Guideline management of Thrombotic Thrombocytopenic Purpura (TTP)

Perinatology Division

Supervisors:

Dr. Homeira Vafaei

Dr. Maryam Kasraiean

Dr. Nasrin Asadi

Dr. Azam Faraji

Student:

Dr. Maryam Zarekhafri

Assistant fellowship of perinatology

Management of thrombotic thrombocytopenic purpura (TTP)

Background and significance:

Disorders that cause thrombocytopenia in pregnancy:

Gestational thrombocytopenia

Pre-eclampsia and HELLP syndrome

Immune thrombocytopenia (ITP)

Secondary ITP: drug-related, Systemic lupus erythematosus (SLE), antiphospholipid syndrome, HIV-related,

Disseminated intravascular coagulation

Haemolytic – uraemic syndrome/thrombotic thrombocytopenic purpura

Acute fatty liver of pregnancy

Folate deficiency

Congenital platelet disorders

Coincidental marrow disease

Type IIb von Willebrand disease

Hypersplenism

Purpose and scope:

These guidelines educate readers about the causes of different types of thrombotic thrombocytopenic purpura and its prenatal counselling and management. It also provides a standardized approach to thrombotic thrombocytopenic purpura, emphasizing the search for prenatally treatable conditions and etiologies.

Target groups:

Perinatologists, Obstetricians, Internist

Thrombotic Thrombocytopenic Purpura

DEFINITIONS:

Thrombotic thrombocytopenic purpura (TTP) and haemolytic – uraemic syndrome (HUS) share the central features of microangiopathic anaemia or MAHA and thrombocytopenia.

Importance:

Thrombotic thrombocytopenic purpura (TTP) is a rare but potentially fatal blood disorder.

These are not pregnancy-specific, although they occur with increased frequency during or in relation to pregnancy. 20% or more of the included patients developed disease during pregnancy or the immediate postpartum period.

PATHOGENESIS and ETIOLOGIES:

▶ Acquire: auto ab inhibitor (95%)

more commonly, TTP is acquired and due to autoantibodies that inhibit plasma ADAMTS13 activity, referred to as immune-mediated TTP

▶ Hereditary: mutation in ADAMS13 (5%)

TTP may be caused by inherited severe deficiency of plasma ADAMTS13 activity resulting from mutations in ADAMTS13, referred to as hereditary or congenital TTP

Diagnosis:

Symptoms:

- ▶ Fatigue
- ▶ Dyspnea
- ▶ Petechia

- Dizziness
- N/W
- Abdominal pain
- ‘CNS, GI
- Fever
- Neurologic Finding (headache, confuse, coma, stroke, SZ)

TTP Pantad:

- MAHA
- Thrombocytopenia
- Fever
- ARF
- Severe neurologic finding

PBS confirm

- Fragment RBC (8 %), schistocyte, > - HPF
- Polychromasia
- NRBC (malignancy)
- Microsherocyte (autoimmune)

Lab data :

- Hemolytic anemia
- High billirubin
- Low hoptoglobin
- High Retic
- High LDH
- Dark urine
- Hemoglobinuria

Neurologic findings:

- Confusion or headache 27%
- Focal abnormality 40%
- SZ 15 %
- Stroke 12%
- Coma 8 %
- Brain CT and MRI often normal, small silent infarction or with PRE

Prenatal management

First all causes of thrombocytopenia should be considered and if diagnosis is confirmed, the initial management of TTP/HUS during pregnancy does not differ from that of the non-pregnant patient. Delivery does not generally cause resolution of TTP and is not routinely indicated, although it may be required if TTP is associated with pre-eclampsia.

Clinical Evaluation

Calculator: PLASMIC score for estimating the likelihood of severe ADAMTS13 deficiency in adults with suspected TTP

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- ☐ Platelet count <30,000/microL
- ☐ One or more indicators of hemolysis:
  - Reticulocyte count (percentage) >2.5%; or
  - Haptoglobin undetectable; or
  - Indirect bilirubin >2.0 mg/dL [>34 mcmol/L]
- ☐ No active cancer in the preceding year
- ☐ No history of solid organ or hematopoietic stem cell transplant
- ☐ Mean corpuscular volume (MCV) <90 femtoliters
- ☐ International normalized ratio (INR) <1.5
- ☐ Creatinine <2.0 mg/dL [<177 mcmol/L]

