XI congresso nazionale

simeu

ROMA 24-26 MAGGIO 2018

sospetto diagnostico e diagnosi differenziale in pronto soccorso

fiorella paladino
&
il gruppo di lavoro ps/obi
aorn cardarelli napoli

overview

- IDENTIFICAZIONE PAZIENTI A RISCHIO
- PERCHE' IMPORTANTE
- PERCHE' DIFFICILE
- SUPPORTO EGDT
- IMPORTANZA APPROCCIO MULTIDISCIPLINARE

Caso clinico

- Paz di 72 aa giunge in PS alle ore 12.26 per vomito insorto da 3 giorni
- No diarrea
- No febbre
- Pregresso k colon operato molti anni prima- in terapia con ASA

EO

- Lieve pallore
- Addome trattabile
- PV nella norma
- Piccoli ematomi della cute delle mani riferiti presenti da mesi

Codice Aux: 13/060625
Accettata il: 11/04/2018 14.38.49

Richiesta : 2018117201
Modalità : **Emergenza**
Diuresi :

Note:

Reparto Dest.: Pronto Soccorso
Richiedente :
Paziente : [redacted]
Data di Nascita :
Codice Triage:
Codice Fiscale : ZZINNT45L57F839Z

Diagnostica Ematologica - 747-3706

Globuli Bianchi	8,53	x10^3/ul	(4,0 - 10,0)
Globuli Rossi	* 3,61	x10^6/ul	(4,2 - 5,4)
Emoglobina	* 10,8	g/dl	(12,0 - 16,0)
Ematocrito	* 32,7	%	(36 - 46)
MCV	90,6	fl	(82 - 97)
MCH	29,9	pg	(26 - 32)
MCHC	33,0	g/dl	(32 - 37)
Piastrine	* 37	x10^3/ul	(150 - 400)

Codice Aux: 13/060625
Accettata il: 11/04/2018 14.38.49

Richiesta : 2018117201
Modalità : **Emergenza**
Diuresi :

Note:

Reparto Dest.: Pronto Soccorso
Richiedente :
Paziente : [redacted]
Data di Nascita :
Codice Triage:
Codice Fiscale :

U.O.S. di Diagnostica delle Coagulopatie - 747-3706

Tempo di Protrombina			
INR	1,16		0.80 - 1.20
Tempo di Tromboplastina Parz.			
Ratio	0,97		0.7 - 1.3
Fibrinogeno	386	mg/dl	150 - 450

Codice Aux: 13/060625
Accettata il: 11/04/2018 14.38.49

Richiesta : 2018117201
Modalità : **Emergenza**
Diuresi :

Note:

Reparto Dest.: Pronto Soccorso
Richiedente :
Paziente : [redacted]
Data di Nascita :
Codice Triage
Codice Fiscale :

U.O.S. di Biochimica Clinica - 747-3705

Glucosio	* 138	mg/dl	70 - 110
Urea	42	mg/dl	15 - 50
Creatinina	* 0,99	mg/dl	0,5 - 0,9
Sodio	* 130	mEq/L	136 - 145
Osmolarita'	267	mOsm/L	260 - 290
Potassio	4,0	mEq/L	3,5 - 5,1
Proteine Totali	6,9	g/dl	6,6 - 8,7
Albumina	4,0	g/dl	3,5 - 5,0
Bilirubina Totale	* 1,96	mg/dl	0,0 - 1,2
Bilirubina Diretta	* 0,70	mg/dl	0,0 - 0,3
Bilirubina Indiretta	* 1,26	mg/dl	0,0 - 0,9
AST (GOT)	21	UI/L	fino a 40
ALT (GPT)	17	UI/L	fino a 40
GGT	15	UI/L	5 - 36
Alfa-Amilasi	* 27	UI/L	28 - 100
Troponina I	0,22	ng/ml	< 0.3
Calcio	9,4	mg/dl	8,6 - 10,2

Ecoaddome neg. Diretta : qualche livellino in centro addome

Antonio Cardarelli
AZIENDA OSPEDALIERA DI RILIEVO NAZIONALE

2018/23886

A.O.R.N. 'A. CARDARELLI'

VERBALE DI PRONTO SOCCORSO

Cartella P.S.: 2018/23886 , 11/04/2018 12:26

Assistito/a: [redacted]
Sesso: F **Na**
Tess.Sanita 339Z
Residenza:
Via: V.POG

Codice Triage: GIALLO
Motivo di accesso: Altri sintomi o disturbi
Modalita' di accesso: Autonomo (arrivato con mezzi propri)
Provenienza: Decisione Propria
Operatore triage: BENEVENTO PATRIZIA

Note d'ingresso:
Lesioni traumatiche:
Data e Ora:
Luogo incidente: -
Cause e circostanze dichiarate:

APERTURA: 11/04/2018 ore:13:22

CHIUSURA: 11/04/2018 ore:16:19

Esito: DIMISSIONE A STRUTTURE AMBULATORIALI
Diagnosi: Nausea con vomito [78701] -
Descrizione aggiuntiva diagnosi:EPIGASTRALGIA E VOMITO TRE GG FA AL MOMENTO ASINTOMATICA
Prognosi di gg:
Referto di Autorita' giudiziaria:
Note e Prescrizioni: gli esami eseguiti in ps hanno evidenziato piatrinopenia (37000), in assenza di sanguinamenti in atto. la pz e' in terapia con asa senza alcun motivo apparente. si consiglia di sospendere cardioaspirina, terapia con deltacortene 25 mg 1 cp per tre giorni consecutivi e gastroprotezione, movicol 1 bust per tre volte al giorno. venerdÃ¬ esegua di nuovo emocromo e visru epatite b e c e li mostri al curante. si raccomanda di restare sotto controllo per pregressa neoplasia colon. si affida al curante

