

## Case Report

# The PLASMIC Score May Be Useful in the Early Diagnosis of Complement-Mediated Thrombotic Microangiopathy via Early Exclusion of Thrombotic Thrombocytopenic Purpura

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Complement-mediated thrombotic microangiopathy is a rare form of thrombotic microangiopathy but has high rates of mortality and morbidity. Effective treatment exists with eculizumab for this condition, but administration of treatment is often delayed because of overlapping symptoms with other causes of thrombotic microangiopathy. We present a case of a 78-year-old male who was eventually diagnosed with complement-mediated thrombotic microangiopathy. We also discuss the use of the PLASMIC scoring model to assist in more rapid diagnosis and discernment between various thrombotic microangiopathies.

## 1. Introduction

Thrombotic microangiopathy (TMA) represents a process where vascular injury in small vessels causes microthrombi to form with subsequent thrombocytopenia, microangiopathic hemolytic anemia (MAHA), and end-organ injury. TMAs are classically divided into two categories: thrombotic thrombocytopenic purpura (TTP) for ADAMTS13 deficiency-mediated TMA and hemolytic uremic syndrome (HUS) for Shiga-toxin-mediated TMAs [1]. Complement-mediated TMA (C-TMA) is the rarest form of TMA and represents a third categorization of TMAs. C-TMA is a disorder where uncontrolled complement activation causes subsequent platelet activation, microvascular endothelial injury, and widespread microthrombotic disease [2]. Without proper treatment, up to 50% of cases progress to end-stage renal disease or irreversible brain damage and 25% may die from the acute phase of the disease [3]. In addition, those that survive the acute phase often require dialysis and are hospitalized more than twice as long compared to those with typical HUS [4]. With the advent of an extremely effective treatment with eculizumab [5], early differentiation from TTP/HUS and treatment is vital in minimizing the morbidity and mortality of the disease. The PLASMIC score is a recently

developed algorithm that has been shown to demonstrate efficacy in identifying patients presenting with TTP based on rapidly obtainable labs (Table 1) [6–8]. This report will review the approach to someone with a suspected TMA and highlight the use of the PLASMIC score in distinguishing between TTP and HUS/C-TMA to allow for more rapid treatment of C-TMA.

## 2. Case Discussion

A 78-year-old male with a history of chronic kidney disease stage 2, systolic heart failure with a biventricular implantable cardioverter-defibrillator in place, coronary artery disease status after a 5-vessel coronary bypass graft, and chronic obstructive pulmonary disease presented to an outside hospital with cough and fever. He had been seen by his primary care physician six days prior to admission to an outside hospital and treated for a bacterial upper respiratory infection with trimethoprim-sulfamethoxazole but continued to have worsening lower extremity swelling and fevers to 103°F. He had no recent travel, sick contacts, or preceding diarrheal illness. During his admission at the outside hospital, further workup was notable for a lactate dehydrogenase

TABLE 1: PLASMIC scoring system.

Variables	Points
Platelet count $<30 \times 10^9/L$	1
Hemolysis present*	1
No active cancer	1
No history of solid organ or stem cell transplant	1
MCV $<90$	1
INR $<1.5$	1
Creatinine $<2.0$ mg/dL	1

INR: international normalized ratio; MCV: mean corpuscular volume.  
 \*Reticulocyte count  $>2.5\%$  or haptoglobin undetectable or indirect bilirubin  $>2.0$  mg/dL.

