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Case Report

Case report of thrombotic thrombocytopenic purpura with severe acquired ADAM TS 13 deficiency in a previously healthy adult male

Jimmy Joseph*

Department of Internal Medicine, Aster DM Healthcare, Dubai, UAE

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***Correspondence:**
Dr. Jimmy Joseph,
E-mail: jimjosephjim@gmail.com

ABSTRACT

This was a 23 years old, previously healthy male, who presented with status epilepticus, fever and hematuria. Peripheral blood smear showed severe hemolytic anemia and thrombocytopenia. Thrombotic thrombocytopenic purpura (TTP) was suspected and treatment initiated with therapeutic plasma exchange and corticosteroids following which patient showed minimal improvement. Subsequently, blood reports showed critically low ADAM TS 13 activity, which confirmed the diagnosis of TTP. Plasmapheresis was continued along with methyl prednisolone and Rituximab, following which patient showed considerable clinical improvement.

Keywords: Hemolytic anemia, Thrombocytopenia, Fever, Hematuria, Plasma exchange

INTRODUCTION

Thrombotic thrombocytopenic purpura is a thrombotic microangiopathy characterized by Microangiopathic Hemolytic Anemia (MAHA) with moderate or severe thrombocytopenia.[1] The classic pentad described in TTP includes thrombocytopenia, microangiopathic hemolytic anemia, neurologic abnormalities, renal dysfunction and fever. TTP maybe congenital due to ADAM TS 13 gene mutation or acquired, which is associated with anti-ADAM TS 13 antibodies.

TTP is distinguished from other thrombotic microangiopathies by deficiency of ADAM TS 13 (A Disintegrin and Metalloproteinase with Thrombospondin Type 1 motif, member 13), a plasma protein that cleaves von Willibrand factor multimers.[2] Peripheral blood smears are usually diagnostic showing signs of intravascular hemolysis like fragmented erythrocytes (schistocytes), nucleated red blood cells and polychromatic red cells.[3] TTP is a rare hematologic emergency with estimated incidence of 2 per million per year.[4] Early diagnosis and treatment is necessary as it has a reported high mortality rate of 90% in untreated cases.[5]

CASE REPORT

A 23 years old male presented with complaints of fever and continued seizures. He was intubated to protect the airway. Overt bleeding was noted from oral cavity during intubation and from puncture sites along with hematuria on urinary catheterization. Two weeks prior to this there was history of fever and diarrhea for which he was treated in outside clinic with ciprofloxacin and loperamide. No past history of seizures.

Investigations

Initial complete blood count showed anemia with hemoglobin of 5.4 g/dl and thrombocytopenia of 12,000/mcl. Peripheral blood smear showed severe hemolytic anemia with anisochromia and schistocytes. Hemolysis studies were positive. Summary of laboratory data and imaging are shown in Table 1.

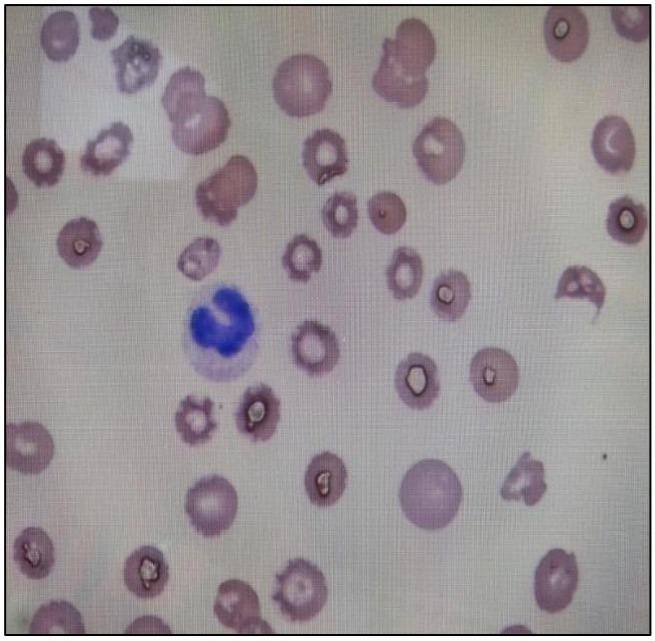

Figure 1: Initial peripheral smear with schistocytes and anisochromia.