- Il giorno successivo ritorna in PS per comparsa di disartria ed ipostenia arto superiore dx

Codice Aux: **13/061625**
Accettata il: 13/04/2018 02.50.13

Richiesta : *2018119148*
Modalità : **Emergenza**
Diuresi :

Note:

Reparto Dest.: Pronto Soccorso

[redacted]A

Codice Fiscale : ZZINNT45L57F839Z

Diagnostica Ematologica - 747-3706

Globuli Bianchi	* 15,67	x10^3/ul	(4,0 - 10,0)
Globuli Rossi	* 3,94	x10^6/ul	(4,2 - 5,4)
Emoglobina	12,0	g/dl	(12,0 - 16,0)
Ematocrito	* 35,9	%	(36 - 46)
MCV	91,1	fl	(82 - 97)
MCH	30,5	pg	(26 - 32)
MCHC	33,4	g/dl	(32 - 37)
Piastrine	* 26	x10^3/ul	(150 - 400)

Striscio: Alcuni schistociti
Coomb negativo
LDH 1400
Prelievo per Adamts 13

Codice Aux: **13/061625**
Accettata il: 13/04/2018 02.50.13

Richiesta : *2018119148*
Modalità : **Emergenza**
Diuresi :

Note:

Reparto Dest.: **Pronto Soccorso**
Richiedente : *Pronto Soccorso*
Paziente : [redacted]
Data di Nascita :
Codice Triage
Codice Fiscale :

U.O.S. di Biochimica Clinica - 747-3705

Glucosio	* 175	mg/dl	70 - 110
Urea	* 59	mg/dl	15 - 50
Creatinina	* 0,96	mg/dl	0,5 - 0,9
Sodio	* 130	mEq/L	136 - 145
Osmolarita'	274	mOsm/L	260 - 290
Potassio	4,6	mEq/L	3,5 - 5,1
Proteine Totali	7,7	g/dl	6,6 - 8,7
Albumina	4,0	g/dl	3,5 - 5,0
Bilirubina Totale	* 3,26	mg/dl	0,0 - 1,2
Bilirubina Diretta	* 0,86	mg/dl	0,0 - 0,3
Bilirubina Indiretta	* 2,40	mg/dl	0,0 - 0,9
AST (GOT)	* 42	UI/L	fino a 40
ALT (GPT)	32	UI/L	fino a 40
GGT	33	UI/L	5 - 36
Alfa-Amilasi	28	UI/L	28 - 100
Troponina I	0,19	ng/ml	< 0.3
Calcio		mg/dl	8,6 - 10,2

SOSPETTO CLINICO DI TMA

DANNO D'ORGANO (almeno 1)

GASTROINTESTINALI
Dolore addominale
Nausea
Diarrea
Diarrea sanguinolenta

S.N.C.
Confusione
Crisi epilettiche
Convulsioni
Coma

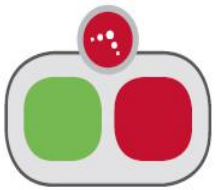
RENALI
Oligo-anuria
Edemi
Creatininemia > V.N.
Proteinuria
Micro/Macroematuria

ALTRI
Affaticamento/astenia
Porpora/Petecchie
Dispnea
Ipertensione
Febbre

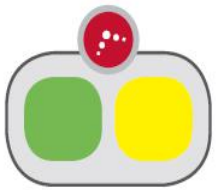
EMOLISI MICROANGIOPATICA

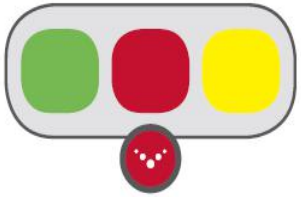
PIASTRINOPENIA
PLT<150.000 o
riduzione PLT<25%

EMOLISI
Aumento LDH>V.N. o
ai limiti superiori V.N.
(se Hb<V.N. verificare LDH)



