UNIVERSITÀ CATTOLICA del Sacro Cuore

CONVEGNO MICROANGIOPATIE TROMBOTICHE UCSC 2016

Roma, 19 febbraio 2016
Fondazione Policlinico Universitario A. Gemelli
Largo Agostino Gemelli, 8 - 00168 Roma (Aula Brasca)

Responsabili scientifici: V. De Stefano - G. Gambaro - L. Pagano - S. Sica

Casistica clinica di PTT e SEU
Aspetti intensivistici

A. Caricato

Reparto di Rianimazione

Fondazione Policlinico Universitario "A. Gemelli"

Early diagnosis

Without treatment mortality rate 90%.

Up to 50% of deaths occurring within the first 24 h of presentation

Overall mortality rate 20%

Time from first clinical manifestation of the disease to the onset of plasmatherapy correlated to prognosis

Early diagnosis
High index of suspicion

- ✓Microangiopathic anemia
- ✓Peripheral thrombocytopenia
- ✓(Organ dysfunction)

Organ involvement and clinical presentation

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

bjh annotation

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A proposal: the need for thrombotic thrombocytopenic purpura Specialist Centres – providing better outcomes

Tina Dutt[1] **and Marie Scully**[2]

[1]*Roald Dahl Haemostasis and Thrombosis Centre, Royal Liverpool University Hospital, Liverpool, and* [2]*Department of Haematology, University College London Hospital, London, UK*

British Journal of Haematology, 2015, **170**, 737–742

Case 1

45 yrs drug abuse
Jaundice, hematuria
Plt 10.000
Diagnosis of sepsis
Transfused
Dead during 2° PEX

Key points

1 Diagnostic challenges exist even for seniors/specialists who are unfamiliar with seeing this patient group.
2 Delayed diagnosis and treatment impacts on survival.

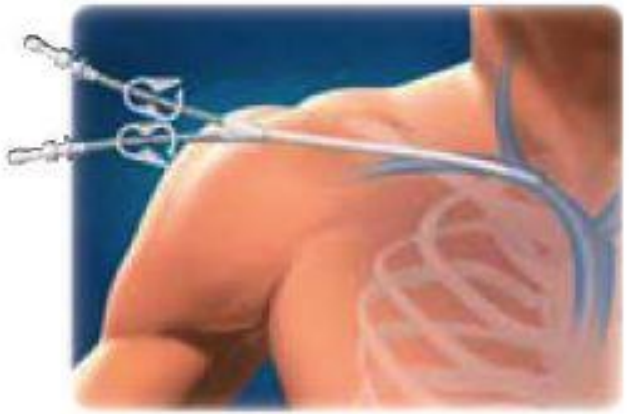
Case 2

43 yrs
Hematuria
Plt 23.000
Urology
Transfused
Day 3 PEX considered
Confused with limb weakness
Dead during transferring

Key points

1 There is a lack of awareness of potentially life threatening causes of thrombocytopenia and the urgent intervention required to diagnose TTP.
2 Neurological features indicate a severe clinical course and poor prognosis.
3 Treatment should not be delayed pending imaging as this rarely alters acute management.

Plasma exchange and CVC positioning



Platelet transfusion ?

VoxSanguinis
The International Journal of Transfusion Medicine

ISBT International Society of Blood Transfusion

Vox Sanguinis (2014) **106**, 161–166

DOI: 10.1111/vox.12090

ORIGINAL PAPER

Characterization of the complications associated with plasma exchange for thrombotic thrombocytopaenic purpura and related thrombotic microangiopathic anaemias: a single institution experience

