Three's (Autoimmune) Company: A Co-occurrence of Thrombotic Thrombocytopenic Purpura, Warm Autoimmune Hemolytic Anemia, and Sjögren's Syndrome

Austin P. Runde, MS; Sanchita Sen, MA; Beatriz Maria Franco Hondermann, MD; Nikitha Nelapudi, MD; Deval Patel, MD

ABSTRACT

Introduction: This case highlights the successful management of atypical, refractory thrombotic thrombocytopenic purpura (TTP), including co-occurring autoimmune conditions, treatment-related adverse effects, and disease sequelae.

Case Presentation: A Hispanic woman in her early 50s presented to the emergency department of an academic, tertiary medical center after a syncopal episode. She reported flu-like symptoms during the preceeding 2 days. Physical examination was remarkable only for scattered ecchymoses on the upper extremities and petechiae of the lower extremities. Despite her clinical stability, she was ultimately found to have refractory TTP, warm autoimmune hemolytic anemia (wAIHA), and Sjögren's syndrome.

Discussion: No reports have described the co-occurrence of TTP, wAIHA, and Sjögren's syndrome. Isolated case reports have described co-occurring TTP and Sjögren's syndrome, as well as co-occurring or sequential TTP and wAIHA, with or without lupus.

Conclusions: We report what is, to our knowledge, one of the first cases of co-occurring TTP, wAIHA, and Sjögren syndrome. This case underscores the importance of multidisciplinary care in the management of refractory TTP and its associated complications.

INTRODUCTION

First described by Moschcowitz in 1924, thrombotic thrombocytopenic purpura (TTP) is a hematologic emergency characterized by severe thrombocytopenia, microangiopathic hemolytic anemia (MAHA), end-organ ischemia, and neurologic abnormalities.[1,2] The annual incidence of TTP is unknown but is estimated at 1 to 13 cases per million people globally, varying by location.[3] TTP is caused either by inherited Upshaw-Schulman syndrome or acquired ADAMTS-13 dysfunction. TTP is typically acquired, occurring secondary to the formation of immunoglobulin (Ig) G, IgA, or IgM autoantibodies (inhibitors) against ADAMTS-13, which block its proteolytic activity or increase its clearance from plasma.1 ADAMTS-13 normally cleaves von Willebrand factor (vWF) multimers into smaller, less prothrombotic fragments. When ADAMTS-13 is impaired, the enzyme is unable to properly cleave vWF, and the aberrant vWF multimers bind platelets avidly. This leads to accumulation of platelet-rich thrombi in the small vessels (thrombotic microangiopathy), causing MAHA and end-organ ischemia. Acquired TTP (aTTP) is twice as common in biological females and can be triggered by malignancy, infection, pregnancy, and drugs, such as nonsteroidal antiinflammatory drugs, estrogen-containing contraceptives, proteosome inhibitors, quetiapine, eptifibatide, and clopidogrel.[1,4]

The MAHA associated with TTP is due to shearing of red blood cells as they traverse thrombi-laden microvasculature, evidenced by schistocytes on peripheral blood smear. Unlike TTP, immune thrombocytopenic purpura (ITP) does not yield schistocytes. Hemolysis mediated by IgG autoantibodies (warm autoimmune hemolytic anemia [wAIHA]) yields spherocytes on blood smear due to the action of splenic macrophages on IgG-bound erythrocytes. An established association exists between wAIHA and ITP, a condition known as Evans syndrome.[5] In contrast, no established association exists between wAIHA and TTP, although case reports have described concurrent disease or sequential presentation, with and without lupus.[6-8]

Like TTP, wAIHA can be caused by cancers (eg, chronic lym-

• • •

Author affiliations: Loyola University Medical Center, Maywood, Illinois (Hondermann, Nelapudi, Patel, Runde, Sen).

Corresponding author: Austin P. Runde; email arunde1@luc.edu; ORCID ID 0000-0002-2583-9502

phocytic leukemia [CLL]), viral infections (eg, Epstein-Barr virus, hepatitis A, B, and C, and HIV), lupus, and drugs.[9]

Sjögren's syndrome results from immune-mediated destruction of the lacrimal and salivary glands, leading to chronic dry eyes and dry mouth (sicca symptoms) and potential involvement other organ systems.[10] Sjögren's syndrome often occurs alongside other autoimmune conditions. The diagnosis is clinical, and Sjögren's syndrome is highly likely when anti-Ro/SSA and/or anti-La/SSB autoantibodies are detected in a patient with sicca symptoms.