SE PRESENTE 1 SOLO TRA PIASTRINOPENIA E EMOLISI, RIPETERE IL DOSAGGIO DOPO 24 ORE





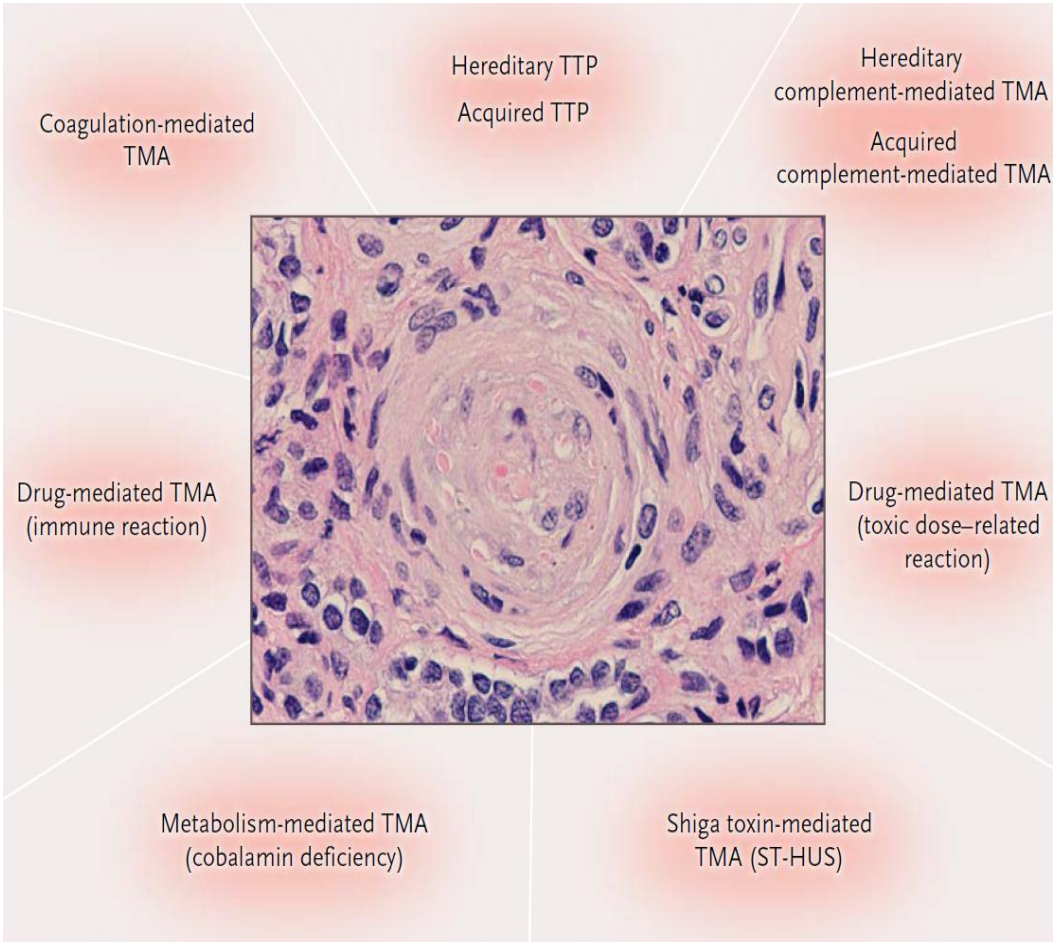
The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