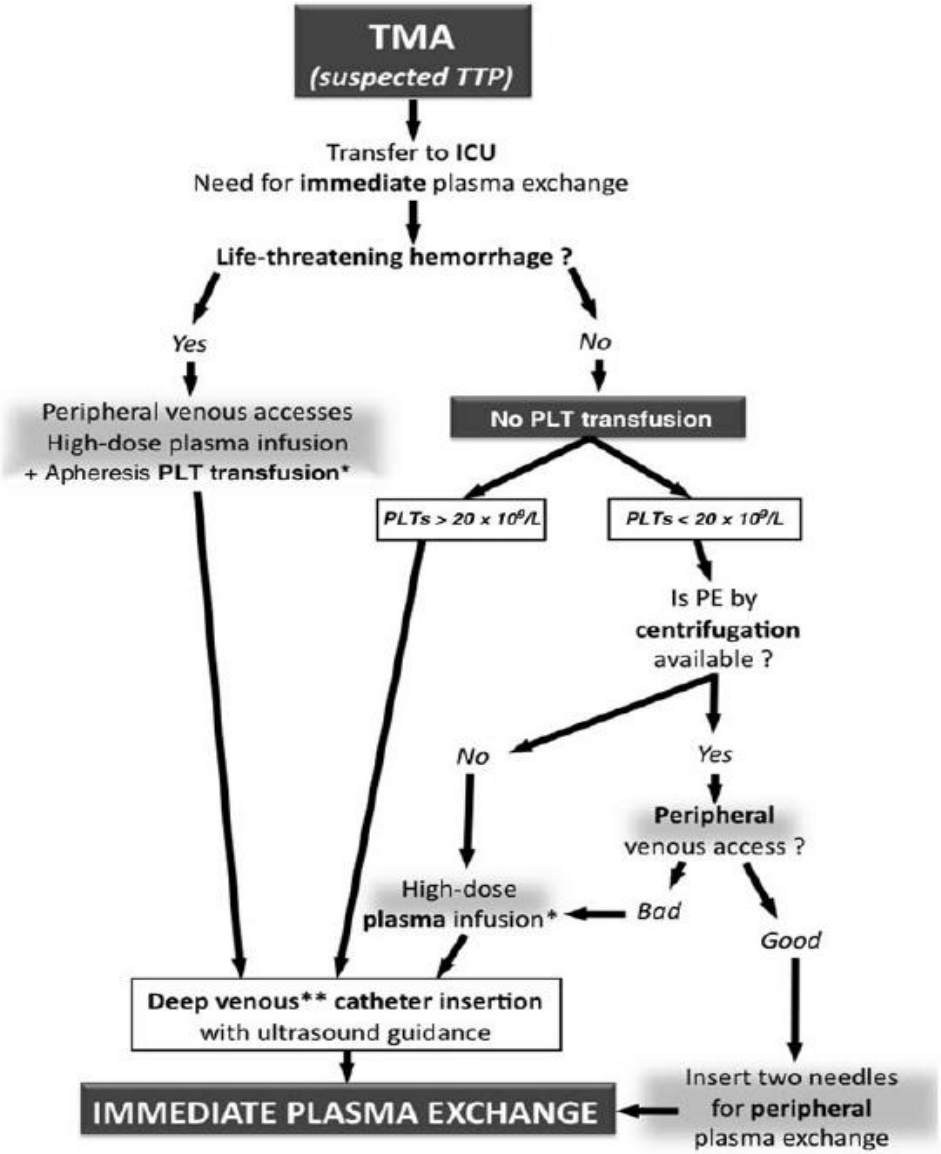
S. McGuckin,[1] J.-P. Westwood,[1] H. Webster,[2] D. Collier,[1] D. Leverett[1] & M. Scully[1]

[1] *University College London Hospitals, London, UK*

[2] *University College London, London, UK*

267 Central Venous Lines
No bleeding
No pneumotorax
13 CVC related sepsis

No platelet approach



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CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

Guidelines 2011

7. Usare la guida ecografica per posizionare i cateteri venosi centrali (ovunque questa tecnologia sia disponibile) così da ridurre il numero di tentativi di incannulamento e le complicanze meccaniche da venipuntura. La guida ecografica dovrebbe essere utilizzata da personale pienamente addestrato nell'utilizzo di questa tecnica. [60–64]. Categoria 1B

RApid CEntral Vein Assessment protocol

GAVeCeLT
Gli Accessi Venosi Centrali a Lungo Termine

Terapia intensiva?

