

Let's talk about TTP: An iberian collaboration for the diagnosis and follow-up of this rare disease



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Congress on Thrombosis

From initial suspicion to long-term follow-up

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Declaration of Conflict Of Interest

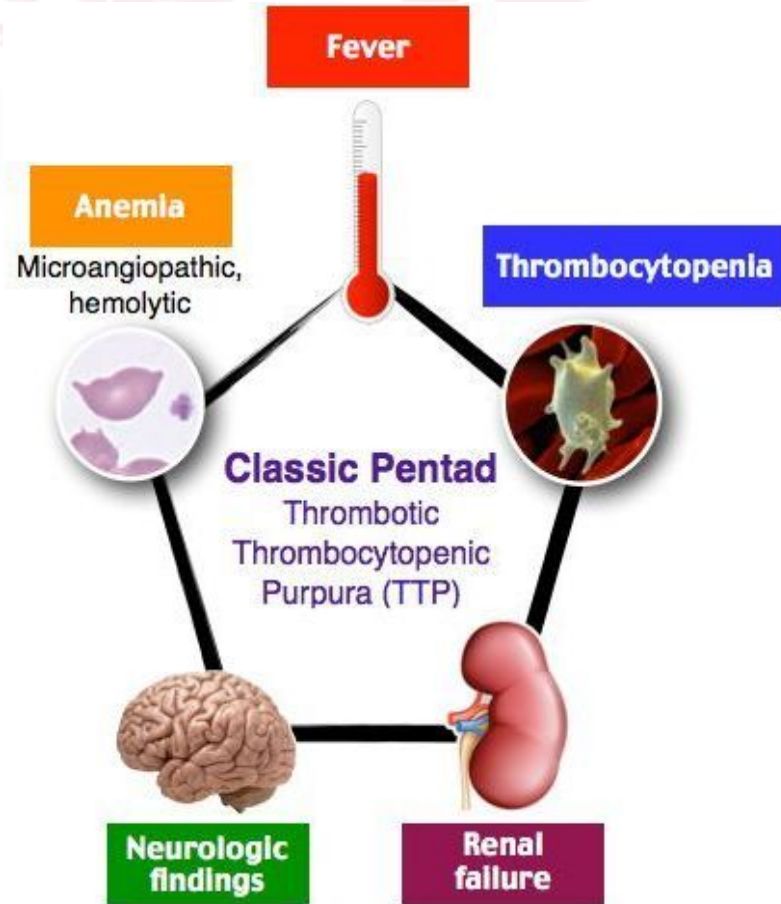
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What is the challenge? The big simulator!

■ Epidemiology and natural history

- Rare disease (aTTP 90% and congenital < 10% - in adults is related with pregnancy)
- 2-4/million
- More frequent in females (2-3:1), and african ancestry
- Plasmapheresis dramatically reduced mortality (up to 5-16%)

What is the challenge? The big simulator!



Signs and symptoms	
Low Platelets	Bleeding symptoms
CNS	Headaches, focal signs of dysfunction
FEVER	
AHMA	Jaundice
Renal lesion	Proteinuria
Cardiac Lesion	Thoracic pain, Rhythm dysfunction
GI	Abdominal pain
General Symptoms	Asthenia, Myalgia

What is the challenge? The big simulator!

■ Diagnosis

- MAT with ADAMTS13 act <10% (acquired form if Ab's positive - Anti-ADAMTS13)
- Not all labs have installed capacity to perform these tests, but the main point is suspicion.



How to suspect? When to suspect?

Table 3. Comparison of clinical prediction scores for severe ADAMTS13 deficiency

	PLASMIC score	French score, points	Bentley score, points
Component of score			
Platelet count	<30 × 10 ⁹ /L: 1 point	≤30 × 10 ⁹ /L: 1 point	>35 × 10 ⁹ /L: -30 points
Creatinine level	<2 mg/dL: 1 point	≤2.26 mg/dL: 1 point	>2 mg/dL: -11.5 points
Parameters of hemolysis	Reticulocyte count >2.5%: 1 point	—	Reticulocyte: >3% +21 points Indirect bilirubin >1.5 mg/dL: +20.5 points
	Haptoglobin undetectable: 1 point Indirect bilirubin >2 mg/dL: 1 point		
Associated conditions	No active cancer: 1 point No history of solid-organ or hematopoietic stem cell transplant: 1 point	—	—
MCV	<90 fL: 1 point	—	—
INR	<1.5: 1 point	—	—
ANA	—	Positive: 1 point	—
D-dimer	—	—	>4 mcg/mL: -10 points
Interpretation			
Risk category, total score			
Low	0-4	0	<20
Intermediate	5	1	20-30
High	6-7	2-3	>30

How to suspect? When to suspect?