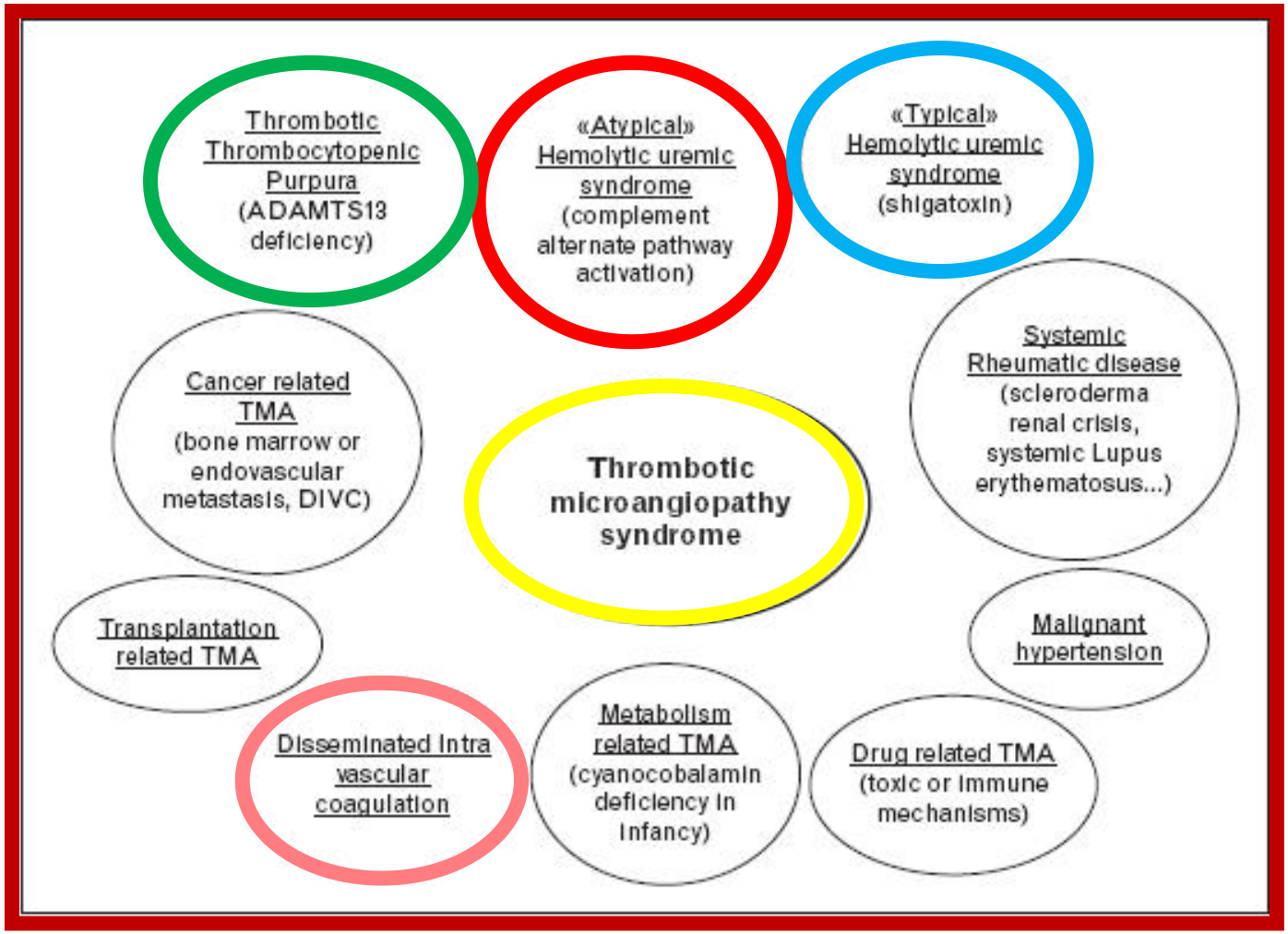
Dan L. Longo, M.D., *Editor*

Syndromes of Thrombotic Microangiopathy

James N. George, M.D., and Carla M. Nester, M.D.



MICROANGIOPATIE TROMBOTICHE



thrombocytopenic purpura Mariotte and Veyradier 2015

Review

Massimo Franchini*

Atypical hemolytic uremic syndrome: from diagnosis to treatment

Abstract: Thrombotic microangiopathy (TMA) is a relatively rare condition but a medical urgency requiring immediate intervention to avoid irreversible organ damage or death. Symptoms on presentation include microangiopathic haemolytic anaemia, thrombocytopenia and organ damage. The most frequent direct causes of TMA are thrombotic thrombocytopenic purpura (TTP) and haemolytic uremic syndrome (HUS). The most common form of HUS is related to Shiga toxin producing *Escherichia coli* (STEC) infection while approximately 10% of cases are due to dysregulation of the complement pathway (atypical haemolytic uremic syndrome, aHUS). Optimal treat-

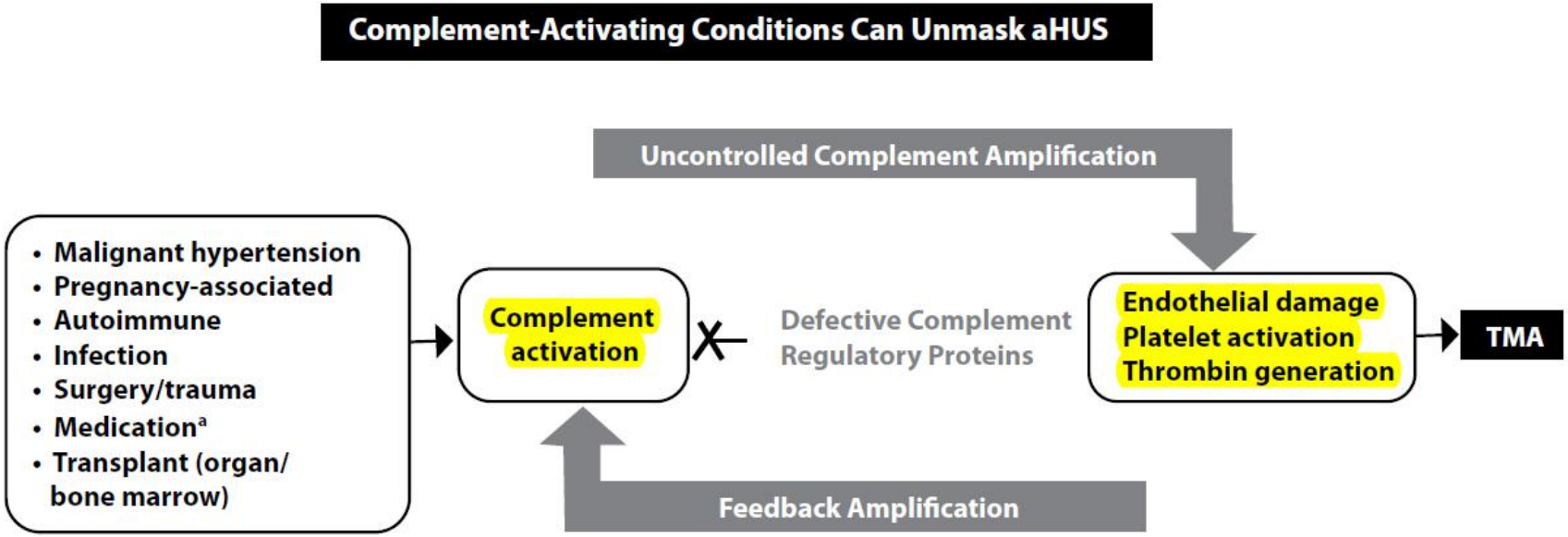


Figure 3. aHUS is a TMA linked to the inability to regulate the alternative complement pathway. This defect sets up a positive feedback loop among generation of the terminal complement components C5a (an anaphylatoxin) and C5b-9 (MAC), endothelial cell activation/injury, and thrombin generation. In approximately two-thirds of cases, a complement-activating condition can be temporally linked to an unmasking of aHUS in a susceptible individual. However, some of those disorders—such as those listed in the box at the left of the diagram—can themselves cause a TMA-like disorder. It is imperative to treat those conditions, but if the signs and symptoms of the TMA do not resolve following such therapy, one should consider a diagnosis of unmasked aHUS. In some situations, renal, cutaneous, or other tissue biopsy may be required.