Indication to ICU

- Organ failure
  - Myocardial ischemia
  - Neurological deterioration
  - Renal impairment
- Hemorrhagic complications
- Hydroelectrolytic balance

Outcome
Univariate analysis

	Survivors (N=248)	Non-survivors (N=33)	P
Ethnicity			
Caucasians	209 (86)	29 (85)	0.70
Afro-Caribbeans	26 (11)	3 (9)	
Others	9 (4)	0	
Age (years old)	39.2±15.7	56.5±19.4	10-6
Females	167 (67)	23 (70)	0.79
Cardiovascular risk factors and pre-existing comorbidities			
Arterial hypertension	25 (10)	11 (33)	5.10^{-4}
Diabetes	16 (6)	3 (9)	0.57
Ischemic stroke	6 (2)	0 (0)	0.37
Ischemic heart disease	11 (4)	5 (15)	0.013
Cerebral involvement	145 (59)	27 (82)	0.018
Headache	62 (25)	5 (15)	0.21
Stupor	34 (14)	10 (30)	0.014
Seizure	16 (6)	7 (21)	0.004
Focal deficiency	41 (17)	10 (30)	0.94
Fever	60 (25)	9 (28)	0.69
Hemoglobin level (g/dL)	7.9±2.0	7.9±2.5	0.73
Reticulocyte count (N=179)	202±126	157±91	0.15
LDH level (xN) (N=232)[$]	5.8±4.2	8.3±4.8	0.06
LDH ≥ 10N (%) (N=232)	22 (9)	6 (21)	0.05
Platelet count ($\times 10^9$/L)[$]	19.1±19.0	20.0±2	0.97
Serum creatinine (µmol/L)[$]	116±88	172±118	0.008
Estimated glomerular filtration rate (mL/min)[$]	72.1±31	50.8±33	5.10-5
ANA (N=253)	114 (50)	13 (52)	0.84
APLA (N=187)	18 (11)	2 (10)	0.86
ADAMTS13 inhibitor (N=177)	118 (74)	13 (72)	0.92
IgG anti-ADAMTS13 Abs (U/mL) (N=90)	97±106	183±366	0.28

Benhamou Haematologica 2012; 212; 97: 1181-1186

Outcome
Logistic regression

Table 4. Association between patients' characteristics and outcome by multivariable analysis.

	Odds Ratio	95% CI	*P*	Score
Cerebral involvement	2.6	[1.0, 6.9]	0.05	+1
Age			8.10^{-6}	
≤40	1	-		+0
41-60	3.4	[1.2, 9.7]		+1
> 60	10.6	[2.0, 32.0]		+2
LDH level ≥ 10N	3.0	[1.3, 11.6]	0.014	+1

Benhamou Haematologica 2012; 212; 97: 1181-1186

Outcome
Logistic regression

Table 3 Association between patients' characteristics and death by multivariable analysis

	Odds ratio (95% CI)	*P*
Troponin-I > 0.25 μg L^{-1}	**2.86 (1.13–7.22)**	**0.024**
Age (years)		
≤ 40	1	0.7
41–60	1.54 (0.49–4.87)	
> 60	1.76 (0.48–6.54)	
Neurologic involvement	1.66 (0.58–4.78)	0.4
eGFR	0.61 (0.23–1.63)	0.32

eGFR, estimated glomerular filtration rate (mL min−1); CI, confidence interval. $P < 0.05$ was considered to be statistically significant. Significant values appear in bold.

Benhamou J Thromb Haemost 2015; 13: 293-302

Unresponsive TTP

Second line treatment
More than 15 PEX
Death

Incidence 43%

	Odds ratio	Confidence interval 95 %	*P* value
Age >60 years old	7.90	1.06–78.34	0.04
Neurological signs at presentation			
Headaches	8.04	1.27–51.03	0.02
Severe symptoms	1.71	0.42–7.09	0.45
Cardiac signs at presentation[a]	3.44	1.63–16.39	<0.01
Platelet rate <15,000/µl at day 2	3.88	1.30–11.62	0.01

Mariotte E: Int Care Med 2013; 39: 1272-81

Supportive care in ICU

- Monitor level of consciousness, cerebral electric activity
- Prevention of cardiac failure
  - Low dose aspirin if PLT > $50*10^9$/l
- Blood transfusion (consider troponin)
- Strict blood pressure control
- Deep vein thrombosis prophylaxis
  - LMWH if PLT > $50*10^9$/l

Dimission from ICU

Clinical remission?

Normalization of neurological examination,
platelet count above 150.000,
normal lactic dehydrogenase (LDH) level,
and increasing hemoglobin level

Improvement?

Improvement of hemolytic activity,
peripheral thrombocytopenia,
and organ ischemia (LDH, troponin level)

Normalization of organ failure indexes?