Vascular micro-thrombotic disease in pregnancy

Sir,

Vascular micro-thrombotic disease (VMTD) includes conditions like thrombotic thrombocytopenic purpura (TTP) and TTP-like syndrome and is associated with adverse outcomes if not promptly diagnosed and treated. Challenges in diagnosing TTP-like syndrome stem from a vague presentation and overlapping features with conditions like pre-eclampsia, HELLP and disseminated intravascular coagulation (DIC). We discuss a case of a pre-eclamptic patient with thrombocytopenia in the postnatal period.

A 39 weeks pregnant patient with controlled pre-eclampsia was admitted for labour. Assisted foetal delivery resulted in third-degree perineal tear which was promptly repaired. Placenta was delivered intact. Slow bleeding continued post-delivery despite uterotonics and a firm fundus. Haemoglobin dropped to 6.6 g/dL and platelets to 101 $\times$ 10^9/L. Coagulation studies showed prolonged prothrombin time (PT), partial thromboplastin time (PTT) and fibrinogen dropped from 200 to 92 mg/dL.

Thromboelastography showed no fibrinolysis. Hepatic function panel was normal. Packed red blood cells, fresh frozen plasma and platelets were given. Blood loss continued, prompting emergent dilatation, curettage and Bakri balloon insertion. Persisting bleeding prompted bilateral uterine artery embolisation. Bleeding was controlled and haematocrit stabilised. The next day, platelets dropped from 58 to 31 $\times$ 10^9/L without active bleeding. Patient remained afebrile and haemodynamically stable. Peripheral blood smear showed few schistocytes. LDH measured >3000 IU/L while fibrinogen and fibrin degradation product levels were normal. Platelets reached a nadir of 13 $\times$ 10^9/L.

Immediate plasmapheresis and steroid yielded improved platelet counts.

Von-Willebrand factor cleaving protease: A disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13 (ADAMTS13) level, and antibodies were normal. Plasmapheresis with steroids was continued till the platelets reached a goal of $>100 \times 10^9$/L.

VMTD is an emerging category of microvascular and macrovascular systemic thrombotic diseases. It includes TTP, TTP-like syndrome, haemolytic uremic syndrome (HUS) as well as other conditions like DIC. TTP/HUS is a diffuse intravascular microthrombotic (DIT) condition exhibiting thrombocytopenia and microangiopathic haemolytic anaemia (MAHA) due to ADAMTS13 protease deficiency. This can arise from congenital deficiency or from acquired antibody formation against ADAMTS13. The kidneys and the brain are the most commonly affected organs.[1]

Pregnancy can be associated with several thrombotic microangiopathies like HELLP, Acute Fatty Liver of Pregnancy (AFLP), DIC, pre-eclampsia and HUS with similar haematomorphology and overlapping features making diagnosis difficult.[2,3]

Endotheliopathy associated with insults like trauma, surgery or infection leads to inflammation and diffuse microthrombotic pathway activation. Platelet activation leads to exocytosis of endothelial ultra-large Von Willebrand Factor (eULVWF) release and formation of microthrombi.[1]

In TTP, the ULVWF are released into circulation affecting kidneys and brain.[1] In TTP-like syndrome, ULVWF are endothelium synthesised (eULVWF) which stay attached to the endothelial cells and, hence, can affect a variety of organs. TTP-like syndrome has the same haematologic manifestations of DIT, MAHA and thrombocytopenia but with minimal haemolysis and, hence, scant schistocytes on peripheral blood smear making it easy to miss the diagnosis.[1]

Plasmic score is a simple, validated clinical scoring system that assists in early diagnosis of TTP; however, it may not diagnose TTP-like syndrome where renal involvement is not always observed, and aetiology is multifactorial.[4]

The atypical presentation and the lack of involvement of typical organs alongside scant schistocytes may cause the diagnosis to be missed and delay treatment.[5]

While plasmapheresis is effective in TTP, in TTP-like syndrome, only early plasmapheresis is effective.[6] Considering the urgency of plasmapheresis initiation in TTP-like syndrome, the diagnosis may rely heavily on the clinical picture and a high index of suspicion. While TTP diagnosis is well known and scored, TTP-like syndrome is a condition with varied risk factors and subtle presentation with poor outcomes. Unlike other conditions, haematopathology may not be reliable for diagnosis and a low threshold for clinical diagnosis is mandated.

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Conflicts of interest
There are no conflicts of interest.

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