REVIEW

Thrombotic thrombocytopenic purpura: from diagnosis to therapy

Eric Mariotte[a] *and Agnès Veyradier*[b]

Curr Opin Crit Care 2015,

Thrombotic thrombocytopenic purpura (TTP) is a rare but challenging disease for intensive care specialists. Patients with acute TTP frequently require admission to the intensive care unit because of organ dysfunctions due to the disease or because of the risk of sudden aggravation at the onset of the disease. This review aims at describing recent evolutions in the diagnosis and for the management of TTP for the use of intensive care specialists.

- Earlier recognition of TMA syndrome in pauci/ asymptomatic patients with early introduction of plasma exchange therapy may continue to improve outcome.

Table 1. Possible organ involvement and clinical presentations of acute thrombotic thrombocytopenic purpur

Organ involvement	Clinical presentation	Biological/radiological presentation
Neurologic	Cephalalgia	Normal radiology
	Focal deficiency	Ischemic/hemorrhagic stroke
	Seizure	Posterior reversible encephalopathy syndrome
	Altered conscience	
Cardiologic	Angina	Nonspecific ECG changes
	Myocardial infarction	Raised cardiac enzymes
	Cardiac failure	Radiologic/echographic signs of cardiac failure
Renal	Hypertension	Uremia
	Oliguria	Hypercreatininemia
	Proteinuria	Acute renal failure
	Hemoglobinuria	
Digestive	Abdominal pain	Digestive tract microangiopathy
	(Bloody) diarrhea	Mesenteric ischemia

Marie Scully,[1] Beverley J. Hunt,[2] Sylvia Benjamin,[3] Ri Liesner,[4] Peter Rose,[5] Flora Peyvandi,[6] Betty Cheung,[7] Samuel J. Machin[8] and on behalf of British Committee for Standards in Haematology

Recommendation

1 The diagnosis of TTP should be treated as a medical emergency (1A).

2 The initial diagnosis of TTP should be made on clinical history, examination and routine laboratory parameters of the patient, including blood film review (1A).

3 In view of the high risk of preventable, early deaths in TTP, treatment with PEX should be initiated as soon as possible, preferably within 4–8 h, regardless of the time of day at presentation, if a patient presents with a MAHA and thrombocytopenia in the absence of any other identifiable clinical cause (1B).

4 Serological tests for HIV, hepatitis B virus and hepatitis C virus, autoantibody screen and when appropriate, a pregnancy test, should be performed at presentation (1A).

5 Pre-treatment samples should be obtained to measure ADAMTS13 activity levels and to detect anti-ADAMTS13 antibodies. Measurement of ADAMTS 13 antigen levels is also useful in congenital TTP cases (1B).

VWF excess and ADAMTS13 deficiency: a unifying pathomechanism linking inflammation to thrombosis in DIC, malaria, and TTP

Michael Schwameis[1]; Christian Schörgenhofer[1]; Alice Assinger[2]; Margarete M. Steiner[1]; Bernd Jilma[1]
[1]Department of Clinical Pharmacology; [2]Centre of Physiology and Pharmacology, Institute of Physiology, Medical University of Vienna, Vienna, Austria

Thrombosis and Haemostasis 113.4/2015

Often TTP follows an acute episode of inflammation, which possibly triggers autoantibody formation (56, 57).

The unifying pathology linking both systemic inflammation and primary TMAs is acute dysfunctional endothelial cell activation, indicated by high VWF antigen (VWFAg) and VWF propeptide (VWFpp) in both sepsis and TTP (58, 59).

	TTP	DIC	Malaria
PLT	↓↓↓*	↓↓(↓)	↓(↓↓)
Anaemia	MHA~	MHA~	§
PT	↔	↑	#
Fibrinogen	↔, ↑	↓↓	#
D-dimer	↔, ↑(↑)	↑↑	#
FRC	↑↑↑**	↑(↑)	#
LDH	↑↑↑	↑(↑↑)	↑(↑↑)#
Thrombus	platelet-rich	fibrin-rich	variable
ADAMTS13	absent	variable	variable

Newly Proposed Sepsis-Induced Coagulopathy Precedes International Society on Thrombosis and Haemostasis Overt-Disseminated Intravascular Coagulation and Predicts High Mortality

Journal of Intensive Care Medicine
1-7

DOI: 10.1177/0885066618773679
journals.sagepub.com/home/jic
SAGE

Abstract

Background: Disseminated intravascular coagulation (DIC) has been recognized as an urgent and critical condition in patients with sepsis. Therefore, unfamiliar and time-consuming tests or a complex scoring system are not suitable for diagnosis. Sepsis-induced coagulopathy (SIC), a newly proposed category delineated by a few global coagulation tests, has been established as an early warning sign for DIC. The purpose of this study was to elucidate the characteristics of SIC, especially in relation to the score of the International Society on Thrombosis and Haemostasis (ISTH) for overt DIC. **Method:** A data set for 332 patients with sepsis who were suspected to have DIC, antithrombin activity <70%, and treated with antithrombin substitution was utilized to examine the relationship between SIC and overt DIC. The performance of SIC calculated at baseline (ie, before treatment) as well as on days 2, 4, or 7 was analyzed in terms of its ability to predict 28-day mortality and overt DIC. **Results:** At baseline, 149 (98.7%) of 151 patients with overt DIC according to the ISTH definition were diagnosed as having SIC. Of the 49, 46 (93.9%) patients who developed overt DIC between days 2 and 4 had received a prior diagnosis of SIC. The sensitivity of baseline SIC for the prediction of death was significantly higher than that of overt DIC (86.8% vs 64.5%, $P < .001$). The sensitivity of SIC on days 2, 4, and 7 was significantly higher than those of overt DIC (96.1%, 92.3%, and 84.4% vs 67.1%, 57.7%, and 50.0%, $P < .001$, .001, and .001, respectively), although the specificity of SIC was lower at all time points.

