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Thrombotic Thrombocytopenic Purpura: A Rare Case Report

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Abstract: Thrombotic thrombocytopenic purpura (TTP) is a rare thrombotic microangiopathy with an estimated incidence of 11 cases/million population per year. Early treatment is essential and is curative in this disease where lack of treatment results in 90% mortality. However, recognition of thrombotic thrombocytopenic purpura can be difficult because of the variety of presentations and lack of specific diagnostic criteria. We describe an atypical case of a patient with TTP who presented to our department for generalized swelling, and was found to have thrombocytopenia with anemia. Occasionally, an unusual clinical presentation makes TTP diagnosis difficult, thus resulting in a delay in the management of TTP. The current treatment is still plasmapheresis and application of steroids.

Keywords: Thrombotic thrombocytopenic purpura (TTP), thrombocytopenia.

INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) was first described by Moschowitz in 1925 as a disease characterized by the pathological findings of hyaline thrombi in many organs [1]. In its classic form, it consists of the pentad of thrombocytopenia, microangiopathic hemolytic anemia, neurologic abnormalities, fever, and renal disease.

Etiologies can include medications, infections, cancers, or transplantation. Currently unexplained thrombocytopenia and microangiopathic hemolytic anemia are the two criteria required to establish the diagnosis of thrombotic microangiopathy and initiate treatment [2, 3]. The current frontline treatment is still plasmapheresis and application of steroids [5, 6]. Therefore, it is vital important to make differential diagnosis with these diseases that evolve with microangiopathic hemolytic anemia in a short time to initiate the plasmapheresis [7]. Although plasmapheresis can effectively reduce the mortality to approximately 20% [8], there is a significant subset of patients with either delayed or absent responses, requiring protracted courses of plasmapheresis with a high rate for the associated complications [9]. The present paper describes one such rare case admitted under our care at the D.Y. Patil Hospital.

CASE REPORT

A 26-year-old male with a 2-week history of generalized swelling and breathlessness presented to the emergency room after having 2 days of diarrhea and diffuse abdominal pain. He had a total of 12 episodes of diarrhoea. The patient complained of fevers, chills, fatigue, poor oral intake, and weight loss. There were no precipitating or relieving factors. He denied any recent travel, sick contacts, pets, raw foods, seafood exposure, antibiotic use, coffee ground emesis, hematemesis, or tenesmus. His past medical history included two episodes of generalized tonic clonic seizure 2 months back.Upon admission, the patient was afebrile 37.1C; pulse rate 117 beats per minute; respirations 26 breaths per minute; and blood pressure 170/96. He appeared to be in some discomfort. His cardiac exam revealed sinus tachycardia without a murmur. There was moderate abdominal distention with diffuse tenderness and decreased bowel sounds. There was bilateral pedal edema. Laboratory examination revealed a white blood cell count of 10,700/µL; hemoglobin of 5.5 g/dL with a mean cell volume of fl, platelet count of 71,000/µL. Peripheral blood smears showing schistiocyte 2% with microcytosis and anisocytosis. Blood chemistry evaluation revealed a138mg/dl urea, 3.7mg/dl creatinine, normal liver function tests except for low albumin level. His LDH was 404 IU/L. Lactic acid level and lipase were all within normal limits. His urine was concentrated and revealed proteinuria with cast cells. USG of abdomen revealed bilateral grade 3 chronic renal parenchymal disease with splenomegaly, massive ascites and bilateral pleural effusion. 24 hours urine proteins were elevated at 1540 mg/24hrs. Ascitic fluid showed transudative in nature with no organism. ANA BLOT test was done to rule out vasculitis and other autoimmune diseases. It was negative for all antigens (Nucleosomes, Ds-DNA, Histones, SmD1, SS-A/Ro, SS-B/La, AMA M2, Jo1). p-ANCA c-ANCA were

negative. HIV, HBsAg, HCV were negative. MRI DWI of brain revealed multile well defined oval lesions scattered in bilateral cerebellar hemispheres with FLAIR hyperintensities involving cortex and subcortical white matter in bilateral parieto-occipital lobes.

On hospital day 3 the platelet count was 76,000/µL with hemoglobin of 7.2 g/dL. On hospital day 7 the platelet count was 39,000/µL and the hemoglobin of 5.7 g/dL. His neurological examination was unremarkable. Hematology consultation was obtained because of the thrombocytopenia.

Schistocytes were observed on the peripheral smear and bone marrow biopsy. Kidney biopsy was done for final diagnosis. It showed thrombotic microangiopathy both glomerular and arteriolar in chronic phase (Figure-1 and 2). ADAMTS 13 was not done due to affordability issue. He was started on steroids followed by plasma exchange. Plasma exchange was initiated immediately along with systemic steroids. Platelets counts improved, the patient remains afebrile and hemodynamically stable. Patient received a total of 5 plasma exchanges and 6 settings of haemodialysis. Patient was sent home on hospital day 30 with fistula.

