Received: 7 January 2021 | Revised: 22 March 2021 | Accepted: 7 May 2021

DOI: 10.1002/ccr3.4364

CASE REPORT

Clinical Case Reports Open Access WILEY

Endocarditis-induced thrombotic thrombocytopenic purpura mimicking preeclampsia: A case report

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Abstract

TTP, Preeclampsia have similar manifestations in pregnancy. Establishing the right diagnosis is essential as the treatment is different. Endocarditis-induced TTP should be suspected when neurological symptoms, thrombocytopenia are present.

KEYWORDS

case report, infection, preeclampsia, pregnancy, thrombotic thrombocytopenic purpura

1 | BACKGROUND

Infective endocarditis is a serious disease, and it might trigger thrombotic thrombocytopenic purpura in some patients. Pregnant women are susceptible to several microangiopathies that might share some clinical presentations. Thrombotic thrombocytopenic purpura and preeclampsia are of special interest as these entities have different treatments, thus establishing the right diagnosis is essential. We present a case of a 29-year-old pregnant woman with left hemiparesis and fever who was diagnosed with preeclampsia. Although the pregnancy was terminated, the patient did not recover, which suggested misdiagnosis and led to further investigations. Low ADAM-TS13 level led to the diagnosis of thrombotic thrombocytopenic purpura. However, due to various failed attempts of treatment, and subsequent investigations, it was clear that thrombotic thrombocytopenic purpura was induced by an infective endocarditis. Then, the patient underwent surgery, treated with antibiotics, and fully recovered. Infective endocarditis imitated two different microangiopathic hemolytic anemia in this patient, which highlights the importance of considering infective endocarditis in such cases.

Thrombotic thrombocytopenic purpura (TTP) is an autoimmune disease that occurs due to the formation of antibodies against a disintegrin and metalloprotease with thrombospondin type 1 motif, member 13 (ADAM-TS13) which is a protease that binds to and cleaves von Willebrand