Variables	Points*
Platelet count $<30 \times 10^9$ per L	1
Hemolysis variable†	1
No active cancer	1
No history of solid-organ or stem-cell transplant	1
MCV <90 fL	1
INR <1.5	1
Creatinine <2.0 mg/dL	1
INR: International normalized ratio. MCV: Mean corpuscular volume.	
†Reticulocyte count $>2.5\%$, or haptoglobin undetectable, or indirect bilirubin >2.0 mg/dL.	

High Risk6

96,2% risk of severe ADAMTS 13 deficiency

Discussion – Our experience with Prediction scores

Comparative Analysis of Clinical Prediction Scores in Acquired Thrombotic Thrombocytopenic Purpura: The superiority of PLASMIC score

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SPH 2020; ASH 2020

Discussion – Our experience with Prediction scores

AIM:

- To compare the discriminative power of the Bentley, French and PLASMIC scores in predicting severe ADAMTS13 deficiency ($\leq 10\%$)
- To evaluate the scores applicability in our center

METHODS:

- We performed a retrospective analysis of patients with ADAMTS13 activity tested between 2008 and 2019.
- ADAMTS13 activity and IgG anti-ADAMStT13 were studied by ELISA (TECHNOZYM®).

SPH 2020; ASH 2020



Discussion – Our experience with Prediction scores

- PLASMIC score was calculated in all patients (119 patients with suspected TTP)
- Due to missing data, Bentley score was only applied in 44.5% (n=53) and French score in 54.6% (n= 65) patients.

Table 3. Correlation between clinical prediction scores and ADAMTS13 activity using a high-risk score cut-off vs low-to-intermediate-risk score

	PLASMIC SC	BENTLEY SC	FRENCH SC
SENSIVITY	80,6%	44,4%	83,3%
SPECIFICITY	78,4%	94,3%	36,2%
PPV	56,8%	80 %	33,3%
NPV	92%	76,7%	85%

- There were not statistically significant differences between PLASMIC and Bentley scores in the ability to predict low ADAMTS13 activity, and both performed better than French score ($p < 0.001$; $p = 0.02$, respectively)