Despite the presence of one autoimmune condition increasing the risk of developing another, no case reports have described the co-occurrence of TTP, wAIHA, and Sjögren's syndrome.[11] While there is a rare but documented association between TTP and Sjögren's syndrome, we present what is, to our knowledge, one of the first reported cases of a patient with co-occurring TTP, wAIHA, and Sjögren's syndrome.[12]

CASE PRESENTATION

The patient is a woman in her early-50s with a past medical history of allergic rhinitis, undifferentiated anemia, vitamin B_{12} deficiency, cholecystitis secondary to cholelithiasis, eczema, and recurrent tonsillitis. Her only home medication was intranasal fluticasone daily. She also reported taking magnesium, turmeric, and ashwagandha supplements daily. Her surgical history was significant only for cesarean delivery, laparoscopic cholecystectomy, and childhood tonsillectomy. She denied recreational drug, tobacco, and alcohol use. Her family history was remarkable only for type 2 diabetes in her biological parents, unspecified colon cancer in one biological parent, and easy bruising beginning after menopause in her sister. She had no known allergies and no history of cancer or solid organ or hematopoietic stem cell transplantation.

Case History

The patient presented to our emergency department (ED) following a collapse witnessed by her husband. She reportedly awoke from sleep and lost consciousness; the first event she recalled was being assisted to the bathroom by her husband. He reported that she stumbled and became "glassy-eyed" and unresponsive for approximately 30 seconds. She reported feeling unwell for 2 days prior to presentation, with malaise, nausea, nonbloody, nonbilious vomiting, and myalgias. Several days before symptom onset, her child had an upper respiratory infection, and she consumed a meatless hamburger that "did not taste right." Review of systems was positive for a 2- to 3-year history of easy bruising and a 1-week history of "pink" urine, oozing epistaxis, and light vaginal bleeding but negative for recent gumline bleeding.

Physical Exam

In the ED, the patient's blood pressure was 129/75 mmHg, pulse 104 beats/minute, respiratory rate 18 breaths/minute, temperature 97.9 °F (36.6 °C), peripheral oxygen saturation 100% on room air, and body mass index 29.39 kg/m². She appeared well, and physical examination was remarkable only for fatigue, stripe-like bruising on the flexor surface of the left wrist, and circumferential bruising of the right bicep that she attributed to a blood pressure cuff. Physical examination was negative for oral petechiae, Grey Turner sign, focal neurologic deficits, and altered mental status.

Table 1. Abnormal Laboratory Results Obtained on Admission

Component	Value	Reference Range
Red blood cell count	3.09 m/uL	3.80–5.20 m/uL
Hemoglobin	9.5 gm/dL	11.5–15.5 gm/dL
Hematocrit	27.4%	34.0%–46.5%
Red cell distribution width	16.9%	11.0%–15.0%
Platelets	6 k/uL	150–400 k/uL
Sodium	135 mmol/L	136–144 mmol/L
Blood urea nitrogen	37 mg/dL	7–22 mg/dL
Blood glucose	160 mg/dL	70–100 mg/dL
Alanine aminotransferase	59 U/L	7–35 U/L
Aspartate aminotransferase	107 U/L	10–40 U/L
Total bilirubin	2.6 mg/dL	0.2–1.4 mg/dL
Direct bilirubin	0.6 mg/dL	0.0–0.3 mg/dL
Serum bicarbonate	22 mm/L	24–30 mm/L
D-dimer	5769 ng/mL FEU	< 500 ng/mL FEU
PLASMIC score[a]	7	0–4
HS-troponin (every 2.5 hours)	593 →709→780→680 ng/L	0–14 ng/L
HS-C-reactive protein	20.31 mg/L	< 1.0 mg/L[b]
Erythrocyte sedimentation rate	45 mm/hr	0–35 mm/hr
Uncorrected reticulocytes	3.3%	0.6%–1.8%
Corrected reticulocytes	2%	0.6%–1.8%
Haptoglobin	< 30 mg/dL	36–195 mg/dL
Lactate dehydrogenase	2122 U/L	108–212 U/L
Ferritin	1403 ng/mL	11–241 ng/mL
Iron	320 ug/dL	35–140 ug/dL
Iron saturation	95%	20%–50%
Vitamin B12	199 pg/mL[c]	180–914 pg/mL[c]
Direct antiglobulin (Coombs) test	(+) polyspecific Coombs antibody; (+) anti-IgG antibody; (+) warm antibody	(–)
ADAMTS-13 activity	< 3%	> 69%
ADAMTS-13 inhibitor	1.9 IU	< 0.5 IU
Antinuclear antibody	1:1280 (speckled pattern)	< 1:40
Complement C4	9 mg/dL	16–38 mg/dL
Anti-Ro/SSA	65 U/mL	< 7.0 U/mL

Abbreviations: anti-Ro/SSA, anti-Ro/Sjögren syndrome-related antigen A autoantibody; FEU, fibrinogen equivalent units; HS, high sensitivity.

