“AVANÇOS NO DIAGNÓSTICO E TRATAMENTO DO SÍNDROMA HEMOLÍTICO URÉMICO”

Outubro 2014

Serviço de Nefrologia

Hospital Prof Dr Fernando Fonseca EPE

CASO CLINICO

Mulher, 45 anos, raça negra.

Antecedentes pessoais:
.HTA há 4 anos, não controlada
.Cirurgia hernia inguinal

Antecedentes familiares: irrelevantes

Medicação habitual:IECA.

Alergias: ⃠

PA 226-136 mm Hg T 36.4 º C
⃠ sobrecarga de volume; ⃠ lesões cutâneas, ⃠ discrasia hemorrágica, ⃠ défices neurológicos, ⃠ sinais meníngeos

Sindroma “gripal”
Hb 10.6 Plaq 135 000
urina II: Hb 1+ prot 100

Alta: Paracetamol, fosfomicina,

Diarreia aquosa, vómitos e dor abdominal

Lab:
Hb 11.5 g/dl Plaq 127 000 Leuc N
sCr 6.5 mg/dl ureia 89 mg/dl Bicarb 22 mmol/L Urina II: prot 100 Hb 1+ LDH 869 /L BilT 1.7 g/dl

Ecografia renal: 95 x98 mm; ↑ ecogenecidade

10.11.12

14.11.12

16.11.12

Lab:
Hb 8.9 g/dl Plaq 112 000 Leuc N
sCr 9.05 mg/dl ureia116 mg/dl

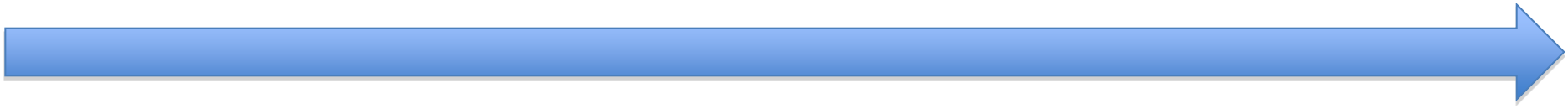
Indução HD

↓

Haptoglobina < 7, bilirrubina N
esquizócitos sangue periférico
Coombs negativo.

→ Anemia hemolítica microangiopática + trombocitopenia + lesão orgão

Microangiopatia trombótica



ceftriaxone → D 3

Diagnóstico Diferencial

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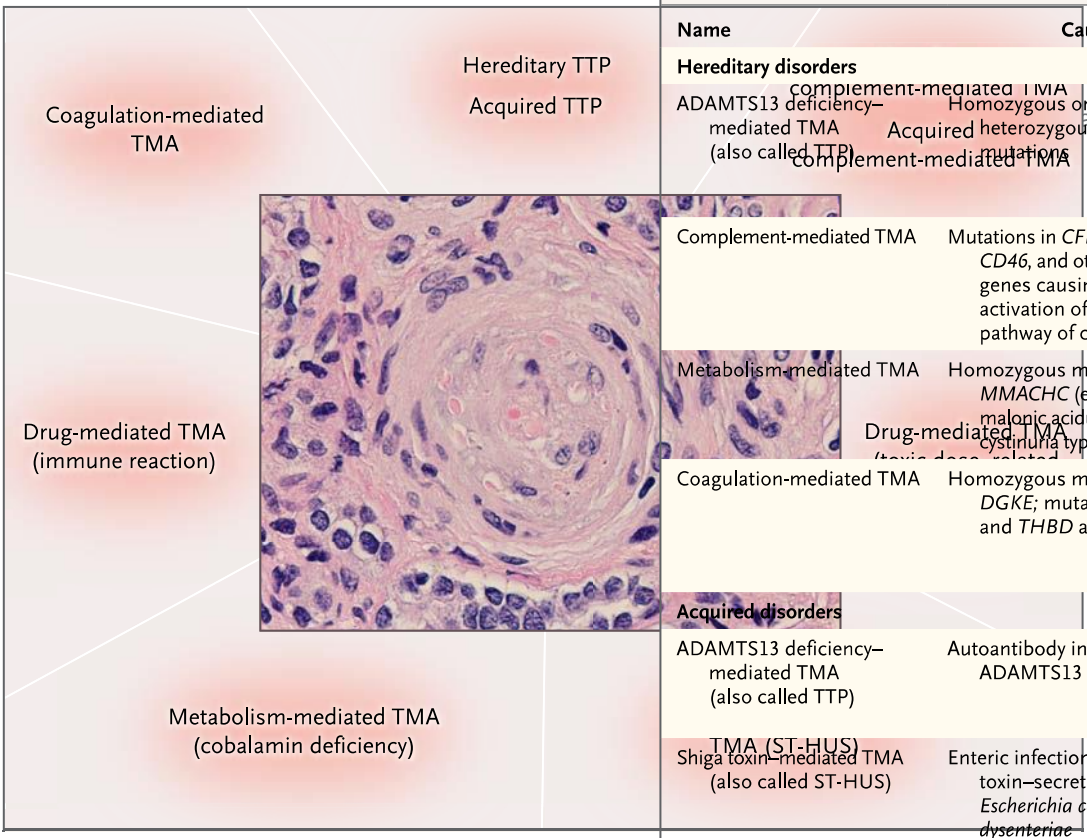