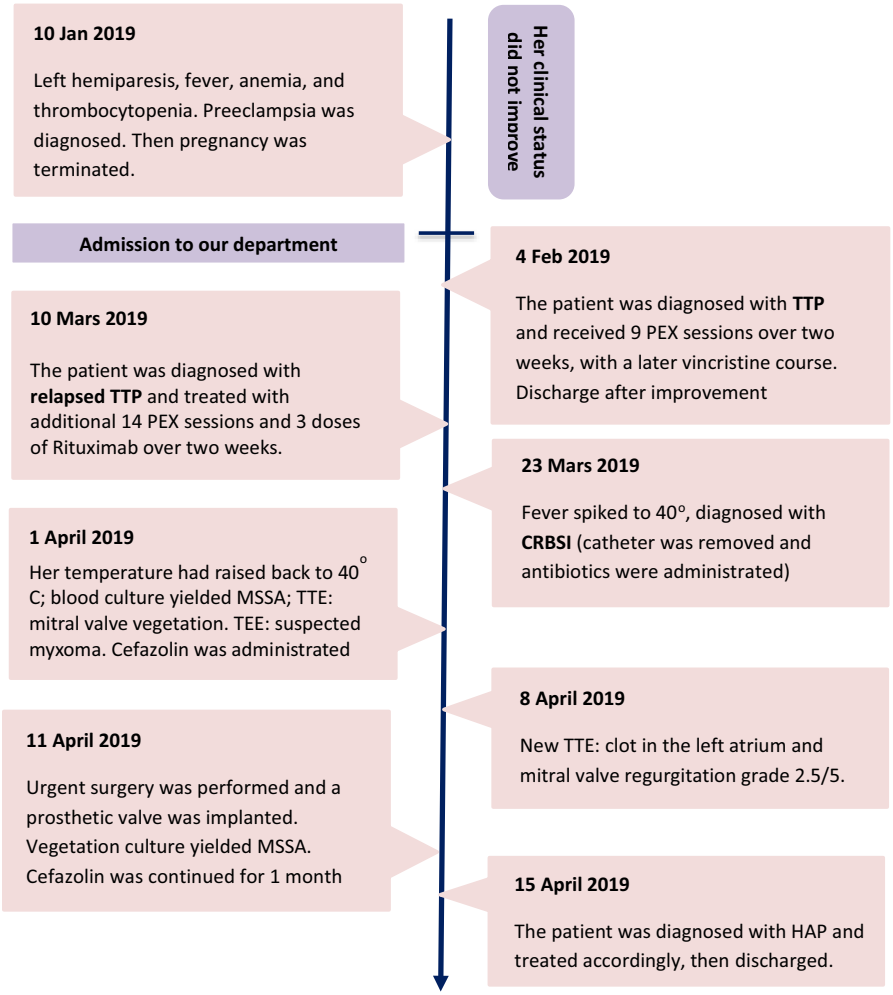

FIGURE 1 Timeline of the patient's case, diagnostic process, intervention, and outcome. TTP: Thrombotic thrombocytopenic purpura, PEX: Plasma exchange, CRBSI: Catheter-related bloodstream infection, MSSA: Methicillin-sensitive Staphylococcus. Aureus, TTE: Transthoracic echocardiography, TEE: Transesophageal echocardiography, HAP: Hospital-acquired pneumonia

factor (vWF).[1,2] When vWF gets exposed to shear stress effect in blood vessels, it undergoes a conformational change and increases its adhesive activity which makes vWF susceptible to ADAM-TS13, especially high molecular weight (HMW) vWF polymer, and then vWF converts to a series of multimers. Smaller particles of vWF have less ability to bind to platelets and less efficiency to enhance thrombosis. But in ADAM-TS13 deficiency, vWF conformational changes happen without the subsequent cleavage by ADAM-TS13, and this results in vWF-platelet aggregations and eventually TTP.[2] One of the known triggers of TTP is infective endocarditis, even though the pathogenesis of very severe thrombocytopenia when it accompanies bacterial endocarditis is still uncertain.[3] TTP is characterized by hemolytic anemia and thrombotic microangiopathies with low platelets count, which makes it challenging to distinguish it from preeclampsia.[1,4] One of the predominant manifestations of microangiopathy is cerebrovascular disease which may cause stroke in 11-34 per 100 000 deliveries. Etiologies of stroke during pregnancy include preeclampsia, HELLP syndrome, TTP, Hemolytic-uremic syndrome (HUS), infective emboli due to infective endocarditis, and central nervous system (CNS) infections.[1,4] Here, we present a challenging case of a pregnant woman with endocarditis-induced TTP that mimicked preeclampsia at presentation.

2 | CASE PRESENTATION

A 29-year-old pregnant woman in her 17th week of gestation with no previous pregnancies, developed left hemiparesis, fever, and dizziness. She was referred to a maternity hospital where her laboratory tests results were as follows: white blood cell (WBC) count 13.5×10^3 µL, red blood cells (RBC) 3.5×10^6 µL, hemoglobin (HB) 8.5 mg/dL, platelets (PLT) 60×10^3 mm^3, lactate dehydrogenase (LDH) 921 IU/L, alanine aminotransferase (ALT) 48 IU/L, and partial thromboplastin time (PTT) 67.5 seconds. Aspartate aminotransferase (AST), international normalized ratio (INR), and reticulocytes were within normal limits. Brain magnetic resonance imaging (MRI) showed multiple cortical infarctions in the right hemisphere, and she was diagnosed with preeclampsia. The medical decision then was to end the pregnancy. After the pregnancy was terminated, no improvement was recorded in her condition. Therefore, she was referred to our hospital (Figure 1).

On arrival, vital signs were within normal limits except for a heart rate (HR) of 100 beats/minute and a temperature of 40°C. Physical examination revealed pale conjunctiva, disseminated bruises on arms, and diffuse purpura. Neurological examination showed that the patient was cognitive and oriented to time, place, and people, with left extremities weakness (strength 3/5) and normal strength (5/5) on the right side. Muscle tone was within normal limits with normal plantar reflexes. Electrocardiography (ECG) and chest X-ray (CXR) were within normal limits. Peripheral blood smear showed few tear-drop cells and low PLT count 30-40 $\times 10^3$ mm^3. Based on the laboratory and blood smear findings, ADAM-TS13 activity was tested and the result revealed a low activity: 2.5% (normal range: 40%-130%). Transthoracic echocardiography was performed to detect the cerebral emboli source, and it showed mild mitral regurgitation with mild prolapse and moderate degenerative myxomatous changes. The leaflet was 8-mm thick, and a patent foramen oval (PFO) was noticed. Carotid arteries Doppler echography was unremarkable.