Differential diagnosis

Initially he was thought to have meningitis due to fever and seizures which was ruled out by normal CT, MRI and MRA brain. Due to hemolysis and thrombocytopenia TTP was suspected. We ruled out other differential diagnoses with similar picture like DIC (due to normal coagulation profile), disseminated malignancy (due to normal chest X-ray and ultrasound abdomen) and malignant hypertension (due to normal blood pressure). Other serology tests for anti-phospholipid antibody (APLA) and complement C3 and C4 were negative thus ruling out SLE.

Treatment and outcome

Plasmapheresis was started. He underwent eight sessions of plasmapheresis. Methyl prednisolone 1 gram i.v was given for 8 days. He was extubated on day 7. Single dose of Rituximab 500 mg i.v was given on Day 10. He responded to the treatment and after 7 sessions of plasmapheresis, his Hb improved to 7.2 g/dl, with absent fragmented RBCs on peripheral blood smear. Platelet count increased to 72,000/mcl and LDH reduced to 700 U/l.

Table 1: Laboratory investiagtions.

Patient data	
Haemoglobin	5.4 g/dl
Platelets	12,000/mcl
Peripheral smear	Peripheral smear showed schistocytes and anisochromia (Figure 1)
Hemolysis studies	↑ Total Bilirubin 2.02 mg/dl
	↑Indirect Bilirubin 1.62 mg/dl
	↑ LDH 1021 U/l (normal 35-225 U/l)
	↓Haptoglobin<0.1 g/l (normal 0.3-2 g/l)
	↑Retic count 6.8% (normal 0.5-3.5%)
Serology	Cold agglutinin positive
Renal function and urinalysis	Normal serum creatinine-1.07 mg/dl
	Normal blood urea nitrogen-34.7 mg/dl
	Urinalysis- 50-55 dysmorphic RBCs/hpf
ADAM TS 13	↓ ADAM TS 13 activity<2% (normal>66.8%)
Coagulation profile	Normal PT 15.7 secs Normal INR 1.11
	↑ aPTT 50 secs
	↓ Fibrinogen 78 mg/dl (normal 197-410 mg/dl)
Infection works up	Blood culture- no growth
CT and MRI brain	Normal
USG Abdomen	Normal

DISCUSSION

Clinical diagnosis of TTP is suspected when microangiopathic hemolytic anemia, thrombocytopenia, with or without neurologic or renal abnormalities are present and without another etiology.[6] The classic pentad of TTP (thrombocytopenia, MAHA, fever CNS involvement and renal insufficiency) is present in less than 10% of patient.[7] ADAM TS 13 Activity level of less than 10% is confirmatory but not essential for diagnosis.[8] Our patient had history of acute diarrheal illness 2 weeks prior to presentation which led us to consider hemolytic uremic syndrome. Relatively normal renal functions and decreased ADAM TS 13 activity level helped to diagnose TTP in our patient which was confirmed later by clinical improvement on treatment with plasmapheresis corticosteroids and rituximab. Daily plasma exchange regardless of ADAM TS 13 activity is recommended until

platelet counts return to normal for two successive days.[9] Use of high dose Methylprednisolone is also suggested owing to autoimmune nature of TTP.[10] The International Society on thrombosis and hemostasis (ISTH) Guidelines of 2020 recommend addition of rituximab to corticosteroids and therapeutic plasma exchange, for patients with TTP having first acute event as it appears to prevent relapses.[11] Al-Khabori et al, in a consensus report from GCC countries reported that currently in the GCC countries that they studied TTP treatment mainly consisted of plasma exchange and corticosteroids with rituximab sometimes added.[12]

The young patient responded favorably to plasma exchange, corticosteroids and rituximab. To date, his outcome is positive.

CONCLUSION

This case report aims to increase awareness among clinicians, about this rare hematologic emergency and to highlight the importance of early recognition and initiation of treatment. Prompt diagnosis and treatment of TTP poses a challenge due to overlap of clinical features of various thrombotic microangiopathies and diverse symptoms at presentation often leading to misdiagnosis.

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