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Secondary Thrombotic Microangiopathy (TMA) in Systemic Lupus Erythematosus (SLE): A Case of Mistaken Identity?

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INTRODUCTION

TMAS ARE A GROUP OF DISORDERS CHARACTERISED BY:

- ✓ Microangiopathic Hemolytic Anemia (MAHA) : Evidenced by schistocytes on peripheral blood film
- ✓ Thrombocytopenia : Platelet count <150 x10^9/L or >25% drop from baseline
- ✓ ± End-organ ischemia: Due to intravascular thrombi

CLASSIFICATION AND DIFFERENTIAL DIAGNOSIS OF TMAs (Figure 1)

TMAs can be broadly classified based on ADAMTS13 activity into:

A. Thrombotic Thrombocytopenic Purpura (TTP)
B. Non-TTP Subtypes (Primary and Secondary Subtypes)

We report a case of a patient with SLE Initially treated as TTP but was later determined to have secondary TMA likely related to SLE and a Differential diagnosis included atypical HUS (aHUS)

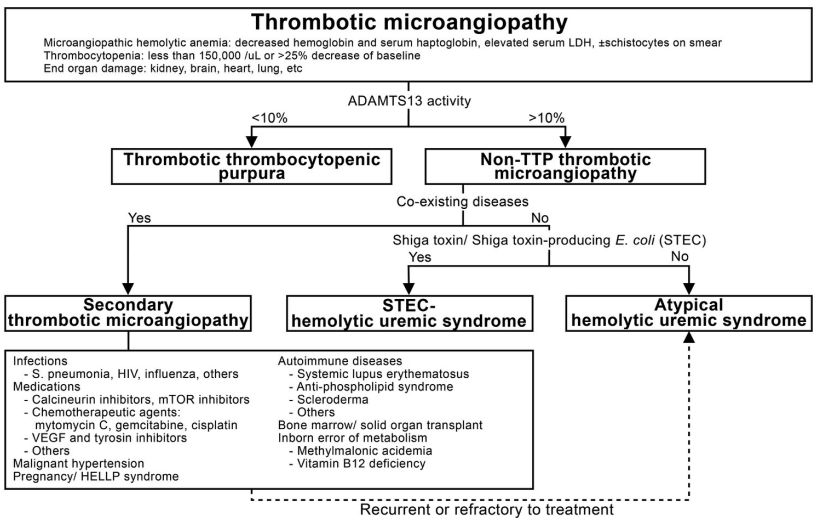

Figure 1 : Algorithm for the differential diagnosis of thrombotic microangiopathy (TMA) [Reproduced from Tseng et al., 2023)

CASE REPORT

An 18-year-old female with SLE diagnosed in 2023 presented with multi-system involvement, including cutaneous lesions, haematological abnormalities (cytopenia), neuropsychiatric lupus (non-convulsive seizures), lupus nephritis (without prior renal biopsy), and constitutional symptoms such as fever. She achieved steroid-free remission in March 2024 on azathioprine but experienced a disease flare in May 2024, requiring prednisolone and a switch to mycophenolate mofetil (MMF).

In late August 2024, she was admitted with worsening acute kidney injury (serum creatinine 250 µmol/L), microscopic haematuria, and nephrotic-range proteinuria (5.84 g/day). Renal biopsy revealed Class IV lupus nephritis with subacute arteriolar TMA. She received intravenous methylprednisolone with partial renal response and no dialysis required. During the admission, she developed altered mental status; CT venogram was normal. Blood film showed red cell fragments and 2.7% schistocytes, consistent with microangiopathic haemolytic anaemia (MAHA). Complement levels were low (C3: 0.2 g/L, C4: <0.08 g/L), but LDH, bilirubin and platelet count remained normal. Based on the presence of MAHA, CNS involvement, and AKI, she was treated presumptively for SLE-associated TTP with five sessions of plasma exchange, another course of methylprednisolone (500 mg daily for 3 days), and a single dose of IV cyclophosphamide (0.75 g/m^2). She improved significantly and was discharged with stable renal function.

Post-discharge, her ADAMTS13 activity sent prior to plasma exchange was normal at 57.5% (reference 40–130%); Antiphospholipid Screening was negative . In light of this and persistent normal platelet counts, her diagnosis was revised to secondary TMA related to SLE, with differential consideration of atypical HUS, characterized by MAHA, CNS involvement, renal impairment, complement activation with a normal ADAMTS13 activity level.

DISCUSSION

- Patient presented with biopsy proven active lupus nephritis Class IV and concurrent TMA on Renal biopsy
- Initially managed as active LN but subsequently developed signs concerning for TTP and was Treated Empirically with PLEX and Immunosuppression with clinical improvement
- Post-Treatment, ADAMTS 13 activity returned normal making TTP unlikely.
- Diagnosis was revised to Secondary TMA due to SLE with active LN
  - Differential diagnosis : atypical HUS
- Renal TMA is not uncommon in Class IV LN and associated with poorer prognosis
- In a cohort study of 148 SLE patients, renal TMA was seen in ~19.5%, independent of APS or malignant hypertension.

DIAGNOSTIC AND THERAPEUTIC CONSIDERATIONS

- TMA subtype differentiation is challenging at initial presentation.
- ADAMTS13 testing is a key component in workup.
- **TTP is a medical emergency:**
  - ~90% mortality if untreated
  - ~50% of deaths occur within the first 24 hours
- Empirical treatment for TTP is critical while awaiting confirmatory testing due to high risk of early mortality.

CONCLUSION

- This case highlights the diagnostic and therapeutic challenges in managing TMA in patients with SLE.
- Early empirical treatment is often warranted given the significant clinical overlap between TTP, aHUS and Secondary TMA, but diagnosis must be refined based on ADAMTS13 levels.
- Prompt recognition of secondary TMA is crucial, as management centres on disease control with immunosuppression.

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