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Case Report

Systemic Lupus Erythematosus

Systemic Lupus Erythematosus Presented by Thrombotic Thrombocytopenic Purpura: A Case Report

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Abstract: Thrombotic thrombocytopenic purpura (TTP) is a life-threatening haematological condition which can be secondary to many disorders. Systemic lupus erythematosus (SLE) can present with thrombotic microangiopathy and the differentiation between them is quite difficult especially in people with no previous history of SLE. Thrombocytopenia and microangiopathic haemolytic anaemia (MAHA) characterized by schistocytes on the peripheral blood smear are the most consistent signs of TTP. Plasma exchange, the main treatment for TTP must be started urgently once the TTP diagnosis is established. We report a case of 20-year-old female with no previous medical problems, who was presented with severe illness and dizziness following tooth extraction and was found to have severe microangiopathic haemolytic anaemia, her platelet count was severely decreased and with subsequent diagnosis as TTP and plasma exchange and steroids were started and fulfilled the European League Against Rheumatism and the American College of Rheumatology 2019 (EULAR/ACR-2019) criteria for SLE. The patient showed satisfactory improvement. This study of case report was made for early diagnosis and immediate treatment of unusual presentation of SLE resulted in a good prognosis.

Keywords: Thrombotic thrombocytopenic purpura, systemic lupus erythematosus, microangiopathic haemolytic anaemia, plasma exchange, autoimmune disease, plasmic score.

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1. INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) is well established as a rare and severe form of thrombotic microangiopathy (TMA) with high mortality rate in spite of appropriate therapeutic management [1], in which ADAMTS13, the Von Willebrand Factor cleaving protease is severely deficient, characterised by microangiopathic haemolytic anaemia (MAHA), marked thrombocytopenia and organ ischemia due to disseminated micro vascular platelet rich-thrombi [2]. Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease that affects many organs in the body, including the hematopoietic system. SLE can present with TMA and differentiation between the two diseases can be quiet difficult, especially in those with no previous history of SLE. TTP may occur before or after the diagnosis of SLE but in a rare case; both can be present concurrently[3] We reported this interesting and challenging case with a rare presentation that should be kept in mind.

2. CASE REPORT

A 20-year-old Saudi female with no history of any chronic medical illness came with a history of gum bleeding after tooth extraction, menorrhagia, and dizziness. She denied any other drug history. The patient had no history of fever, cough, shortness of breath, change in the level of consciousness. There was no history of bleeding from any orifices. The patient had not experienced a similar illness before. She denied a history of autoimmune diseases within her family. Her surgical, family, and social histories were unremarkable.

2.1 Past history

Had no similar complaints as now.

2.2 Family history

No significant illness nor autoimmune diseases.

2.3 Personal history

Normal mixed diet, No smoking and alcohol.

2.4 Physical examination

The patient was stable and not in acute distress. Her vital signs, including orthostatic, were normal. Pallor and pale conjunctivae were found but not jaundiced.

2.5 On examination

The chest was clear with equal air entry and no added sounds. An abdominal examination revealed no tenderness, lax and no hepatosplenomegaly when palpated. There were bruising and purpuric eruptions on the abdominal wall and the lower extremities and the back. A neurological examination was normal. There was no evidence of active oral, nasal or rectal bleeding.

2.6 Lab investigations

Initial complete blood count showed white blood cells (WBCs) of 14.5×10^3 /µL (normal range, $4.5–11\times10^3$ /µL), profound anaemia, haemoglobin of 65 g/L (normal range, 130–170g/L) and a very low platelet of 3×10^9 /L (normal range, $150–410\times10^9$ /L). Schistocytes of 8 % were found on a peripheral blood smear (Figure 1). The workup for haemolysis was positive. Therefore, the patient was confirmed with thrombotic TTP due to thrombocytopenia, microangiopathic haemolytic anaemia and schistocytes in the peripheral blood film, negative direct coombs test. The PLASMIC score was 7, which meant that the patient had a high risk of severe ADAMTS13 deficiency. A summary of the laboratory data and imaging: (Table 1)

2.7 CBC

↓Haemoglobin, 6.5 g/dL (normal range, 13–17 g/dL) Normal MCV, 90.0 fL (normal range, 83–100 fL) ↑ RDW, 17.3% (normal range, 11%–14%) ↓ Platelet, 3×10^3 /µL (normal range, $150–410\times10^3$ /µL) ↑ WBC, 14 600×10^3 /µL (normal range, $4.5–11\times10^3$ /µL)

2.8 Haemolysis workup

↑ Total bilirubin, 45.0 µmol/L (normal range, 0–20 µmol/L) ↑ Indirect bilirubin, 25.3 µmol/L (normal range, 0–8.6 µmol/L) ↑ LDH, 850 U/L (normal range, 125–220U/L) Haptoglobin (not available), ↑ absolute reticulocyte count, 8.5% (normal range, 0.3%–1.5%), Negative direct Coombs test