Total criteria point count: 0

Reset form

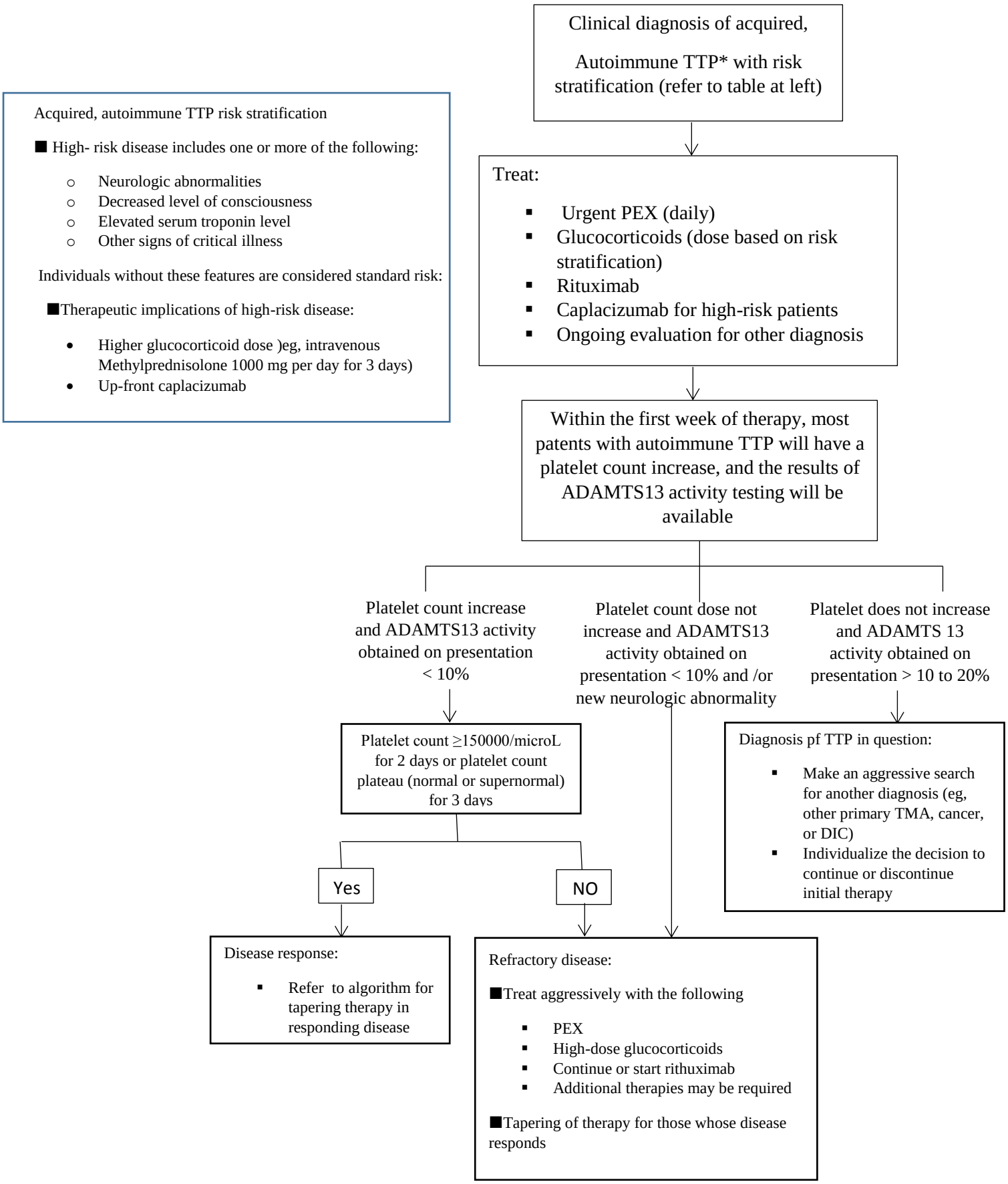
Interpretation

PLASMIC score (points)	Risk of severe ADAMTS13 deficiency
0 to 4	Low risk
5	Intermediate risk
6 to 7	High risk