level of 6500, total bilirubin 4.0 (unconjugated), platelet count  $27K/\mu L$ , fibrinogen 193, international normalized ratio 1.4, and mean corpuscular volume 103.6—all of which raised concern for hemolysis with a total PLASMIC score of 4. A peripheral blood smear demonstrated schistocytes, and his creatinine rose to 3.0 from a baseline of 1.0 despite adequate urine output. He was then transferred to our institution on hospital day 3 for initiation of plasma exchange therapy for suspected TTP. The patient's ADAMTS13 level, which was collected at the previous hospital, returned at 47% on his fifth day of hospitalization; this was inconsistent with TTP. Thus, plasma exchange therapy was never initiated. Workup for systemic lupus erythematosus, cobalamin C deficiency-mediated TMA, heparin-induced thrombocytopenia, drug-induced TMA, autoimmune hemolytic anemia, disseminated intravascular coagulation (DIC), typical HUS, HIV, and malignancy returned negative. His condition continued to deteriorate, with creatinine peaking at 7.4 and continued decrease in hemoglobin and platelet counts, requiring multiple blood transfusions; he was started on eculizumab for clinical evidence of C-TMA on hospital day 6. However, within 24 hours of administration of eculizumab, he had a non-ST-elevation myocardial infarction with a troponin level of 16.78. He was urgently transferred to the intensive care unit and was subsequently intubated for worsening tachypnea and increased work of breathing. The decision was then made by his family to transition to comfort care given evidence of acute right ventricular failure complicated by profound acidosis requiring multiple pressors with minimal hope of recovery.

### 3. Discussion

The syndromes of TMAs have great overlap and can be difficult to discern in a clinical setting. TMAs should be suspected in patients presenting with signs of MAHA (elevated LDH, low haptoglobin, thrombocytopenia, and schistocytes on blood smear). Once TMA is confirmed, systemic causes such as DIC, HELLP/preeclampsia, infections, lupus, and malignancy must be ruled out. It is reasonable to begin plasma exchange therapy for empiric treatment of TTP, as TTP has the highest urgency for treatment, while undergoing workup for other causes of the TMA.

Recent research has demonstrated the efficacy of the PLASMIC scoring system in evaluation of possible TTP. When dichotomized into high risk (PLASMIC score  $>5$ ) versus low risk (PLASMIC score 0–5), the model predicted severe ADAMTS13 deficiency correlating to TTP with a positive predictive value of 72%, a negative predictive value of 96%, a sensitivity of 90%, and a specificity of 92% [8].

Once the PLASMIC score has established the patient as having a low likelihood for TTP, other etiologies of TMA outside of TTP can be considered while awaiting ADAMTS13 results. In our patient, drug-induced TMA (DITMA) was a consideration given prior exposure to antibiotics; however, DITMA is either very acute (from drug reaction, occurring over hours) or very chronic (from drug toxicity, occurring over weeks to months). TMA secondary to occult malignancy takes place over weeks to months, and Shiga-toxin HUS usually has a preceding diarrhea illness. This patient had a subacute presentation over a few days without diarrheal illness, normal fibrinogen, and a negative ANA, lowering the likelihood of DIC, drug-induced, HUS, lupus-induced, or occult malignancy-induced TMA. Next, metabolism-induced TMA can be evaluated by checking for homocysteine and methylmalonic acid, as vitamin B12 deficiency has been shown to rarely induce TMAs [9]. Our patient had normal vitamin levels. In the setting of continued worsening renal failure, C-TMA is the next consideration. If the clinical suspicion for C-TMA is high, eculizumab should be started empirically as early treatment is important for minimization of kidney damage. It is important to keep in mind that eculizumab inhibits C5, and as such vaccination and prophylaxis against meningococcal infections is crucial. In an acute setting such as C-TMA, vaccination with a quadrivalent meningococcal vaccine and a four-week course of either penicillin V (250 mg every 12 hours) or ciprofloxacin (500 mg daily) are appropriate [10].

Our patient presented with generalized malaise and shortness of breath with laboratory findings consistent with a TMA with MAHA. In this patient, eculizumab administration was delayed to pursue treatment for TTP. In addition, the slow turnaround for ADAMTS13 assays created further delays in treatment of a potential C-TMA. Given the low PLASMIC score of 4 at the outside hospital, an alternative cause of TMA should have been considered and empiric treatment with eculizumab initiated.

### 4. Conclusion

TMAs have a variety of causes, notably, TTP, Shiga-toxin HUS, and C-TMA. Rapid diagnosis of the cause is crucial; effective treatment exists and acute mortality remains high. C-TMA remains an important consideration of patients presenting with TMA and MAHA with worsening kidney function, and early administration of eculizumab has been shown to be effective. Future use of the PLASMIC model may help expedite diagnosis.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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