Table 1. SIC and ISTH Overt DIC Scoring Systems.[a,b]

Points	SIC	ISTH Overt DIC
Platelet count ($\times 10^9$/L)		
2	<100	<50
1	≧100, <150	≧50, <100
FDP or D-dimer		
3	–	Strong increase
2	–	Moderate increase
1	–	–
Prothrombin time (PT)		
2	>1.4	≧6 seconds
1	>1.2, ≦1.4	≧3, <6 seconds
Fibrinogen (g/mL)		
1	–	<100
Total SOFA score		
≧2	2	–
1	1	–

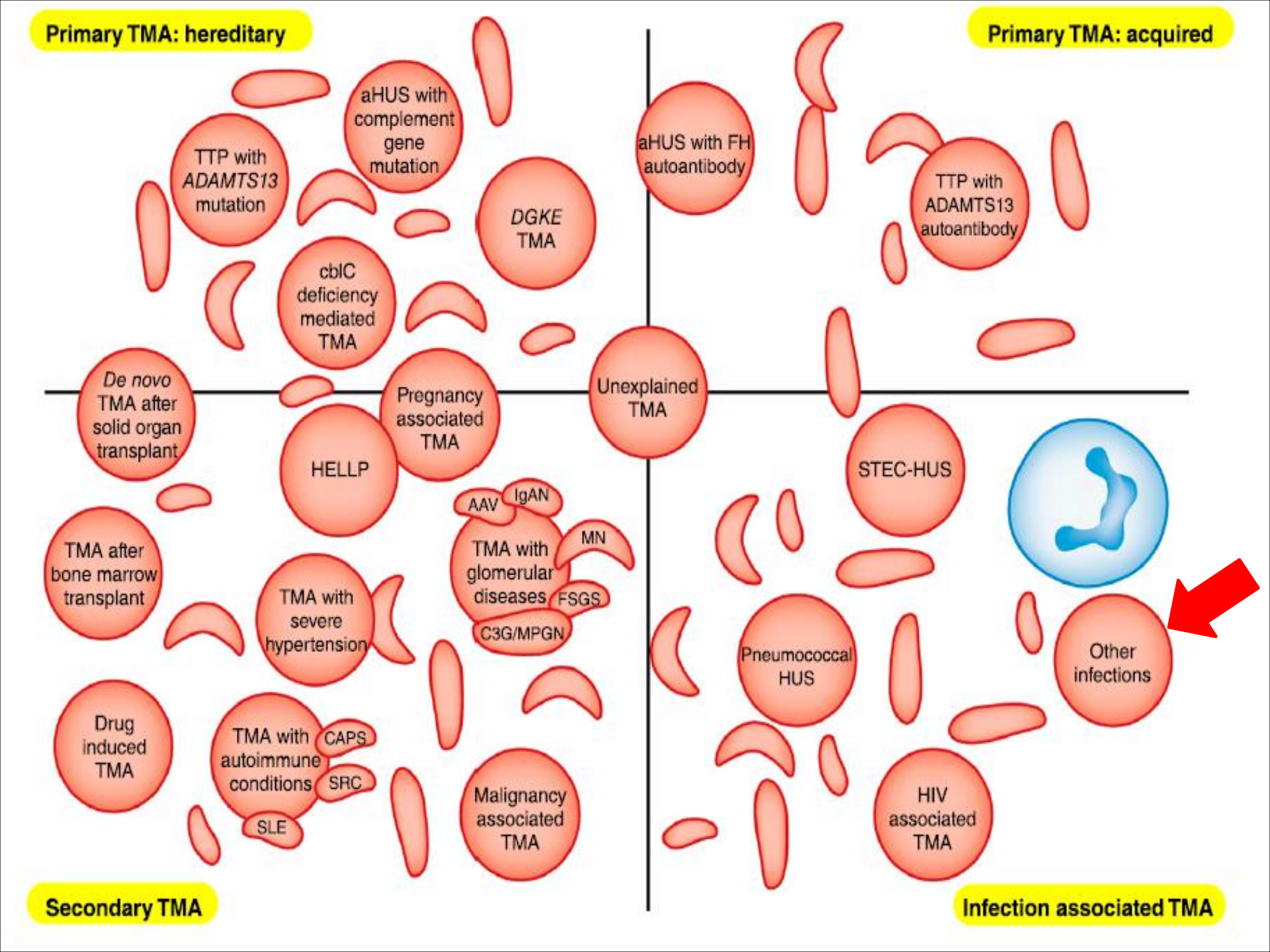
SOFA Score

The European Society of Intensive Care Medicine

SOFA score	0	1	2	3	4
Respiration PaO_2FiO_2 or SaO_2/FiO_2 mmHg	>400	<400 221-301	<300 142-220	<200 67-141	<100 <67
Coagulation	>150	<150	<100	<50	<20
Liver Birilubin(mg/dl)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular Hypotension	No hypotension	MAP <70	Dopamine ≤5 or any	Dopamine >5 or notepinephrine ≤0.1	Dopamine >15 or norepinephrine >0.1
CNS (GCS)	15	13-14	10-12	6-9	<6
Renal Creatinine (mg/dl) or urine output (ml/d)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or <5.00	>5.0 or <200