Based on the clinical features and investigation, the patient was diagnosed with TTP and was treated with nine sessions of plasma exchange (PEX) over 2 weeks with clinical and laboratorial improvement. Her left extremities strength after the last PEX session was 4/5. Laboratory tests improved except for LDH 701 IU/L and C-reactive protein (CRP) 7.4 mg/L, so the decision was made to start a vincristine course (2 mg/weak).

Three weeks later, the patient developed jaundice and generalized fatigue, laboratory tests were as follows: WBC count 12.8 $\times 10^3$ µL, PLT 34 $\times 10^3$ mm^3, and LDH 1700 IU/L. Blood smear showed anisopoikilocytosis, polymorphic, hyperchromic RBCs, schistocytes 6-8/field, 6 reticulocytes per high power field, few target cells, spherocytes, late erythroblasts, and low PLT count 30-40 $\times 10^3$ mm^3 (Figure 2). The patient was diagnosed with relapsed TTP, and additional 14 PEX sessions were started with rituximab for a 3-week dose. The patient's fever did not abate but spiked to 40°C, then she was diagnosed with intravascular catheter-related bloodstream infection. Empiric treatment with vancomycin and meropenem was initiated for 6 days without obtaining blood culture samples, due to unavailability of culture materials at the time of sampling, and her clinical status has slightly improved after removing the catheter. However, after the 6-day antibiotics course, her clinical condition had deteriorated, her temperature had raised back to 40°C, and the left hemiparesis had worsened. Laboratory tests showed WBC 47.4 $\times 10^3$ µL and PLT 39 $\times 10^3$ mm^3. Blood cultures yielded methicillin-sensitive *Staphylococcus aureus* (MSSA). Transthoracic echocardiography showed a 0.9 × 1.7 cm vegetation on the anterior mitral leaflet and PFO. Transesophageal echocardiography revealed a suspected myxoma in the left atrium. The treatment was adjusted to intravenous (IV) cefazolin 2 grams (g) every 8 hours daily for 1 week. Transthoracic echocardiography after 1 week to assess the efficacy of treatment showed a hypoechoic nonfixed mass that suggests a newly formed clot in the left atrium, and mitral valve regurgitation grade 2.5/5. Urgent surgery was performed in which a large vegetation was seen on the left posterior commissure that extended to the anterior mitral leaflet (1.5 × 1.2) cm, with another small vegetation measuring about 4 mm on the posterior leaflet's ring. The vegetations were removed, and the mitral valve was replaced with a prosthetic mechanical valve. Vegetation cultures also revealed MSSA, and the pathology test was consistent with valvulitis. After the surgery, IV cefazolin was continued.

During treatment with cefazolin, the patient developed hospital-acquired pneumonia (HAP) followed by septic shock and was treated empirically with colistin and meropenem for 1 week with clinical and laboratorial improvement. ADAM-TS13 activity at this time point was 2.5%. Cefazolin was continued for 1 month after surgery with clinical and laboratorial improvement. After 16 months of follow-up, the patient is still under regular visits and she is now pregnant with no recurrent complaints.

3 | DISCUSSION

Thrombotic thrombocytopenic purpura can either be congenital or acquired, both characterized by severe deficiency in ADAM-TS13.[5] While congenital TTP is caused by an inherited deficiency of ADAM-TS13, the acquired TTP is due to autoantibodies directed against ADAM-TS13.[5] One study

