Thrombotic Microangiopathies with Rheumatologic Involvement

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KEYWORDS

• Thrombotic microangiopathies • Systemic lupus erythematosus
• Antiphospholipid antibody syndrome • Scleroderma

KEY POINTS

- Thrombotic microangiopathies are a heterogeneous group of disorders, of which autoimmune diseases are one subtype.
- Thrombotic microangiopathy is characterized by endothelial cell injury leading to vascular thrombosis and organ ischemia.
- Complement system dysregulation and the development of autoantibodies against the von Willebrand factor cleaving protease ADAMTS13 play a key role in the pathogenesis of thrombotic microangiopathy.
- Systemic lupus erythematosus, antiphospholipid antibody syndrome, and scleroderma are commonly associated with thrombotic microangiopathy.
- Treatment involves immunosuppression to treat the underlying autoimmune disease and the use of renin–angiotensin–aldosterone system inhibitors to treat hypertension associated with chronic thrombotic microangiopathy.

Thrombotic microangiopathy (TMA) is a clinicopathologic diagnosis defined as microangiopathic hemolytic anemia (MAHA) with associated features of thrombocytopenia and end-organ ischemia, including the kidneys, central nervous system, and lungs.[1,2] The kidney is particularly susceptible to the endothelial injury of TMA owing to its highly specialized vascular capillary network, the glomerulus.[3] There is a growing appreciation for the vital role of complement system dysregulation and the development of autoantibodies against the von Willebrand factor cleaving protease, ADAMTS13, in the pathogenesis of TMA[4] (**Fig. 1**).

Renal TMA is characterized by endothelial cell injury leading to vascular thrombosis and organ ischemia. Histologically, TMA presents as fibrin thrombi (fragmented red cells) trapped in glomerular endothelium and mesangium[5] (**Figs. 2–4**). Other light microscopic features include mesangiolysis and mesangial cell interposition leading to glomerular basement duplication characteristic of membranoproliferative

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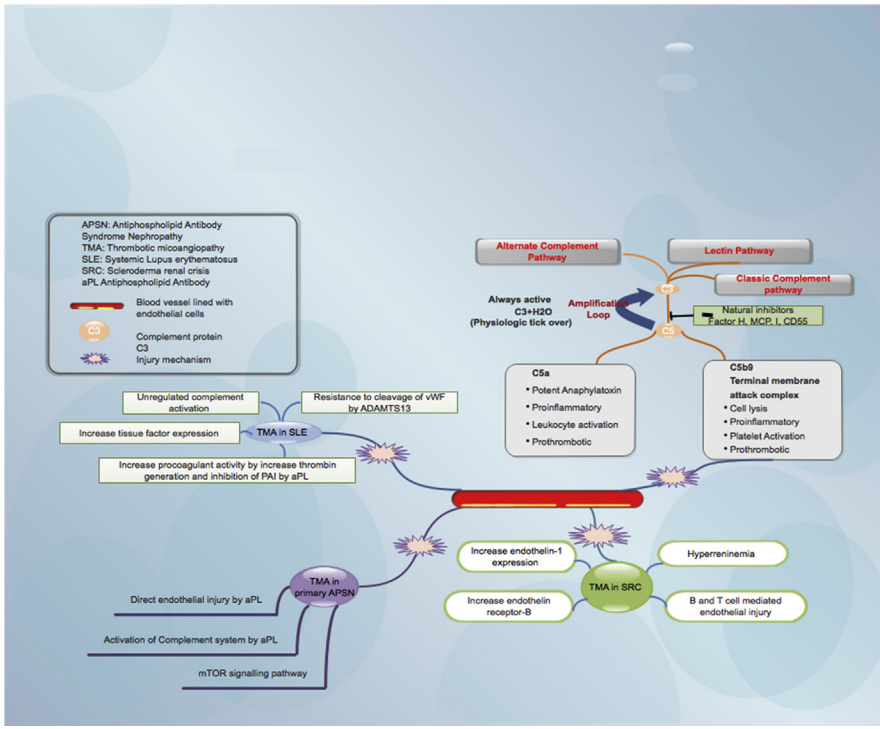

Fig. 1. Pathogenic mechanisms of thrombotic microangiopathy in rheumatic diseases. There is a role for dysregulated complement, resistance to cleavage of von Willebrand's factor by ADAMTS13 and direct endothelial cell injury by antiphospholipid antibody.

glomerulonephritis pattern of injury.[5] In chronic TMA, arteries and arterioles can have intimal proliferation with mucoid changes and entrapped red blood cell fragments or frank necrosis and/or fibrin thrombi.[5] Immunofluorescence studies shows positive staining for fibrin thrombi and occasional nonspecific staining for C3, IgM, or IgG. On electron microscopy, there are features of endothelial cell swelling with loss of

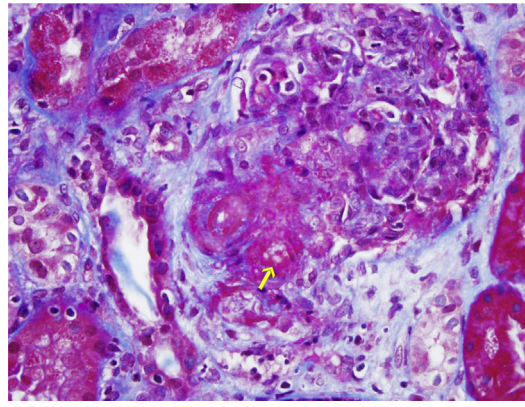

Fig. 2. A 20X Masson trichrome stain. Arteriolar thrombus (*Yellow arrow*) in the glomerulus in a patient with underlying class IV lupus nephritis with thrombotic microangiopathies (TMA). SLE, systemic lupus erythematosus.