[a] Platelet count, combined hemolysis variable, absence of active malignancy, absence of solid organ or stem cell transplant, mean corpuscular volume, international normalized ratio, and creatinine score.

[b] >10.0 reflects acute inflammatory process.

[c] <200 considered low by many institutions.

Laboratory Results

Abnormal results from the comprehensive metabolic panel, complete blood cell count (CBC), mixed venous blood gas, and ancillary testing are listed in the Table.[13] Prothrombin time, interna-

tional normalized ratio, and activated partial thromboplastin time were within normal limits, as were phosphorus, magnesium, and hemoglobin A1C (HbA1c).

Respiratory pathogen polymerase chain reaction (PCR) testing was negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), influenza A/B, respiratory syncytial virus, adenovirus, coronavirus 229E/HKU1/NL63/OC43, human metapneumovirus, human rhinovirus/enterovirus, parainfluenza virus types 1 through 4, *Bordetella pertussis* and *Bordetella parapertussis, Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*.

Viral testing was negative for active cytomegalovirus and Epstein-Barr virus infection; HIV 1/2 antibodies and antigens; acute hepatitis A, B, and C; anti-hepatitis B core antibody; and coxsackie A antibodies. Nasal PRC testing was negative for methicillin-resistant *Staphylococcus aureus*.

Gastrointestinal pathogen PCR testing was negative for *Campylobacter*, toxigenic *Clostridioides difficile* A/B, *Pleisomonas shigelloides*, *Salmonella*, *Vibrio* spp., *Yersinia enterocolitica*, enteroaggregative *Escherichia coli* (E coli), enteropathogenic *E coli,* enterotoxigenic *E coli*, Shiga-toxin producing E coli, *Shigella*/invasive *E coli*, *Cryptosporidium*, *Cyclospora*, *Entamoeba histolytica*, *Giardia lamblia*, adenovirus F40/41, astrovirus, and norovirus GI/GII.

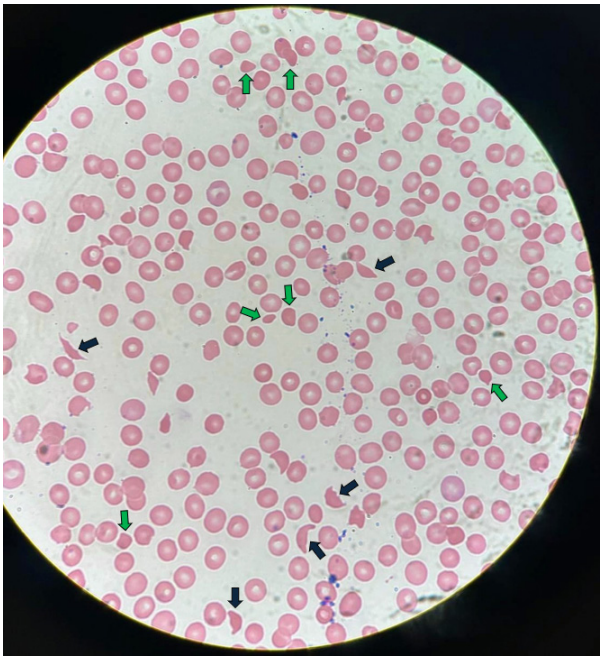
Complement C3 was within normal limits. Rheumatologic workup was negative for rheumatoid factor, lupus anticoagulant, cardiolipin, β2-glycoprotein 1, Smith, La/SSB, Scl-70, Jo-1, and double-stranded DNA autoantibodies. During rheumatology evaluation, the patient reported a 1-year history of dry eyes without other rheumatologic symptoms.

Admission electrocardiography (ECG) revealed sinus tachycardia (QT/QTcB, 318/414 ms) and low-voltage QRS complex. ECGs throughout admission continued to demonstrate a low-voltage QRS complex and occasional nonspecific T-wave abnormalities.