piastrine

Krongdaiu@nu.ac.th


Primary TMA: hereditary
Primary TMA: acquired
aHUS with complement gene mutation
TTP with ADAMTS13 mutation
DGKE TMA
cblC deficiency mediated TMA
aHUS with FH autoantibody
TTP with ADAMTS13 autoantibody
De novo TMA after solid organ transplant
Pregnancy associated TMA
Unexplained TMA
HELLP
STEC-HUS
AAV
IgAN
MN
TMA with glomerular diseases
FSGS
C3G/MPGN
TMA after bone marrow transplant
TMA with severe hypertension
Pneumococcal HUS
Other infections
Drug induced TMA
TMA with autoimmune conditions
CAPS
SRC
SLE
Malignancy associated TMA
HIV associated TMA
Secondary TMA
Infection associated TMA

Dewitte *et al. Ann. Intensive Care (2017) 7:115*
DOI 10.1186/s13613-017-0337-7

Annals of Intensive Care

REVIEW Open Access

Blood platelets and sepsis pathophysiology: A new therapeutic prospect in critical ill patients?

Antoine Dewitte[1,2*], Sébastien Lepreux[1,3], Julien Villeneuve[4], Claire Rigothier[1,5], Christian Combe[1,5], Alexandre Ouattara[2,6] and Jean Ripoche[1]

Abstract

Beyond haemostasis, platelets have emerged as versatile effectors of the immune response. The contribution of platelets in inflammation, tissue integrity and defence against infections has considerably widened the spectrum of their role in health and disease. Here, we propose a narrative review that first describes these new platelet attributes. We then examine their relevance to microcirculatory alterations in multi-organ dysfunction, a major sepsis complication. Rapid progresses that are made on the knowledge of novel platelet functions should improve the understanding of thrombocytopenia, a common condition and a predictor of adverse outcome in sepsis, and may provide potential avenues for management and therapy.

LA DIAGNOSI DIFFERENZIALE DELLE MICROANGIOPATIE TROMBOTICHE (TMA)

SOSPETTO CLINICO DI TMA

DANNO D'ORGANO (almeno 1)

GASTROINTESTINALI
Dolore addominale
Nausea
Diarrea
Diarrea sanguinolenta

S.N.C.
Confusione
Crisi epilettiche
Convulsioni
Coma

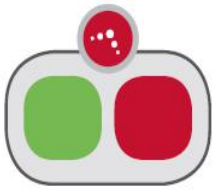
RENALI
Oligo-anuria
Edemi
Creatininemia > V.N.
Proteinuria
Micro/Macroematuria

ALTRI
Affaticamento/astenia
Porpora/Petecchie
Dispnea
Ipertensione
Febbre

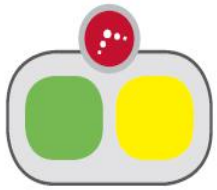
EMOLISI MICROANGIOPATICA

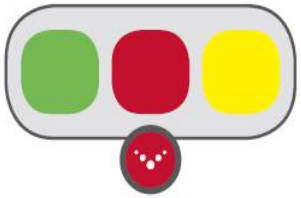
PIASTRINOPENIA
PLT<150.000 o
riduzione PLT<25%

EMOLISI
Aumento LDH>V.N. o
ai limiti superiori V.N.
(se Hb<V.N. verificare LDH)



SE PRESENTE 1 SOLO TRA PIASTRINOPENIA E EMOLISI, RIPETERE IL DOSAGGIO DOPO 24 ORE





CONFERMA DIAGNOSTICA

SCHISTOCITOSI: presenza di schistociti allo striscio periferico (specificare % e numero/campo)

APTOGLOBINA: riduzione dei livelli ematici<V.N.

TEST DI COOMBS: negatività al test (se positivo escludere possibile autoimmunità)

COAGULAZIONE: test nel range di normalità

N.B.: conservare campione di plasma e campione di feci in questa fase prima di qualsiasi trattamento
Modalita'di raccolta prelievo, richiesta in direzione sanitaria di invio prelievo, corriere convenzionato tel:081 19312346.
chiamarlo subito per prenotare ritiro giorno successivo con pacco e ghiaccio secco.
CENTRO DI RICERCA "Rene e Trapianto" UOC Nefrologia Dialisi e Trapianto AO Cosenza
Per SAGGIO ELISA ADAMTS-13

DIAGNOSI DIFFERENZIALE TMA

VALUTARE L'ATTIVITÀ DELL'ADAMTS-13 E LA PRESENZA DI SHIGA-TOX/EHEC *(Escherichia Coli Enteroemorragico)*

Attività ADAMTS-13<5%	Attività dell'ADAMTS-13>5%	Positività alla Shiga-tox/EHEC Laboratorio di biochimica Dott. .....
PTT	**SEUa**	**STEC-SEU**


TRATTAMENTO
SU VALUTAZIONE DEL CLINICO NEL COMPLESSO DELLA PRESENTAZIONE SINDROMICA
Eventuale Plasma Exchange/Plasma Infusion come trattamento empirico se esclusa STEC-SEU e in attesa di ADAMTS-13
PTT
SEUa
STEC-SEU
Plasma-Exchange
Eculizumab
Osservazione/Idratazione-SEU

Table 3. Recommendations for management of adult patients with suspected aHUS in the ICU.

