Case Report
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An Unusual Presentation of Thrombotic Thrombocytopenic Purpura with Preserved ADAMTS13: A Case Report

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Abstract

Background: Thrombotic Thrombocytopenic Purpura (TTP) is a rare, potentially fatal disease with multisystem involvement. ADAMTS13 assays are often used for supporting the diagnosis, here we present a rare case of TTP with normal ADAMTS13 levels.

Case presentation: A 39-year-old female presents with syncopal episodes, blurred vision in both eyes during a patch test, headaches, and tenderness over the abdomen, all against a backdrop of hypertensive emergency. She had a history of chronic hypertension managed on medications, iron deficiency secondary to fibroid and an episode of provoked deep vein thrombosis and pulmonary embolism with negative work-up of thrombophilia. Labs revealed low hemoglobin of 9.8 mg/dl, platelet in the range of 52,000/ ml, 3 mEq/L potassium, with high levels of Creatinine (Cr) 6.7 mg/dl and Blood Urea Nitrogen (BUN) levels of 59 mg/dl. Due to the clinical triad of thrombocytopenia, hemolysis pattern and neurological manifestation, ADAMTS13 essay was ordered. Thrombophilia work-up showed haptoglobin was less than 20 mg/dl, LDH of 752 U/L, and a normal ADAMTS13 level. PLASMIC score was 5, suggestive of moderate risk. With high levels of abnormal creatinine levels and BUN, renal biopsy was done to look for the cause of acute kidney injury in the setting of suspected TTP which revealed diffuse thrombotic microangiopathy, along with moderate to chronic changes with greater than 50% tubular atrophy and interstitial fibrosis. CT scan of the brain was negative for detecting any cause of syncope; MRI showed lacunar infarcts secondary to thromboembolism. A provisional diagnosis of TTP with normal ADAMTS13 level was made and she was started on plasma exchange. Drastic symptom improvement was noted with FFP and 8 units of plasma exchange.

Keywords: Hypertensive emergency • ADAMTS13 level • Blood urea nitrogen • Thromboembolism

Introduction

Thrombotic Thrombocytopenic Purpura (TTP), is a rare disorder characterized by Thrombotic Microangiopathy (TMA) resulting in Microangiopathic Hemolytic Anemia (MAHA) [1]. With an incidence of 2 persons per million per year, TTP is a life-threatening disease if not treated immediately causing severe thrombocytopenia due to the formation of platelet-rich thrombi and leading to ischemic end-organ damage [2]. Hallmark of this condition is the severe deficiency of a protease enzyme which cleaves von Willebrand factor (vWF) multimers called ADAMTS13. With the lack of ADAMTS13 proteolytic activity, there is a build-up of vWF multimers which accumulate and initiate platelet adhesion and aggregation, leading to disseminated microthrombosis, severe thrombocytopenia, and ischemic end-organdamage [3]. Prompt treatment with emergency exchange oftherapeutic Plasma Exchange (PEX) is the core for managing such a condition [4]. It becomes important to recognize TTP early due to its associated clinical complications such as permanent neurological abnormalities. Diagnosis can be challenging, with varied clinical presentations from nonspecific symptoms to even ischemic damage to the brain leading to neurologic abnormalities, measuring ADAMTS13 activity becomes essential and helps in confirming [5]. ADAMTS13 activity and level can be measured using various assays. Initially, ADAMTS13 assays used plasma-derived VWF multimers and consumed a lot of time for the final conformational changes in unfolding and involving various other agents [6]. However, with the advancement, nowadays the most used assays measuring ADAMTS13 activity use an Enzyme-Linked Immunosorbent Assay (ELISA) or Fluorescence Resonance Energy Transfer (FRET)-based technology [7,8]. Although

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these are advantageous in the early detection of TTP, there might be conditions where ADAMTS13 levels may not be detected and one needs a clinical perspective to diagnose such a condition to prevent end-organ damage. One of the reasons could be due to the presence of some antibodies that may inhibit its detection, however, they are usually associated with autoimmune conditions [9]. Here, in this case, we present a rare presentation of late-onset TTP where the patient was clinically presenting with the signs and symptoms of TTP but had a negative ADAMTS13 level assay.