Chest radiography was negative for consolidation. Noncontrast computed tomography (CT) of the head was unremarkable. CT of the cervical spine without IV contrast was negative for fracture or subluxation. CT of the chest, abdomen, and pelvis with IV contrast was remarkable only for diverticulosis. There were no acute abnormalities or lymphadenopathy.

Peripheral blood smear revealed schistocytes, microspherocytes, and severe thrombocytopenia (Figure 1). Type and screen confirmed O-positive blood type and was negative for alloantibodies. Direct antiglobulin test was negative for complement antibodies.

Figure 1. Image of Patient's Peripheral Blood Smear



Schistocytes (blue arrows), microspherocytes (green arrows), and severe thrombocytopenia are evident (1000x).

Hospital Course

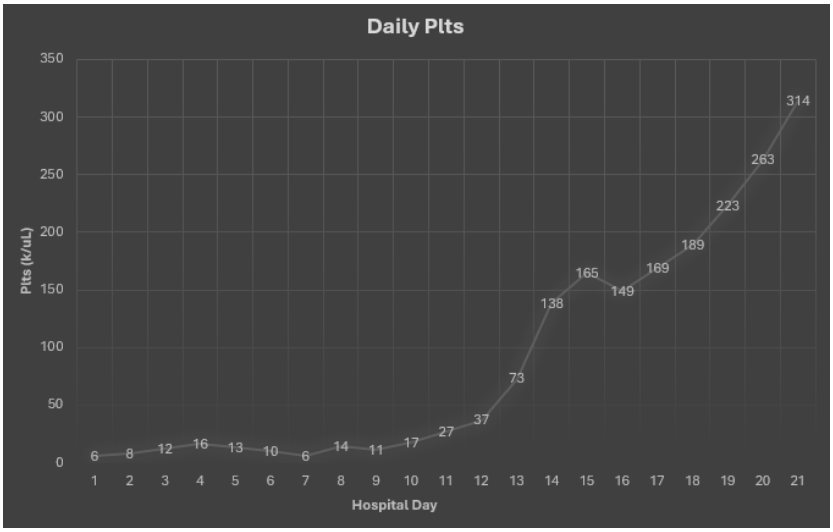
Methylprednisolone was initiated at a dosage of 1000 mg daily for 3 days followed by prednisone 80 mg daily for 4 days. Therapeutic plasma exchange (PLEX) at a rate of 1.0 plasma volume was initiated on hospital day 1 and planned daily until a platelet count of at least at least 140 k/uL (reference range, 150–400 k/uL) was achieved for 2 consecutive days. However, the patient's platelet count failed to rise above 20 k/uL after 7 PLEX sessions. PLEX therefore was escalated to 1.5 plasma volumes daily for 5 sessions before being reduced to 1.0 plasma volume. Prednisone was replaced with methylprednisolone 125 mg daily for 3 days before being tapered to 80 mg daily. Rituximab was initiated on the final PLEX session (hospital day 16) and scheduled for 375 mg/m^2 weekly for an additional 4 doses. Caplacizumab-yhdp was prepared but ultimately not required. Daily platelet counts from admission to discharge are shown in Figure 2. Cyanocobalamin 1000 mcg and folate 1 mg daily were initiated in the setting of hemolytic anemia.

On hospital day 3, the patient began to experience transient ischemic attacks (TIAs) characterized by syncope and focal deficits, including dysarthria, facial hemiparesis, and lower-extremity drift. Transthoracic echocardiography (TTE) revealed a dilated inferior vena cava and a small pericardial effusion. Cardiology diagnosed myocarditis and effusive-constrictive pericarditis based on TTE findings, troponinemia, and elevated erythrocyte sedimentation rate/high-sensitivity C-reactive protein levels; the patient's ongoing glucocorticoid therapy was expected to ameliorate the cardiac inflammation. CT angiography and perfusion imaging of the head with and without IV contrast revealed no abnormalities. Aspirin 81 mg daily was initiated for secondary prevention of ischemic neurologic events. TIAs continued during the following week, prompting magnetic resonance imaging

(MRI) of the head without contrast. MRI demonstrated 2 punctate foci of diffusion restriction in the posterior right frontal lobe, consistent with acute ischemia, and a small signal abnormality in the subcortical white matter of the right insula without diffusion restriction on fluid-attenuated inversion recovery sequence. The TIAs and focal deficits resolved as the platelet count recovered.