SPH 2020; ASH 2020



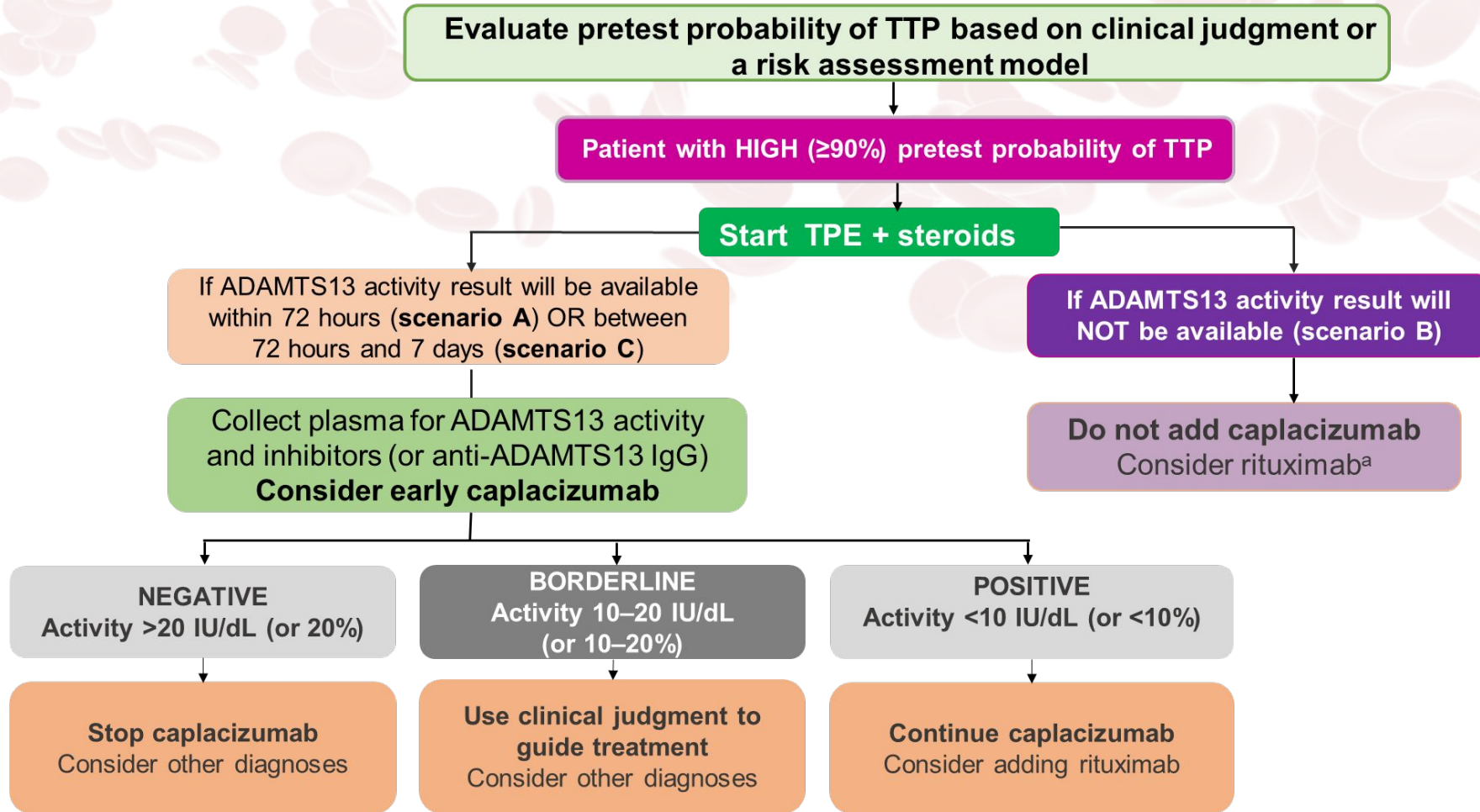
Treatment strategies

General

Blood collection: activity and Ab's anti-ADAMTS13 (BEFORE ANY INTERVENTION)

- ❑ Plasma Exchange (1,0 volemia with inac Human Plasm)
- ❑ Corticotherapy - 1mg/Kg/dia of PDN
- ❑ Folic acid 5mg id

Treatment strategies



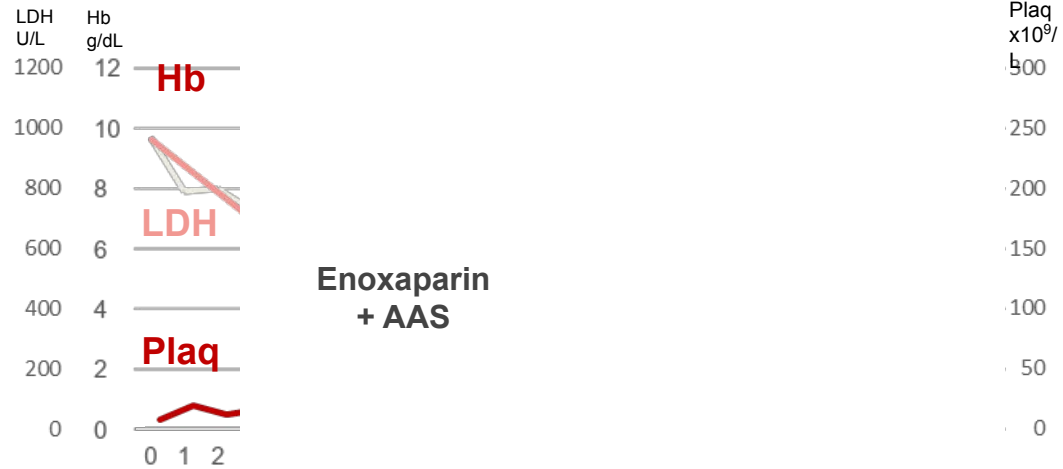
Treatment strategies

♀, 46 years
Abdominal pain
Jaundice
Confusion

Plat $7 \times 10^9/L$
Hb 9,7g/dL
VGM 84,3fL
Reti $112 \times 10^9/L$ (3,5%)
INR 1,0
Cr 0,82mg/dL
LDH 960U/L (N<247)
BRB total 5,1mg/dL
BRB indiret 4,3mg/dL
TAD negativ



PDN 1mg/Kg/dia



**Rituxima
b**

ADAMTS13 0%
ab 79U/mL

PlasmaEx

**Caplacizuma
b**

PlasmaEx
Bidaily

ADAMTS13 26%
ab 12U/mL

aTTP score 7