Figure 1. Pathological Features of the Nine Primary Thrombotic Mic

Table 1. Primary Thrombotic Microangiopathy (TMA) Syndromes.*

Name	Cause	Clinical Features	Initial Management
Hereditary disorders			
ADAMTS13 deficiency–mediated TMA (also called TTP)	Homozygous or compound heterozygous *ADAMTS13* mutations	Initial presentation is typically in children but may also be in adults; possible evidence of ischemic organ injury; acute kidney injury is uncommon; patients with heterozygous mutations are asymptomatic.	Plasma infusion
Complement-mediated TMA	Mutations in *CFH, CFI, CFB, C3, CD46*, and other complement genes causing uncontrolled activation of the alternative pathway of complement	Initial presentation is often in children but may also be in adults; acute kidney injury is common; patients with heterozygous mutations may be symptomatic.	Plasma infusion or exchange, anti-complement agent
Metabolism-mediated TMA	Homozygous mutations in *MMACHC* (encoding methylmalonic aciduria and homocystinuria type C protein)	Initial presentation is typically in children <1 year of age; also reported in one young adult with hypertension and acute kidney injury.	Vitamin B_{12}, betaine, folinic acid
Coagulation-mediated TMA	Homozygous mutations in *DGKE*; mutations in *PLG* and *THBD* also implicated	Initial presentation with acute kidney injury is typically in children <1 year of age with *DGKE* mutations; clinical features of disorders associated with other mutations have not been described.	Plasma infusion
Acquired disorders			
ADAMTS13 deficiency–mediated TMA (also called TTP)	Autoantibody inhibition of ADAMTS13 activity	Initial presentation is uncommon in children; often presents with evidence of ischemic organ injury; acute kidney injury is uncommon.	Plasma exchange, immunosuppression
Shiga toxin–mediated TMA (also called ST-HUS)	Enteric infection with a Shiga toxin–secreting strain of *Escherichia coli* or *Shigella dysenteriae*	Initial presentation is more common in young children, typically with acute kidney injury; most cases are sporadic; large outbreaks also occur.	Supportive care
Drug-mediated TMA (immune reaction)	Quinine and possibly other drugs, with multiple cells affected by drug-dependent antibodies	Initial presentation is a sudden onset of severe systemic symptoms with anuric acute kidney injury.	Removal of drug, supportive care
Drug-mediated TMA (toxic dose–related reaction)	Multiple potential mechanisms (e.g., VEGF inhibition)	Gradual onset of renal failure occurs over weeks or months.	Removal of drug, supportive care
Complement-mediated TMA	Antibody inhibition of complement factor H activity	Initial presentation is acute kidney injury in children or adults.	Plasma exchange, immunosuppression, anticomplement agent

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.