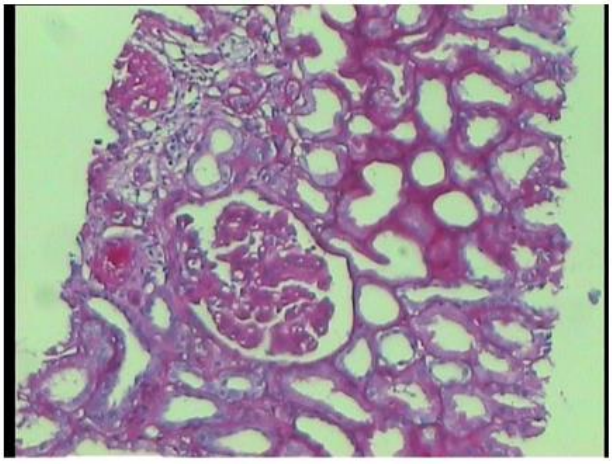

Fig-1: TMA in Chronic Phase

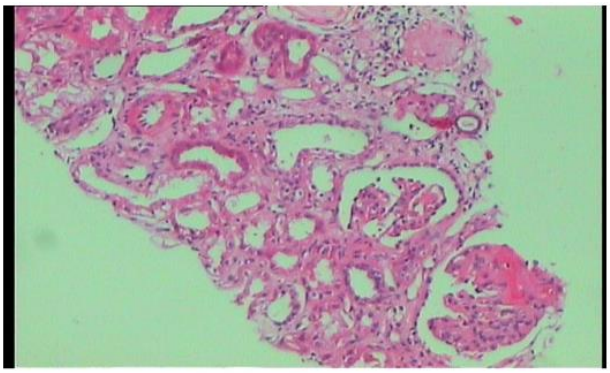

Fig-2: TMA in Chronic Phase

DISCUSSIONS

Thrombotic Thrombocytopenic Purpura is an acute lifethreatening syndrome characterized by thrombocytopenia and microangiopathic hemolytic anemia. There is often multi-organ involvement with neurological and renal abnormalities being most common and potentially the most serious [5]. A classic pentad of thrombocytopenia, MAHA, fever, neurological abnormalities and renal dysfunction has been described but is rarely seen in its entirety nowadays [4]. Predominant neurological symptoms and signs (such as headache, confusion, seizures, focal abnormalities, transient ischaemic attack, stroke and coma) are suggestive of TTP, whereas severe renal failure is more suggestive of HUS.

TTP is associated with a deficit in the activity of ADAMTS13, a von Willebrand factor cleaving protease, which produces platelet clumping and subsequent microvascular thrombosis with fibrin deposition, red blood cell fragmentation (schistocytes), release of inflammatory cytokines, high levels of plasminogen-activator inhibitor type 1 and other prothrombotic mediators. TTP can be idiopathic, acquired or due to congenital ADAMTS13 deficiency. ADAMTS13 deficiency (<10%) and the presence of ADAMTS13 inhibitor distinguish idiopathic and acquired TTP from the congenital form [6].

Testing ADAMTS13 deficiency is not recommended for confirming the diagnosis because it can be present in other conditions such as sepsis with disseminated intravascular coagulation or ischaemic organ failure [7]. However, ADAMTS13 deficiency can anticipate the long-term relapse risk, because patients with severe ADAMTS13 deficiency relapse more frequently [8].

The first line treatment for TTP is plasma exchange. The objective is to remove the auto antibodies, and replace them with Fresh Frozen Plasma (FFP) [9]. Complete plasma exchange, replacing 1-1.5x the patient's calculated volume occurs daily until platelets and organ function normalize [10]. This can often take weeks, as the neurological sequelae resolve, then the anemia, and finally renal normalization. LDH is also a keen marker for treatment response, as it indicates hemolysis and tissue damage [11]. If plasma exchange is not possible, FFP infusions are an acceptable bridging therapy until the patient can be transferred [12].

Twenty percent of patients will not respond to plasma exchange [13], making our first line treatment significantly flawed17. On a side note, it is postulated that the majority of patients who do not respond to plasma exchange, developed TTP from atypical etiologies such as malignancy [14]. As a second line treatment and for severe cases, immuno suppressants are used. The mainstays of this treatment are steroids and rituximab [14]. Response to treatment with rituximab is usually seen within fourteen days [15]. After platelets have normalized, treatment should be continued for at least 2 more days to insure efficacy [10].

CONCLUSION

This case report will highlight the importance of unusual presentation, early diagnosis and early aggressive treatment for patients with TTP to avoid a poor outcome by decreasing morbidity and mortality.

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