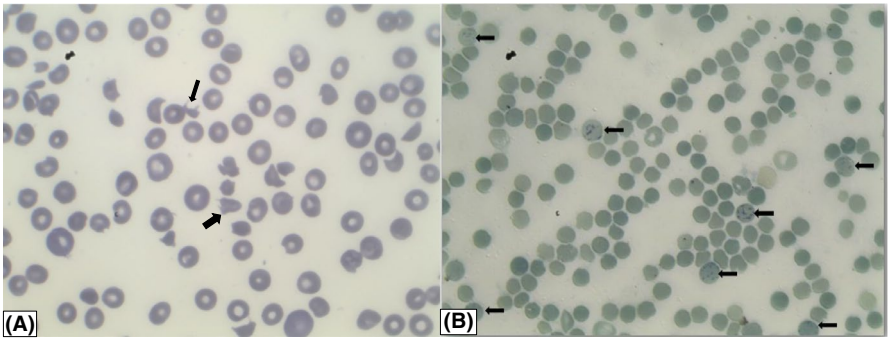

FIGURE 2 A, Peripheral blood smear showing anisopoikilocytosis, polymorphic, hyperchromic red blood cells, schistocytes (black arrows), and low platelets count. B, Peripheral blood smear showing reticulocytes (black arrows)

has showed that infections were the most prevalent cause (27%) while pregnancy triggered TTP in 4% of women.[6] About 10 to 25% of TTP patients are either pregnant women, especially during the second and third trimesters, or in their postpartum period.[7] Our patient was pregnant and had latent infective endocarditis; two of the main triggers of TTP.

The challenge in managing TTP in pregnant women is to achieve the correct diagnosis, as it can be simply overlooked because pregnant women are more exposed to many medical conditions that clinically manifest by signs of other microangiopathies.[7] It is very important to distinguish between TTP and other pregnancy-related microangiopathies as their treatments are different.[7]

Notably, our patient presented initially with thrombocytopenia and neurologic abnormalities associated with severe deficiency of ADAM-TS13 without any evidence of microangiopathic hemolytic anemia (MAHA) such as elevated bilirubin or presence of schistocytes in blood film or reticulocytosis. Later on, the patient developed typical clinical features of TTP. This unusual clinical scenario is rare in TTP syndrome but still possible.[8]

The most important diagnostic test that led us to the diagnosis and treatment was ADAM-TS13 activity.[7] PEX sessions were started, as plasma exchange is the key treatment, then followed by vincristine, which is a supplementary therapy. The PEX sessions were repeated due to incomplete response to the initial treatment, and rituximab was added as it is currently the drug of choice in refractory disease.[5] Partial recovery with persistence of the infectious state made it essential to look for another underlying cause, which was discovered to be the valvular vegetation and infective endocarditis diagnosis in accordance with the modified Duke criteria.[1] Valvular dysfunction and cerebral infarctions due to emboli were indications for surgical intervention followed by antimicrobial treatment.

In our patient, endocarditis and vegetation were not detected on presentation, though we cannot exclude their presence and attribute to all the TTP manifestations, especially without being able to test ADAM-TS13 inhibitor due to limited resources in Syrian health centers. Moreover, ADAM-TS13 activity <10% has been reported in several previous case reports of patients that may have acute and severe neurologic abnormalities before MAHA and thrombocytopenia were reported as a result of bacterial endocarditis.[8,9] A last argument is the presence of MSSA which is more probably to be community acquired, an aspect that may suggest the presence of underlying endocarditis.

4 | CONCLUSION

Thrombotic thrombocytopenic purpura and preeclampsia might have similar manifestations in pregnant women. Establishing the right diagnosis is essential as the treatment is different. Endocarditis-induced TTP should be suspected in the presence of neurological manifestations and thrombocytopenia. Moreover, repeating cardiac echocardiography should be considered in light of high clinical suspicion, and all efforts have to be made in order to exclude infectious context in unexplained recurrent TTP.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

All authors: contributed to the design of this manuscript. AI, MK, and OAA: wrote the first draft. TA, LA, and AA: wrote the final manuscript. RA and AS: scientifically reviewed the manuscript.

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor in Chief of this journal.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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How to cite this article: Issa A, Kouli M, Awwameh R, et al. Endocarditis-induced thrombotic thrombocytopenic purpura mimicking preeclampsia: A case report. *Clin Case Rep*. 2021;9:e04364. https://doi.org/10.1002/ccr3.4364