Table 2. Common Disorders Associated with Microangiopathic Hemolytic Anemia and Thrombocytopenia.*

Systemic infection
Systemic cancer
Severe preeclampsia, eclampsia, HELLP syndrome
Severe hypertension
Autoimmune disorders (e.g., systemic lupus erythematosus, systemic sclerosis, antiphospholipid syndrome)
Hematopoietic stem-cell or organ transplantation

Exames Complementares Diagnóstico

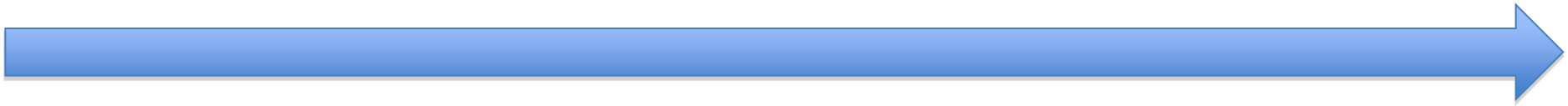
- Fundoscopia: exsudados algodonosos, sem edema da papila (grau III).
- Estudo HTA secundária negativa.
- TP e aPTT normais.
- C3 ↓ C4 N; ANA, dsDNA negativo; ANCA negativo
- Serologias HIV, HCV, HBV negativas. IgM CMV, adenovirus, HSV negativa
- Coproculturas negativas;
- Hemoculturas negativas.

Biópsia renal:
-infiltrado intersticial e glomerular exuberante;
-trombos intracapilares e edema endotelial
IF: C3 na IF

1.Plasmaferese 1.5 V x 5 sessões substituição PFC
2. HD

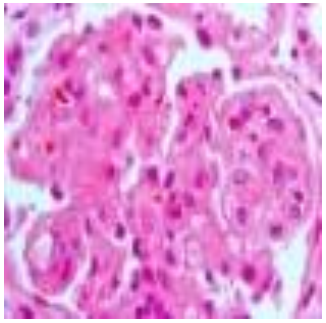
Estudo genético:
Mutação no gene CHF

Suspendeu HD após 18 dias.
Alta
sCr 4.14 mg/dl RAC 3

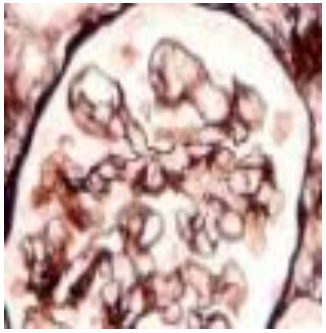


D 5

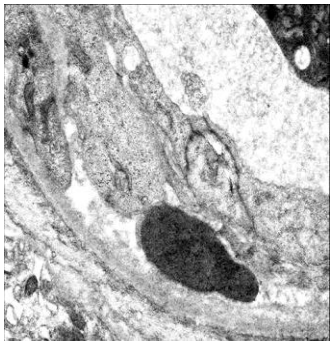
D 32



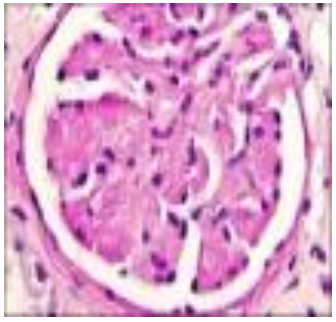
Global capillary oedema



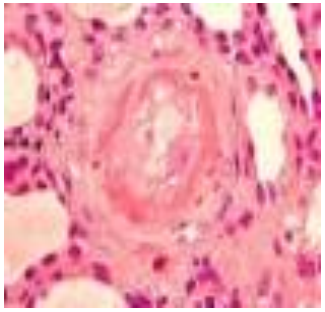
Double contours (Jones's silver)