1. Obtain adequate diagnostic samples before plasma therapy
2. Make use of multidisciplinary care, including nephrologists and haematologists
3. Initiate plasma therapy within 4–8 h of admission or diagnosis of TMA. For patients with an initial presentation of TMA, switch to eculizumab as soon as a diagnosis of aHUS is confirmed (ADAMTS13 > 10% and STEC negative); for patients with a history of previous aHUS, initiate eculizumab immediately upon admission to the ICU
4. Careful ICU monitoring should be offered as organ dysfunction may appear or worsen until remission
5. Owing to the increased risk of *Neisseria meningitidis* infection with eculizumab treatment, patients should be vaccinated against serotypes A, C, Y and W135 and subtype B 2 weeks before eculizumab is initiated; unvaccinated individuals should receive prophylactic antibiotics upon eculizumab initiation until at least 2 weeks after *Neisseria meningitidis* vaccination (please refer to country-specific guidelines).

Expert statements on the standard of care in critically ill adult patients with atypical haemolytic uraemic syndrome

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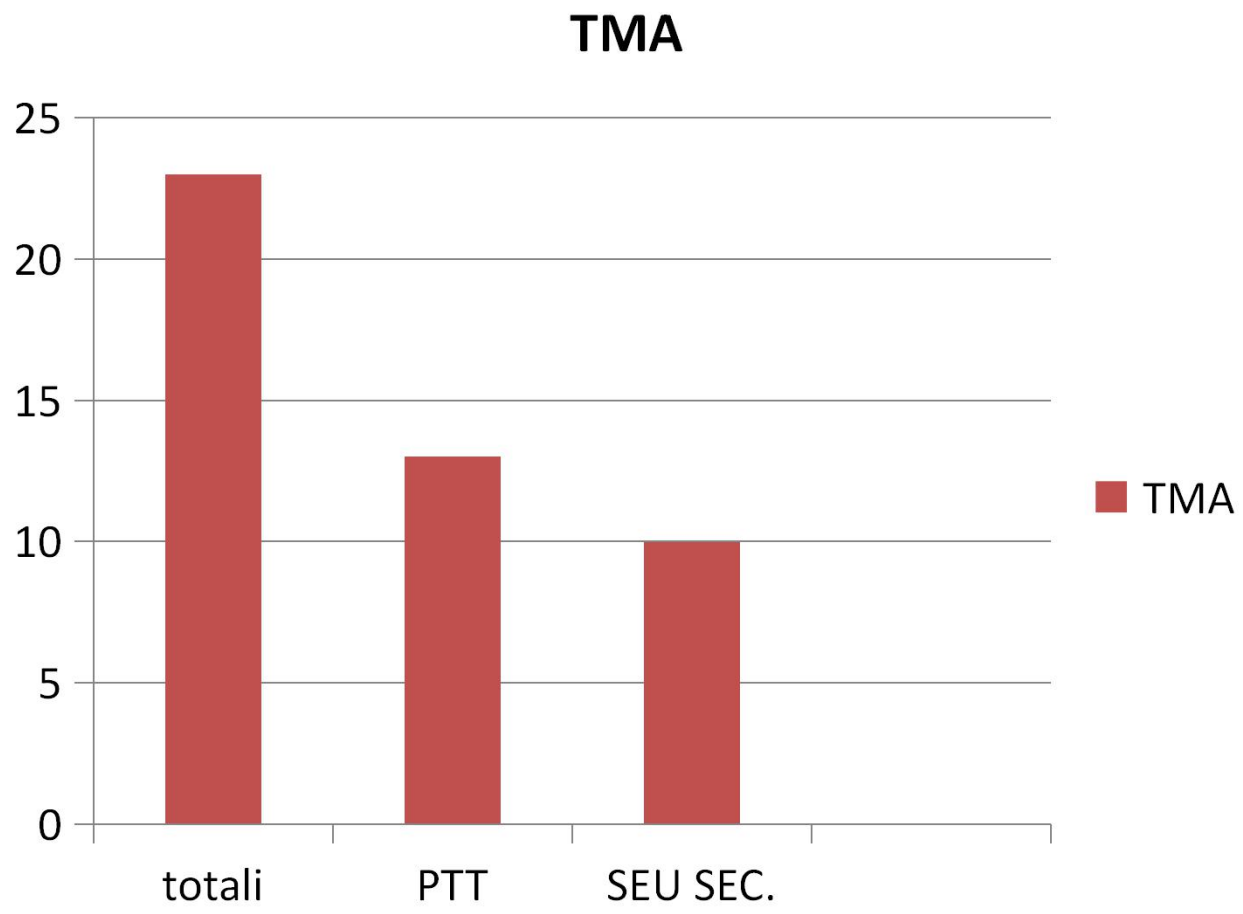
Nostra esperienza dall' 1/3/17 al 1/05/18



Accessi totali 42671

Considerazioni

- TMA vera emergenza e forse non così rara
- Necessaria più capillare diffusione culturale e ruolo del medico d'urgenza
- Protocolli condivisi con ematologi, nefrologi, trasfusionali ed infettivologi
- Audit clinici