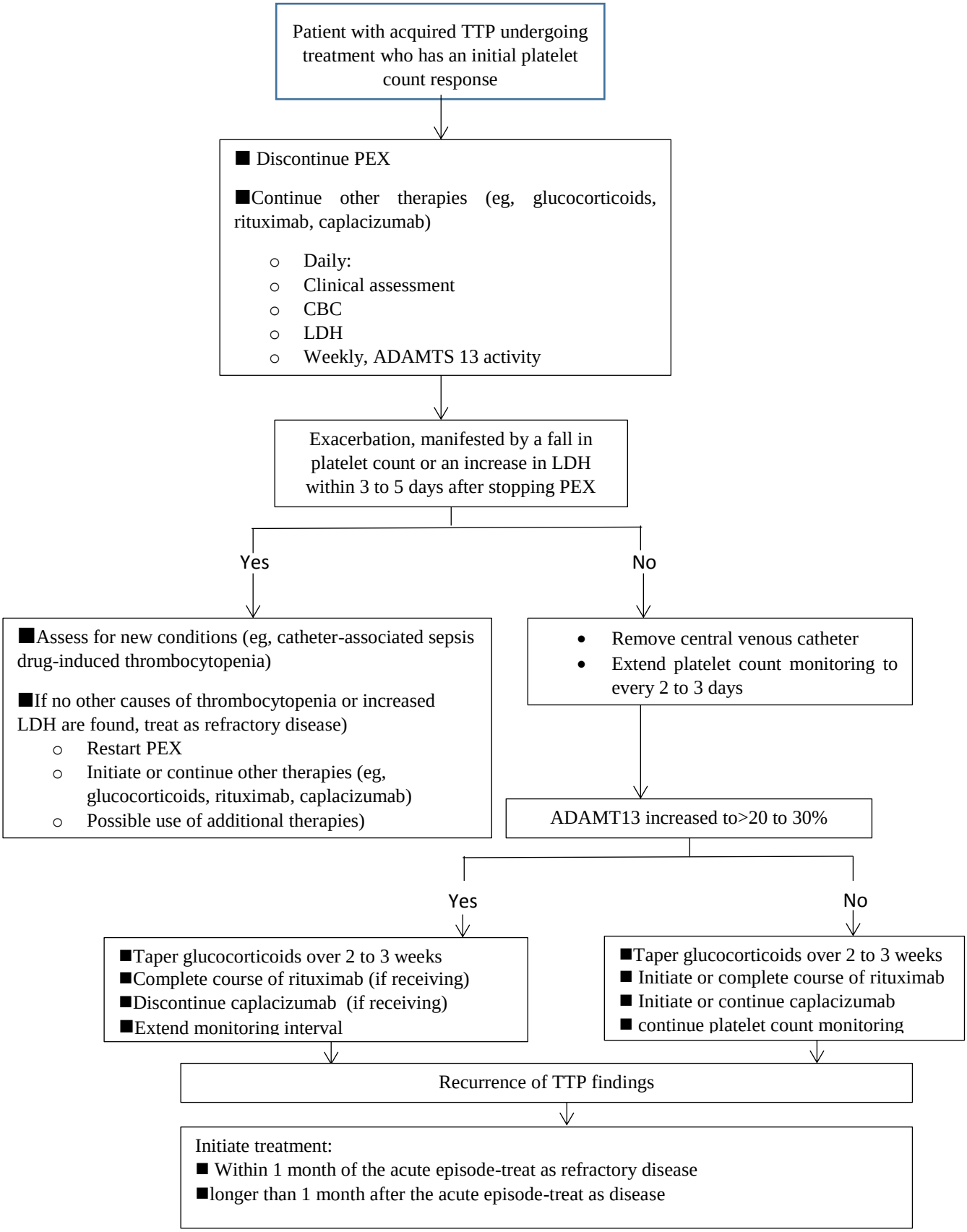
Notes

Invasive Investigation, Management

Algorithm for the initial treatment of acquired, autoimmune thrombotic thrombocytopenic purpura (TTP)


Clinical diagnosis of acquired,
Autoimmune TTP* with risk stratification (refer to table at left)
Acquired, autoimmune TTP risk stratification
■ High- risk disease includes one or more of the following:
Neurologic abnormalities
Decreased level of consciousness
Elevated serum troponin level
Other signs of critical illness
Individuals without these features are considered standard risk:
■Therapeutic implications of high-risk disease:
Higher glucocorticoid dose)eg, intravenous Methylprednisolone 1000 mg per day for 3 days)
Up-front caplacizumab
Treat:
Urgent PEX (daily)
Glucocorticoids (dose based on risk stratification)
Rituximab
Caplacizumab for high-risk patients
Ongoing evaluation for other diagnosis
Within the first week of therapy, most patents with autoimmune TTP will have a platelet count increase, and the results of ADAMTS13 activity testing will be available
Platelet count increase and ADAMTS13 activity obtained on presentation < 10%
Platelet count dose not increase and ADAMTS13 activity obtained on presentation < 10% and /or new neurologic abnormality
Platelet does not increase and ADAMTS 13 activity obtained on presentation > 10 to 20%
Platelet count ≥150000/microL for 2 days or platelet count plateau (normal or supernormal) for 3 days
Diagnosis pf TTP in question:
Make an aggressive search for another diagnosis (eg, other primary TMA, cancer, or DIC)
Individualize the decision to continue or discontinue initial therapy
Yes
NO
Disease response:
Refer to algorithm for tapering therapy in responding disease
Refractory disease:
■Treat aggressively with the following
PEX
High-dose glucocorticoids
Continue or start rithuximab
Additional therapies may be required
■Tapering of therapy for those whose disease responds

Algorithm for tapering therapy after an initial response in a patient with acquired, autoimmune thrombotic thrombocytopenic purpura (TTP)



Prognosis

Pregnancy in TTP :

- Most pregnancy after recovery of TTP are successfully
- Risk of PE and relapse
- Hematologist and perinatology : close follow up
- CBC and ADAMS13 activity
- PLT < 100000 : evaluation
- Before pregnancy ADAMS 13 activity check
- If < 20 % start TX
- If remain < 20 no absolute contraindication for pregnancy but increase risk of and relapse and close absorb monitoring
- PE 38 %
- Increase risk of IUFD , pregnancy lost , FGR
- The same TX in non pregnant

Conclusion, Pregnancy in TTP:

- Near term and several weeks post partum
- Normal BP and neurologic finding
- Severe hemolysis
- AST – ALT normal
- Kidney injury mild
- Not improve after delivery (trigger of relapse)
- Flare of lupus : AKI

REFERENCES