Case Presentation

Here we present a case of a 39-year-old female with the chief complaints of syncopal episodes, blurred vision associated with headaches, generalized abdominal pain and hypertensive emergencies. The patient was known for chronic hypertension medically managed with a combination of hydrochlorothiazide and valsartan, iron deficiency secondary to the fibroid, and the episode of provoked deep vein thrombosis and pulmonary embolism with a negative work-up on thrombophilia. The patient was also taking Vitamin D and Vitamin C supplements. Tenderness on palpation was noted over the whole abdomen, along with blurred vision in both eyes with a patch test on a physical examination. The laboratory investigations at that point revealed a low hemoglobin count of 9.8 mg/dl, low platelet in the range of 52,000 per microliter, low potassium of 3 mEq/L, high levels of Creatinine (Cr) 6.7 mg/dl with increased Blood Urea Nitrogen (BUN) levels of 59 mg/dl. Due to clinical triads such as thrombocytopenia, hemolysis pattern, and neurological manifestation, we ordered ADAMTS-13 level. On her thrombophilia work-up, haptoglobin was less than 20 mg/dl, with an LDH of 752 U/L and an average ADAMTS13 level. The PLASMIC score, which predicts ADAMTS13 deficiency in patients with suspected Thrombotic Thrombocytopenic Purpura (TTP), was 5, suggesting moderate risk. With high levels of abnormal creatinine levels and BUN, renal biopsy was done to look for the cause of acute kidney injury in the setting of suspected TTP, which revealed diffuse thrombotic microangiopathy, along with moderate to chronic changes with greater than 50% tubular atrophy and interstitial fibrosis. CT scan of the brain was negative for detecting any cause of syncope. However, MRI showed lacunar infarcts secondary to thromboembolism. A provisional diagnosis of TTP with an average ADAMTS13 level was made, and the patient was started on plasma exchange. Drastic improvement in the symptoms was noted with FFP and eight units of plasma exchange (Figure 1).

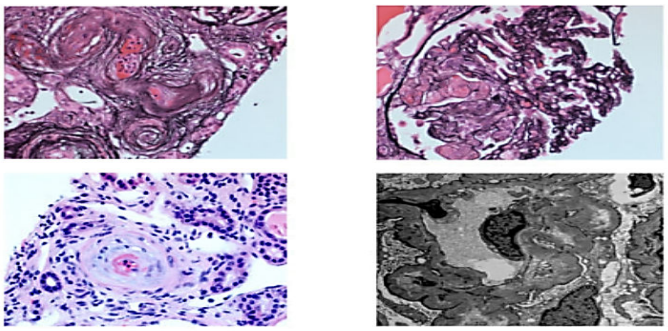

Figure 1. MRI showing features supporting the diagnosis of spinal cord and vertebrae involvement in Thrombotic Thrombocytopenic Purpura (TTP).

Discussion

ADAMTS 13 is a critical enzyme responsible for dividing the multimers of the von Willebrand factor. The ADAMTS13 level of less than 10% or less has a sensitivity value of 97% and a specificity value of 100% to diagnose TTP in suspected individuals [2]. Despite that, some patients whose clinical presentations are consistent with TTP but whose lab work shows normal levels [10]. Despite average enzyme level, inhibitory acquired autoantibodies to ADAMTS13 called acquired TTP usually block the enzyme's ability to divide the multimers. An alternate explanation could be genetic alteration and mutations in the ADAMTS13 enzyme, which leads to the loss of the enzyme's functional capacity [11]. For some patients who receive plasma exchange therapy, redistribution of anti-ADAMTS antibodies between intra and extravascular space leads to fast neutralization of infused plasma ADAMTS13 levels [12]. In these cases, patients can be found as usual or mild to decrease ADAMTS13 level [13]. TTP diagnosis could be challenging based on the enzyme level and one must carefully evaluate the clinical presentation, laboratory, and imaging findings and apply the prediction score like PLASMIC after ruling out other possible alternative diagnoses. Timely and appropriate treatment of TTP, regardless of ADAMTS level, is essential as it can significantly decrease the risk of complications and improve overall prognosis.

Conclusion

Our case is a rare presentation of acquired TTP where ADAMTS13 levels were found to be normal. As TTP may eventually cause severe renal, neurological complications, mucocutaneous bleeding, or intravascular bleeding, it is important to look at the clinical presentation with a triad of thrombocytopenia, hemolysis patterns, and neurological presentation even with normal ADAMTS13 levels in an elderly population.

Appendix

Rare presentation of thrombotic thrombocytopenic purpura

Objective of case report: (1) Want to discuss about rare complaint;(2) In TTP case, ADAMTS Normal

Chief complaint

Syncope, Blurry Vision, Headache, Hypertensive Emergency, Generalized abdominal pain

Past medical history

Provoked DVT and PE (Hold AC due to thrombocytopenia) Thrombophilia work up neg Hypertension

Iron deficiency secondary to fibroid

Medication

Hydrochlorothiazide 25 mg OD

Valsartan 160 mg BID

Vit D/Vit C supplement

Significant physical examination

Tenderness on palpation over whole abdomen

Blurred vision both sides with patch test

Relevant lab

Platelet 52

Hb 9.8

BUN 59

Cr 6.7

K 3

Normal ADAMTS level

Haptoglobin less than 20 LDH 752

PLASMIC score 5 moderate risk

Renal biopsy from AKI in the setting of TTP - Diffuse thrombotic microangiopathy.

Moderate chronic changes with greater than 50% tubular atrophy and interstitial fibrosis

Relevant imaging

CT brain neg for syncope

MRI lacunar infarction - secondary to thromboembolism

Treatment

Plasma exchange with symptom improvement

FFP Had PEX 8 Unit

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