On hospital day 9, *Proteus vulgaris* bacteremia was detected via blood cultures obtained in the setting of altered mental status. Levofloxacin was initiated after testing revealed ceftriaxone resistance. Repeat blood cultures obtained shortly thereafter confirmed clearance of bacteremia. Sulfamethoxazole-trimethoprim 800-160 mg 3 times weekly and pantoprazole 40 mg daily were initiated because of high-dose glucocorticoid therapy.

Figure 2. Run Chart Depicting Patient's Daily Platelet Count From Admission to Discharge



Plasma exchange was performed daily from hospital day 1 to 16.

On hospital day 14, the patient reported somatic concerns, intermittently declined to speak or eat, displayed a flat affect, and demonstrated thought content concerning for Cotard delusion. Given the absence of prior psychiatric history, the psychiatry team deemed her sudden behavior change likely glucocorticoid-induced depression. Mirtazapine was initiated at 7.5 mg nightly with a target dose of 15 mg. However, she deteriorated over the next day, displaying signs of psychosis and catatonia (Bush-Francis Catatonia Rating Scale [BFCRS] score = 8). Mirtazapine was discontinued and clonidine 0.05 mg was prescribed as needed up to 3 times daily. Her BFCRS score quickly decreased to 3, although she continued to display signs of psychosis; therefore, olanzapine 2.5 mg nightly was added. She responded well to olanzapine, which was continued until 1 week after completion of glucocorticoid therapy. She subsequently developed elevated blood glucose levels reaching 200 to 250 mg/dL, for which insulin was initiated during inpatient hospitalization and metformin 500 mg was prescribed after discharge until glucocorticoid cessation.

After a 21-day admission, the patient was discharged with a platelet count of 314 k/uL, ADAMTS-13 activity of 23%, and an undetectable ADAMTS-13 inhibitor level. At her final rituximab infusion (1 month postdischarge), she reported feeling closer to her baseline status and complete resolution of psychiatric symptoms without neurologic deficits. Abnormal values from CBC, comprehensive metabolic panel, and hemolysis studies performed at follow-up were red blood cell count 3.53 × 106/μL, MCV 112.5 fL (reference range, 82.0–99.0 fL [88.7 fL on admission]), mean corpuscular hemoglobin 36.0 pg (reference range, 27.0–34.0 pg), mean platelet volume 8.9 fL (reference range, 9.0–13.0 fL), absolute neutrophil count 8.3 (reference range, 1.5–7.0 k/mm^3), lactate dehydrogenase 272 U/L, blood glucose 160 mg/dL, and alanine aminotransferase 48 U/L.

DISCUSSION

Our patient presented with a challenging case of TTP. Despite initially appearing well enough to suggest ITP, she ultimately was diagnosed with refractory TTP complicated by co-occurring wAIHA and Sjögren's syndrome. Patients with TTP frequently present with altered mental status, focal neurologic deficits, gastrointestinal symptoms, acute kidney injury (AKI), bleeding secondary to thrombocytopenia, abdominal pain, fever, and headache.[3,14] Although reported frequencies vary, the classic Amorosi-Ultmann TTP pentad of thrombocytopenia, MAHA, fever, AKI, and neurologic abnormalities is present in only 5% to 35% of cases.[3,14]

Guidelines for the management of aTTP were reviewed in 2024 by the International Society on Thrombosis and Haemostasis (ISTH).[15] For an initial episode of aTTP, ISTH-recommends frontline treatment with PLEX with glucocorticoids, rituximab, and caplacizumab. Given the patient's clinical complexity and elevated risk of adverse events, PLEX and glucocorticoids were initiated first, whereas rituximab and caplacizumab were considered subsequently.

Before ADAMTS13 testing became available, the patient's presentation was highly suggestive of TTP based on the PLASMIC score, a validated clinical prediction tool used to estimate the likelihood of severe ADAMTS13 deficiency in patients with suspected thrombotic microangiopathy.[13] Our patient met multiple high-risk criteria, including severe thrombocytopenia, laboratory evidence of hemolysis, absence of active malignancy, absence of transplant

history, normal coagulation studies, and preserved renal function, supporting prompt initiation of empiric PLEX while definitive testing was pending.

CONCLUSIONS

Despite the well-established observation that the presence of one autoimmune disease increases the risk of developing additional autoimmune diseases, we found no reports documenting co-occurring TTP, wAIHA, and Sjögren's syndrome. Herein, we describe the successful treatment of a highly complex case, highlighting the importance of multidisciplinary care and providing support for use of the PLASMIC score to justify empiric PLEX.

Financial disclosures: None declared.

Funding/support: None declared.

