

A Patient with Thrombotic Thrombocytopenic Purpura and Crohn Disease

Gülden Sincan¹, İlhami Kiki¹, Suat Sincan²

¹Department of Hematology, Medical School, Ataturk University, Erzurum, Turkey

²Adnan Menderes Family Health Center, Erzurum, Turkey

*Corresponding author

Gülden Sincan

Email: guldensincan@gmail.com

Abstract: Thrombotic thrombocytopenic purpura is a rare disease characterized with microangiopathic hemolytic anemia, thrombocytopenia, fever, kidney damage and neurologic symptoms. Thrombotic thrombocytopenic purpura was reported in the course of many causes such as inflammatory diseases, malignancies, infections, autoimmune disorders, stem cell transplantation and drug administrations. There are only few cases of thrombotic thrombocytopenic purpura associated with crohn disease was reported in the literature. We describe a 30 year old patient who presented with thrombotic thrombocytopenic purpura associated with crohn disease. She was treated successfully with plasmapheresis.

Keywords: Crohn Disease; Thrombotic Thrombocytopenic Purpura.

INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is an acute disease, rarely seen. TTP is characterised with pentad of thrombocytopenia, neurological manifestations, hemolytic anemia due to microangiopathy, fever and renal failure [1]. It described firstly by Moschowitz in 1925 [2]. The most important findings is thrombocytopenia, fragmented erythrocytes and schistocytosis of TTP. Crohn's disease is a type of inflammatory bowel disease that may affect any part of the gastrointestinal tract from mouth to anus. Signs and symptoms include abdominal pain, diarrhea, fever and weight loss. Other complications are anemia, skin rashes, arthritis, inflammation of the eye. There are no medications or surgical procedures that can cure Crohn's disease. Treatment options help with symptoms, maintain remission, and prevent relapse.

TTP can be congenital or acquired. The most common form of acquired idiopathic. TTP is usually seen in healthy people. But it can develop secondary to malignancies, bacterial or viral infections, autoimmune disorders, pregnancy, stem cell transplantation and drug administrations such as ticlopidine, clopidogrel, cyclosporine A and hormone therapy [3-7]. Crohn disease is one of the rare causes of TTP [8-10]. Microvascular thrombosis plays an important role in the pathogenesis of thrombotic thrombocytopenic purpura. Patients with inflammatory bowel disease have an increased frequency of microvascular thrombosis. Therefore; TTP/HUS seen in patients with crohn disease. We describe a 30 year old patient who presented with TTP associated with crohn disease. She responded well to plasmapheresis.

CASE REPORT

A 30 year old female patient was admitted to emergency department with petechial lesions on her body and headache. Her past medical history included of crohn disease for 3 years. She was treated with 5-aminosalicylic acid, but this treatment was stopped 6 months ago by herself. There was no complaint of the patient's associated with gastrointestinal tract and she was not taking any medication for crohn disease. The informed consent was obtained in this patient.

On physical examination there were petechial lesions on her body, blood pressure was 100/70 mmHg, pulse was 90 beats/min, no fever and without any other significant findings.

Laboratory findings were as follows; level of hemoglobin was 9.2 gr/dl, hematocrit 26.3%, white cell count 7900/mm³, platelets 7000/mm³. Level of serum urea was 14 mg/dl, creatinine 0.7 mg/dl, sodium 135 mEq/L, potassium 3.7 mEq/L, uric acid 3.8 mg/dl, C-reactive protein 2.9 mg/l, aspartate amino transferase 25 UI/L, alanine amino transferase 12 UI/L, gamma glutamyl transferase 15 U/L, alkaline phosphatase 49 U/L, lactate dehydrogenase 610 U/L, indirect bilirubin 2.5 mg/dl. She had a negative direct and indirect coombs test, a normal fibrinogen level, an elevated reticulocyte count of 3.6% (0.5-2.0%). There were fragmented erythrocytes, schistocytosis, sferocytosis and polychromasia in the peripheral blood smear. Serological tests for brucella, cytomegalovirus, rubella, toxoplasma, hepatitis A, B, C, human immune deficiency virus, ebstein-barr virus, and parvovirus were negative. Anti nuclear antibody (ANA), anti-ds DNA, anticardiolipin antibodies, antiphospholipid antibodies, lupus anticoagulants, c-antineutrophil

