TTP & the Thrombotic Microangiopathies

MAHA + thrombocytopenia · Do not wait for ADAMTS13 to start treating

PLASMIC ≥ 6
= treat as TTP

RECOGNIZE THE MICROANGIOPATHY *two findings open the whole differential*

THE CORE FINDING

Microangiopathic hemolytic anemia plus thrombocytopenia, with no other explanation. **Schistocytes** on the film · **raised LDH** · **low haptoglobin** · raised indirect bilirubin · **negative direct antiglobulin test** (this is mechanical, not immune, hemolysis).

DO NOT WAIT FOR THE PENTAD

The classic pentad — MAHA, thrombocytopenia, fever, renal failure, neurological signs — is **present in a minority** and describes untreated, late disease. **Waiting for it is how people die.** Two findings are enough to act.

CRITICALLY, THE COAGS ARE NORMAL

PT, aPTT and fibrinogen are typically normal in TTP — this is what separates it from **DIC**, where they are deranged. An abnormal coagulation screen should send you looking for a different diagnosis.

SCORE AND CONFIRM *PLASMIC guides action while the assay is pending*

Step	Detail
PLASMIC score	A score **> 6** (or a French score of 2) indicates a **high probability of ADAMTS13-deficient TTP**. Validated clinical scores are endorsed to aid diagnosis and **early management** precisely because the assay takes time.
Send ADAMTS13 first	Draw the **ADAMTS13 activity and inhibitor before plasma exchange**, since exchange replaces the enzyme and destroys the result. **But do not delay treatment waiting for it.**
Interpreting it	**ADAMTS13 < 10 IU/dL** confirms TTP — continue caplacizumab and rituximab. **≥ 20 IU/dL** should prompt you to **consider stopping caplacizumab and seek an alternative diagnosis**.
Immune or congenital	Most adult TTP is **immune-mediated**, from an autoantibody inhibitor. Congenital TTP (Upshaw-Schulman) presents earlier or in pregnancy and is treated with plasma or recombinant ADAMTS13, not immunosuppression.

TREAT IMMEDIATELY *the modern regimen is a combination, started together*

1. **Therapeutic plasma exchange** — the intervention that changed TTP from almost uniformly fatal to survivable. **Start the same day.** If exchange is not immediately available, give **plasma infusion** as a bridge while arranging transfer.
2. **Corticosteroids** — high dose, started at the same time as exchange, to suppress the autoantibody.
3. **Rituximab** — given up front alongside the other agents in immune TTP. Frontline use also reduces inhibitor boosting during caplacizumab treatment.
4. **Caplacizumab** — an anti-von Willebrand factor nanobody. **Start as soon as possible, without waiting for ADAMTS13 to return.** Adding it to exchange, steroids and rituximab is supported for therapeutic efficacy and potential survival benefit. It causes mucocutaneous bleeding, so watch for it.
5. **Monitor daily** platelets, LDH, hemoglobin, creatinine and neurological status. **Platelet recovery is the main response marker.** Continue exchange until the count is sustained, then taper.

THE OTHER MICROANGIOPATHIES *same picture, completely different treatment*

HUS

STEC-HUS: children, bloody diarrhea, prominent **renal failure**. Management is **supportive**, with dialysis as needed. **Avoid antibiotics and antimotility agents**, which may increase toxin release and worsen outcomes. **Atypical HUS:** complement dysregulation. Treated with **eculizumab or ravulizumab** — vaccinate against meningococcus and cover with antibiotics.

ALWAYS EXCLUDE

DIC (abnormal coagulation) · **HELLP and pre-eclampsia** in pregnancy · **malignant hypertension** · **drug-induced TMA** (quinine, gemcitabine, calcineurin inhibitors, VEGF inhibitors) · disseminated malignancy · severe B12 deficiency, which mimics hemolysis with a high LDH · mechanical valve hemolysis.

AFTER THE ACUTE EPISODE *immune TTP is a relapsing disease*

Element	Detail
Monitor ADAMTS13 in remission	A **falling ADAMTS13 activity predicts relapse** before the platelet count moves. Serial measurement identifies patients who need pre-emptive rituximab, which is far safer than treating a fully declared relapse.
Pre-emptive rituximab	Given for a significant fall in ADAMTS13 during clinical remission, to prevent an acute episode. This is one of the main reasons to keep these patients in specialist follow-up rather than discharging them.
Long-term sequelae	**Cognitive impairment, depression, hypertension and stroke** are commoner than historically appreciated, even after apparently full recovery. Ask about them at follow-up.
Pregnancy	Pregnancy can trigger both first presentations and relapse. **Distinguish from HELLP and pre-eclampsia**, which usually resolve with delivery. Congenital TTP frequently declares itself in a first pregnancy. Plan future pregnancies with hematology and obstetrics jointly.
Patient safety net	Give the patient written information and a clear route back in. **Relapse can be rapid**, and recognition by a patient who knows their diagnosis is often faster than by a new clinician.

THE BEDSIDE SEQUENCE *what to do in the first hour*

FIRST HOUR

Blood film urgently and confirm schistocytes · full coagulation screen to exclude DIC · **LDH, haptoglobin, bilirubin, reticulocytes, direct antiglobulin test** · creatinine and troponin · **calculate PLASMIC** · **send ADAMTS13 before any plasma** · contact hematology and the apheresis service.

WHILE YOU WAIT FOR APHERESIS

Start **corticosteroids** and give **plasma infusion** if exchange will be delayed. **Withhold platelet transfusion.** Monitor for cardiac and neurological involvement — **troponin rise and confusion are markers of severity** and should accelerate transfer.

PEARLS & PITFALLS

- **Do not transfuse platelets in TTP** unless there is life-threatening bleeding — it is classically described as fuelling further microvascular thrombosis.
- **Normal PT, aPTT and fibrinogen with schistocytes points to TTP, not DIC.** That single distinction redirects the entire management.
- **Send ADAMTS13 before exchange**, then start treatment without waiting for the result.
- **Any unexplained thrombocytopenia with anemia deserves a blood film**, urgently. Schistocytes change everything.
- **Neurological signs can be subtle and fluctuating** — confusion or headache, not necessarily a stroke. Do not require a deficit before acting.
- **ADAMTS13 ≥ 20 IU/dL should make you revisit the diagnosis** rather than continuing TTP-directed therapy by momentum.

References: ISTH Guidelines for the Diagnosis and Management of Thrombotic Thrombocytopenic Purpura (2020) and the 2025 focused update · PLASMIC score derivation and validation · HERCULES caplacizumab trial.

Educational aid; verify against local hematology protocol and patient factors.

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