Acknowledgements: The authors wish to thank their Loyola University Medical Center colleagues and extend special thanks to Hematology/Oncology, Transfusion Medicine/Blood Banking/Apheresis, and Critical Care for services rendered, as well as Harshavardhan Tathireddy, MD, and Angela Ai, MD, for providing the patient's blood smear.

REFERENCES

1. Sukumar S, Lämmle B, Cataland SR. Thrombotic thrombocytopenic purpura: pathophysiology, diagnosis, and management. *J Clin Me*d. 2021;10(3):536. doi:10.3390/jcm10030536

2. Moschcowitz, E., An acute febrile pleiochromic anemia with hyaline thrombosis of the terminal arterioles and capillaries: an undescribed disease. *Arch Intern Med (Chic)*. 1925;36(1):89-93. doi:10.1001/archinte.1925.00120130092009

3. Stanley M, Killeen RB, Michalski JM. Thrombotic thrombocytopenic purpura. In: *StatPearls*. StatPearls Publishing; January 2023. Updated April 7, 2023. Accessed October 1, 2025. https://www.ncbi.nlm.nih.gov/books/NBK430721/

4. Medina PJ, Sipols JM, George JN. Drug-associated thrombotic thrombocytopenic purpura-hemolytic uremic syndrome. *Curr Opin Hematol.* 2001;8(5):286-293. doi:10.1097/00062752-200109000-00004

5. Audia S, Grienay N, Mounier M, Michel M, Bonnotte B. Evans' syndrome: from diagnosis to treatment. *J Clin Med.* 2020;9(12):3851. doi:10.3390/jcm9123851

6. Bruns L, Völker L, Klamroth R, Kuhlmann MK, Jabs WJ. Concomitant presentation of thrombotic thrombocytopenic purpura, immune thrombocytopenia, and autoimmune hemolytic anemia in a patient with newly diagnosed systemic lupus erythematosus. *Clin Nephrol Case Stud*. 2023;11:147-153. doi:10.5414/CNCS111193

7. Morgensztern D, Kharfan-Dabaja MA, Tsai HM, Lian EC. Warm-antibody autoimmune hemolytic anemia developing after thrombotic thrombocytopenic purpura. *Acta Haematol.* 2002;108(3):154-156. doi:10.1159/000064706

8. Al-Kadhimi M, Wah F, Al-Dawoodi T, Peguero J, Campos LT. Autoimmune hemolytic anemia presenting concurrently with thrombotic thrombocytopenic purpura. *Case Rep Int.* 2016;5:36-39. doi:10.5348/crint-2016-27-CR-9

9. Fattizzo B, Barcellini W. Autoimmune hemolytic anemia: causes and consequences. *Expert Rev Clin Immunol.* 2022;18(7):731-745. doi:10.1080/1744666X.2022.2089115

10. Carsons SE, Blum MA. Sjogren disease. In: *StatPearls*. StatPearls Publishing; January 2023. Updated July 6, 2025. Accessed October 1, 2025. https://www.ncbi.nlm.nih.gov/books/NBK431049/

11. Cojocaru M, Cojocaru IM, Silosi I. Multiple autoimmune syndrome. *Maedica (Bucur).* 2010;5(2):132-134.

12. Carvalho JF, Shoenfeld Y. Sjögren's syndrome associated with thrombotic thrombocytopenic purpura: a case-based review. *Rheumatol Ther.* 2021;8(1):621-629. doi:10.1007/s40744-020-00265-w

13. Bendapudi PK, Hurwitz S, Fry A, et al. Derivation and external validation of the PLASMIC score for rapid assessment of adults with thrombotic microangiopathies: a cohort study. L*ancet Haematol*. 2017;4(4):e157-e164. doi:10.1016/S2352-3026(17)30026-1

14. Page EE, Kremer Hovinga JA, Terrell DR, Vesely SK, George JN. Thrombotic thrombocytopenic purpura: diagnostic criteria, clinical features, and long-term outcomes from 1995 through 2015. *Blood Adv.* 2017;1(10):590-600. doi:10.1182/bloodadvances.2017005124

15. Zheng XL, Al-Housni Z, Cataland SR, et al. 2025 focused update of the 2020 ISTH guidelines for management of thrombotic thrombocytopenic purpura. *J Thromb Haemost.* 2025;23(11):3711-3732. doi:10.1016/j.jtha.2025.06.002

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 2379-3961) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

© 2026 Board of Regents of the University of Wisconsin System and The Medical College of Wisconsin, Inc.

Visit www.wmjonline.org to learn more.