2.9 Renal function and urinalysis

Normal: BUN, 6.7mmol/L (normal range, 2.5–7.5mmol/L) Normal creatinine, 80 µmol/L (normal range, 50–110 µmol/L), Normal dipstick: +++ blood (menstruating)

3. SPECIAL INVESTIGATIONS:

3.1 Serology

CRP: negative, ESR, 2mm/1st hour (normal range, 0–10mm/1st hour), positive ANA 1/320 (fluorescence pattern Speckled) and anti-dsDNA: positive, anticardiolipin, β–2 glycoprotein I antibody and lupus anticoagulant: Negative, ANCA screening: Negative, anti-Smith: Normal, C3: normal and C4: low, rheumatoid factor and anti-CCP: normal, Negative thyroglobulin antibody.

3.2 ADAMTS 13

Not available

3.3 Coagulation

Normal PT, INR, PTT and fibrinogen level, ↑ D-dimer 1.8 µg/mL (normal range, < 0.5 ug/ml)

3.4 Infection workup

↑ Ferritin: 560 ng/mL (normal range, 18–270 ng/mL) Negative blood culture, urine culture, anti-HIV, anti-HBV and anti-HCV

3.5 Malignancy workup

Normal range of B-HCG, CEA, CA 19-9

3.6 Imaging

Chest X-ray: normal, CT of the chest, abdomen and pelvis: normal, for chest, normal lungs and no PE, CT of the brain: normal study and no evidence of bleeding or ischaemia, normal echocardiography.

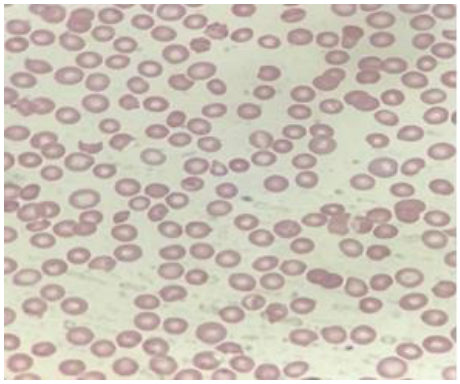

Fig 1: Peripheral blood smear showed 8 % schistocytes

The above mentioned figure 1 shows that the patient got 8% schistocytes in the investigation of peripheral blood smear. A haematological emergency that requires prompt review and investigation for thrombotic microangiopathy (TMA).

Table 1: Lab Investigations

TEST	Result	REFRENCE RANGE
HGB	6.5 g/dL	13-17 g/dL
MCV	90 fL	83-100 fL
RDW	17.3%	11-14%
Platelets	3×10^3	$150–410\times10^3$
WBC	$14\ 600\times10^3$	$4.5–11\times10^3$ /µL
Total Bilirubin	45.0 µmol	0–20 µmol/L
Indirect bilirubin	25.3 µmol/L	0–8.6 µmol/L
LDH	850 U/L	125–220U
Haptoglobin	NA	NA
Absolute reticulocyte count	8.5%	0.3%–1.5%
Direct Coombs test	Negative	
BUN	6.7mmol/L	2.5–7.5mmol/L
Creatinine	80 µmol/L	50–110 µmol/L
dipstick	+++ Blood (menstruating)	
CRP	Negative	
ESR	2mm/1st hour	0–10mm/1st hour
ANA	1/320 (fluorescence pattern Speckled)	
Anti-dsDNA	Positive	
Anticardiolipin	Negative	
β–2 glycoprotein I antibody	Negative	
Lupus anticoagulant	Negative	
ANCA screening	Negative	
Anti-Smith	Normal	
C3	Normal	
C4	Low	
Rheumatoid factor and Anti-CCP	Normal	
Thyroglobulin antibody	Negative	
ADAMTS 13	NA	
PT, INR, PTT	Normal	
Fibrinogen level	Normal	
D-dimer	1.8 µg/mL	< 0.5 ug/ml
Ferritin	560 ng/mL	18–270 ng/mL
blood culture	Negative	
Urine culture, anti-HIV,	Negative	
Anti-HBV and anti-HCV	Negative	

ANA, antinuclear antibodies; ANCA, antineutrophil cytoplasmic antibodies; C complement; B-HCG, beta human chorionic gonadotropin; BUN, blood urea nitrogen; CA 19-9, cancer antigen 19- 9; CBC, complete blood count; CCP, cyclic citrullinated peptide; CEA, carcinoembryonic antigen; CRP, C reactive protein; dsDNA, double-stranded DNA; ESR, erythrocyte sedimentation rate; HBV, hepatitis B virus; HCV, hepatitis C virus; INR, international normalised ratio; LDH, lactate dehydrogenase; MCV, mean corpuscular volume; PT, prothrombin time; PTT, partial thromboplastin time; RDW, red cell distribution width; WBC, white blood cell.

