Thrombotic Microangiopathy (TMA)

TMAs are a group of disorders characterized by thrombocytopenia, microangiopathic hemolytic anemia, and organ dysfunction, which can affect the brain, kidneys, heart, pancreas, liver, lungs, eyes, and skin



Patients may present with the following signs and symptoms

Thrombocytopenia 1-3

- Purpura
- Petechiae
- Prolonged bleeding
- Bleeding from gums or nose
- Blood in urine or stool, or bleeding from rectum
- Abnormal vaginal bleeding
- Headaches
- Easy bruising, retinal hemorrhage, and hemoptysis

Microangiopathic hemolytic anemia4

- Fatique
- Dyspnea
- Dark urine
- Back pain

- Jaundice
- Paleness
- Resting tachycardia with flow murmur

Organ injury/AKI^{3,5}

- Acute kidney injury
 - Listlessness
 - Confusion
 - Fatigue
 - Anorexia
 - Nausea
 - Vomiting
 - Proteinuria
 - Weight gain

- Edema
- Oliguria/Anuria
- Uremic encephalopathy
 - Decline in mental status, asterixis, neurologic symptoms
- Anemia
- Uremic platelet dysfunction
- Microhematuria

Patients may also present with other signs and symptoms^{3,4,6-8}

- CNS symptoms: Weakness, transient focal neurologic abnormalities, confusion, headache, paresis, aphasia, dysarthria, visual problems, encephalopathy, seizures, altered consciousness, coma
- Cardiac symptoms: Chest pain, heart failure, hypotension, hypertension, myocardial infarction
- GI symptoms: Severe abdominal pain, diarrhea, pancreatitis, vomiting
- Pulmonary symptoms: Dyspnea, pulmonary hemorrhage, pulmonary edema







TMAs require rapid differential diagnosis⁹⁻¹²

Thrombocytopenia
Platelet count <150 × 10⁹/L or
>25% decrease from baseline

AND

Microangiopathic hemolysis
Schistocytes and/or
Elevated LDH and/or
Decreased haptoglobin and/or
Decreased hemoglobin

Plus 1 or more of the following

Common Signs and Symptoms

Neurological symptoms

Confusion and/or Seizures and/or Stroke and/or Other cerebral abnormalities

Renal impairment

Elevated creatinine level and/or Decreased eGFR and/or Elevated blood pressure and/or Abnormal urinalysis results

GI symptoms

Diarrhea ± blood and/or Nausea/vomiting and/or Abdominal pain and/or Gastroenteritis/pancreatitis

Other Signs and Symptoms

CV symptoms

MI and/or Hypertension and/or Arterial stenosis and/or Peripheral gangrene

Pulmonary symptoms

Dyspnea and/or Pulmonary hemorrhage and/or Pulmonary edema

Visual symptoms

Pain and blurred vision and/or Retinal vessel occlusion and/or Ocular hemorrhage



Evaluate ADAMTS13 activity and Shiga toxin/EHEC test^a

While ADAMTS13 results are awaited, a platelet count $>30 \times 10^{\circ}$ /L and/or sCr >1.7 to 2.3 mg/dL almost eliminates a diagnosis of severe ADAMTS13 deficiency (TTP)

≤5%^b ADAMTS13 activity

>5% ADAMTS13 activity

Shiga toxin/EHEC positive

TTP

Atypical-HUS

STEC-HUS

TMA can also manifest in the presence of clinical conditions such as the following

- Pregnancy-postpartum
- Malignant/severe hypertension
- Solid organ transplantation

- Autoimmune disease (eg, SLE, scleroderma)
- Hematopoietic stem cell transplantation

^aShiga toxin/EHEC test is warranted with history/presence of GI symptoms. ^bRange found in published literature is <5%-10%.

ABBREVIATIONS

ADAMTS13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif member 13; AKI, acute kidney injury; CNS, central nervous system; CV, cardiovascular; EHEC, enterohemorrhagic Escherichia coli; eGFR, estimated glomerular filtration rate; GI, gastrointestinal; HUS, hemolytic uremic syndrome; LDH, lactate dehydrogenase; MI, myocardial infarction; sCr, serum creatinine; STEC, Shiga toxin-producing Escherichia coli; TMA, thrombotic microangiopathy; TTP, thrombotic thrombocytopenic purpura.

REFERENCES

1. National Heart Lung and Blood Institute. Thrombocytopenia. https://www.nhlbi.nih.gov/ health-topics/thrombocytopenia. Accessed May 20, 2019. 2. Gauer RL, Braun MM. Am Fam Phys. 2012;85:612-622. 3. Scully M, et al. Br J Haematol. 2012;158:323-335. 4. Dhaliwal G, et al. Am Fam Phys. 2004;69:2599-2606. 5. Rahman M, et al. Am Fam Phys. 2012;86:631-639. 6. Sakari Jokiranta T, et al. BMC Nephrol. 2017;18:324. 7. George JN, Nester CM. New Engl J Med. 2014;371:654-666. 8. Brocklebank V, et al. Clin J Am Soc Nephrol. 2018;13:300-317. 9. Goodship THJ, et al. Kidney Int. 2017;91:539-551. 10. Azoulay E, et al. Chest. 2017;152:424-434. 11. Laurence J, et al. Clin Adv Hematol Oncol. 2016;14:2-15. 12. Asif A, et al. J Nephrol. 2017;30:347-362.

