients with hemolytic anemia combined with thrombocytopenia, unless there is an obvious alternative etiology. Therefore, under the specialized consultation of hematology, the ADAMTS13 activity test was accomplished, and bone marrow aspiration and other tests were performed, which clarified that it was thrombotic thrombocytopenic purpura, which is one type of microvascular thrombotic lesion[5].

The pathogenesis of TTP is clear, and, as previously described, it is due to genetic or immunologic ADAMTS13 deficiency[6]. Each acute episode of TTP puts the TTP patient at risk of death. For this reason, prevention of acute TTP episodes is a top priority for TTP patients in remission. Depending on the cause of the episode, there are different treatment options for it, so it is important to differentiate between cTTP and iTTP to help guide treatment as well as follow-up.

Congenital TTP is the result of a pure heterozygote mutation or compound heterozygote mutation in the ADAMTS13 gene, leading to congenital ADAMTS13 deficiency or reduced activity. Therefore, in cTTP, patients have a sustained decrease in ADAMTS13 activity over time, which in turn leads to an acute onset of the disease, and therefore patients with cTTP are treated with replacement therapy in the form of plasma infusion supplemented with exogenous ADAMTS13, patients are expected to have complete recovery of ADAMTS13[2]. In iTTP, on the other hand, it is due to the production of anti-ADAMTS13

autoantibodies in the patient's body, which inhibit ADAMTS13 activity or lead to ADAMTS13 deficiency in the patient's body by accelerating ADAMTS13 clearance. Therefore, plasma replacement becomes the first line of treatment during the acute onset of iTTP patients and glucocorticoids may be used as appropriate. The patient in the case, whose anti-ADAMTS13 antibody was positive, was considered to be immune thrombotic thrombocytopenic purpura, so plasma exchange therapy was performed in the first instance to promptly remove ADAMTS13 inhibitors or IgG antibodies and other curative factors from the blood, and shock therapy with glucocorticoids and immunoglobulins was performed, which could reduce inflammatory reactions, protect organ function, and inhibit autoantibody production. And after the above treatment, the patient's symptoms improved significantly, platelets and hemoglobin recovered gradually, renal function recovered and creatinine level decreased. The rest of the treatment of TTP includes biologics application such as rituximab and capucelizumab[7], other immunosuppressant agents, and so on. It is important to note that blind platelet transfusion due to thrombocytopenia can be fatal for TTP patients, as it may increase microvascular thrombosis and aggravate ischemic organ damage. Platelet transfusion should be considered only in the setting of life-threatening bleeding after plasma exchange or after weighing the pros and cons[8].

4. Conclusion

TTP is rare in clinical practice, but it is a medical emergency and rapid diagnosis as well as initiation of treatment can be of significant benefit to the patient. However, in early diagnosis, few patients with TTP present with a complete quintet of signs at the initial stage, so it is important to promptly identify and diagnose patients who present clinically with multiple thrombotic thrombocytopenias with hemolytic anemia with multiple systemic involvement. Therefore, a complete understanding of the disease mechanism and clinical manifestations of thrombotic thrombocytopenic purpura is needed, which can improve early diagnosis and lead to a better prognosis for the patient.

Patient Consent

Written informed consent for the publication of this case report was obtained from the patient.

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