4. DIAGNOSIS

Thrombotic thrombocytopenic purpura (TTP) secondary to SLE.

5. PROGNOSIS

The early diagnosis of Thrombotic thrombocytopenic purpura and immediate treatment resulted in a good prognosis as it is a haematological emergency.

6. TREATMENT PLAN

A central venous catheter was inserted, and plasma exchange with fresh frozen plasma started immediately at the emergency department level, combined with a first dose of methylprednisolone (1000 mg daily for 3 days) followed by oral steroids 1mg/kg /d. The patient was admitted to the intensive care unit, and management continued there. Next day, there is improvement was noticed in lactate dehydrogenase (LDH) and platelet count. ANA, anti-DNA antibodies and other autoimmune markers were ordered, and plasma exchange was continued together with the oral prednisone 40 mg/day. ANA was positive 1/320, anti-DNA was positive, low C4 so the patient fulfilled European League Against Rheumatism and the American College of Rheumatology 2019 (EULAR/ACR-2019) criteria for SLE. Here, our patient was diagnosed as SLE and TTP like syndrome., after seven sessions she was markedly improved, her platelet count became 180 $\times 10^9$, Hb 9 gm%. LDH 290 u/L shifted to the ward and followed by daily CBC, LDH, blood smear. Unfortunately, the patient developed right lower limb swelling, hotness and tense calf muscles on the same side of femoral catheter. Doppler ultrasound done and revealed acute deep vein thrombosis. Anticoagulants was started and the femoral catheter removed, jugular catheter inserted. Plasma exchange was gradually discontinued. There was a total of 13 sessions of plasma exchange conducted with prednisolone (40 mg for 2 weeks tapered to 10 mg every week). Normalisation of the platelets was reached 252×10^9 and LDH. Rheumatology consultation was done and recommended to continue the management. The patient refused rituximab therapy and she preferred to postpone it and was then discharged home as she had improved with follow up with rheumatology.

7. DISCUSSION

TTP is one of the thrombotic microangiopathies (TMA), considered haematological emergencies. Although TTP and SLE are different diseases, they may present as overlapping for each other [4]. There are many several disorders and diseases associated with Thrombotic Microangiopathies. There are many hypotheses being found to explain this association include abnormal endothelial activation, elevated levels of D-dimers, ADAMTS13-resistant von Willebrand Factor and defects in the complement system regulation [5]. TTP is a life threatening disease with haematological condition which must be diagnosed earlier and treated. SLE can be presented with symptoms resembling those of TTP making the differentiation very difficult, especially since our patient didn't have any history or symptoms suggesting lupus before [3]. We suspect TTP in our patient even before completing the classical pentad of TTP, as this historical pentad of fever, thrombocytopenia, microangiopathic haemolytic anaemia (MAHA), neurological symptoms, and renal abnormalities which used for TTP diagnosis becomes obsolete because less than 10% of patients with an acute TTP are presented with these 5 symptoms. Only severe thrombocytopenia and MAHA characterised by schistocytes on the blood smear are the most consistent signs of TTP [6,7] Although our patient had no previous history of SLE and we did not measure a reduction in ADAMTS13 activity as it is not available in our hospital, we depend on clinical data which meet with features of TTP, she also fulfils the 2019 EULAR/ACR criteria for SLE such as high titre of ANA, Anti-DNAs, haematological findings and low C4, neurological symptoms in form of headache and psychosis which make the diagnosis of SLE as it was presented by TTP. The management of these critical conditions of patients is made according to the treatment guidelines. The patient treatment plan has been made according to standard treatment guidelines by improving the CBC levels and by adding steroids and other suitable drugs[8]. This case shows the satisfactory recovery for TTP. SLE presenting as TTP is rare and the purpose of this case study is emphasizing the importance of looking out for the association, early diagnosis and aggressive management with plasma exchange and immunosuppression which is life-saving to ensure better outcomes.

8. ETHICAL APPROVAL STATEMENT

We got the required permission from the institution and the respected person for the conduction of a case report study. The work has received the approval of the Research Ethics Committee of Qassim. The informed consent form was received from the patient regarding the collection of data and enquiry to the participant as well as her parents for the conduction and publishing of the report.

9. AUTHORS CONTRIBUTION STATEMENT

Samah A. Elshweikh conceptualized the study. Samah A. Elshweikh, Abdurahman Aldubaikhi, Sultan Albaybi, Rayan Alsedrani designed the study. Abdurahman Aldubaikhi, Sultan Albaybi, Rayan Alsedrani collected the data. All the authors involved in analyzing the data and Asayel Alqahtani provided the statistical inputs Abdurahman Aldubaikhi, Sultan Albaybi, Rayan Alsedrani prepared the draft manuscript and Samah A. Elshweikh and Asayel Alqahtani provided the inputs and finalized the manuscript. All the authors read and approve the final version of the manuscript.

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11. CONFLICTS OF INTEREST

Conflicts of interest declared none.

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