cytoplasmic antibody (c-ANCA) and p-ANCA were negative. Immunoglobulin levels were within normal ranges. Prothrombin time and partial thromboplastin time and international normalized ratio (INR) were normal. The level of ADAMTS-13 was not examined. Due to these findings, we thought that, the diagnosis was thought as TTP and plasma exchange (PE) with equal volume of fresh frozen plasma was initiated daily. Increase was seen in platelet count in the second days of treatment. Frequency of PE was decreased after fourteen days. In total she received 19 sessions of plasmapheresis. Endoscopic and colonoscopic examination was performed to the patient, due to history of crohn disease. There was no evidence associated with crohn disease in upper and lower gastrointestinal tract. We thought it was in remission of Crohn's disease. In follow up platelet count, hemoglobin level, LDH, and reticulocyte count came to normal range, general condition of patient became better so the patient was discharged.

DISCUSSION

TTP is characterised with pentad of thrombocytopenia, neurological manifestations (convulsion, coma, hemiplegia, paresthesias, visual disturbance and aphasia), microangiopathic hemolytic anemia, fever, and renal failure. Only the minority of TTP patients (20-30%) present with the classic pentad. Currently unexplained thrombocytopenia and microangiopathic hemolytic anemia are the two criteria that required to establish the diagnosis of thrombotic microangiopathy and initiate treatment. In our patient, microangiopathic hemolytic anemia, thrombocytopenia and headache suggested the diagnosis of TTP.

In the last 15 years there has been a marked increase in the understanding of the pathogenesis of TTP. TTP is characterized by deficiency of the von Willebrand factor (vWF) cleaving protein, also known as ADAMTS13 [11]. Accumulation of ultralarge vWF multimers leads to excessive platelet aggregation and microvascular thrombosis with associated end organ damage. Microthrombosis triggered by autoimmune disorders can be the main cause in the development of TTP in patients with CD [12]. Specific coagulation abnormalities have been recorded in patients with inflammatory bowel disease that may lead to a thromboembolic event. Levels of factors V, VII and VIII, lipoprotein (a) and fibrinogen increase in patients with CD. In addition, a reduction in natural anticoagulant factors including antithrombin III, protein C and protein S may develop. Another possible pathomechanism is that IL-12 and Th1-mediated IFN- γ may play the central role in the pathogenesis of TTP associated with CD [13,14]. An increased risk of major thromboembolism has been described in patients with inflammatory bowel disease. Several case reports have been reported previously with CD and TTP. In our case, she has crohn disease for 3 years. But the treatment of crohn disease was stopped 6 months ago by herself.

Crohn disease was in remission in our patient. We thought; crohn disease may be cause for TTP. But the combination of crohn disease and TTP may be accidental in our case.

Plasma exchange with fresh frozen plasma has decreased the mortality rate in acute TTP significantly from more than 90% to less than 25%. Patients who do not respond well to plasma exchange usually require other treatment modalities. Rituximab and high-doses of corticosteroids are widely used therapeutic options indicated in refractory/relapsing disease. Other immunosuppressive agents have been also considered, such as vincristine, cyclosporine, and intravenous immunoglobulins. In this case, we thought that the diagnosis was TTP and we applied plasma exchange (PE) with equal volume of fresh frozen plasma was initiated daily. In the second days of treatment, it was seen that increased in platelet count. Frequency of PE was decreased after fourteen days. 19 sessions of plasmapheresis were applied to the patient in total. In follow up platelet count, hemoglobin level, LDH, reticulocyte count came to normal range.

CONCLUSION

Although rare, TTP is an important complication that leads to a poor prognosis in CD patients. Hemolytic anemia and thrombocytopenia in patients with Crohn disease; TTP should be considered. Crohn disease may cause TTP or crohn disease and TTP may incidentally together.

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