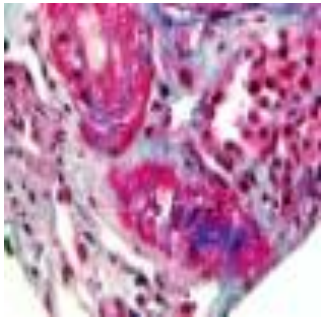
Oedema and erythrocyte in GCW



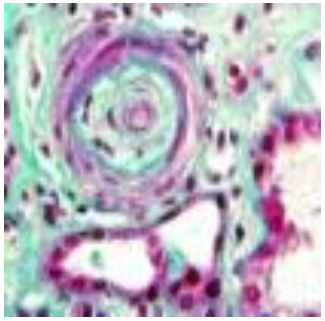
Global ischemic collasse. (PAS)



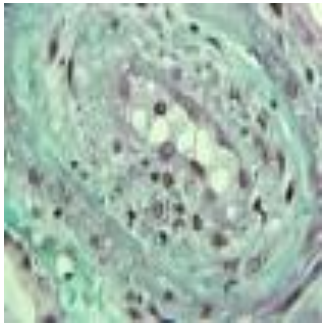
Intimal insudation and erythrocytic infiltration of arteriole



Fibrinoid necrosis of arteriole (Trichrome)



Severe reduction of arteriolar lumen, intimal oedema



Intimal oedema arteriole. (Trichrome)

SHUa Serviço de Nefrologia HFF

Patients	Mutações					Clinica			
	CFH	*MCP*	*CFI*	*CFB*	*C3*	Admissão	Último FU	Outcome	GFR (ml/min)
HUS_IF						08-07-01	18-09-01	HUS Dead	CRRT
HUS127	**c.89insA c.178T>C**	--	--	--	--	05-12-05	28-10-12	CKD5 D	RRT
HUS128	--	--	--	--	--	25-03-03	26-11-13	Partial recovery	40
HUS129	--	--	--	--	--	26-01-02	21-03-14	Total recovery	110
HUS143	**c.89insA**	**c.623T>C**	--	--	--	02-11-2003	28-03-14	2º HUS 2012	38
HUS143_P1	**c.89insA**	**c.623T>C**	--	--	--	01-10-2005	29-04-14	2º HUS 2010	49
HUS352	**c.3469T>C**	--	--	--	--	10-11-2012	06-10-2014	GNC3 Eculizumab	40
HUS_C	**c.493 G>T**	--				14-8-14	21-10-14	Partial recovery	17
C3_HUS						28-8-13	12-5-14	HUS Dead	RRT

Evolução

sCr 2.7 mg/dl CKD EPI 23 ml/min
RAC 0.7 sem hematuria
Hb 11.7 g/dl plaquetas N LDH N

sCr 3.9 mg/dl RAC 1 hematuria
Hb 10.0 g/dl haptoglobina ↓
HTA

2ª biopsia:
-Esclerose 6/15 gl
-Hipercelularidade mesangial MN
-Infiltrado intersticial intenso 30%
-IF: C3

Eculizumab 7 ciclos
até 08/14

sCr 2.9 mg/dl RAC 0.4
Hb 12.7 haptoglobina N

Out 2013 | Jan 2014 | Fev 2014 | Maio 2014 | Out 2014

Use of eculizumab for atypical haemolytic uraemic syndrome and C3 glomerulopathies

Julien Zuber, Fadi Fakhouri, Lubka T. Roumenina, Chantal Loirat and Véronique Frémeaux-Bacchi on behalf of the French Study Group for aHUS/ C3G

Zuber, J. *et al. Nat. Rev. Nephrol.* 8, 643–657 (2012);

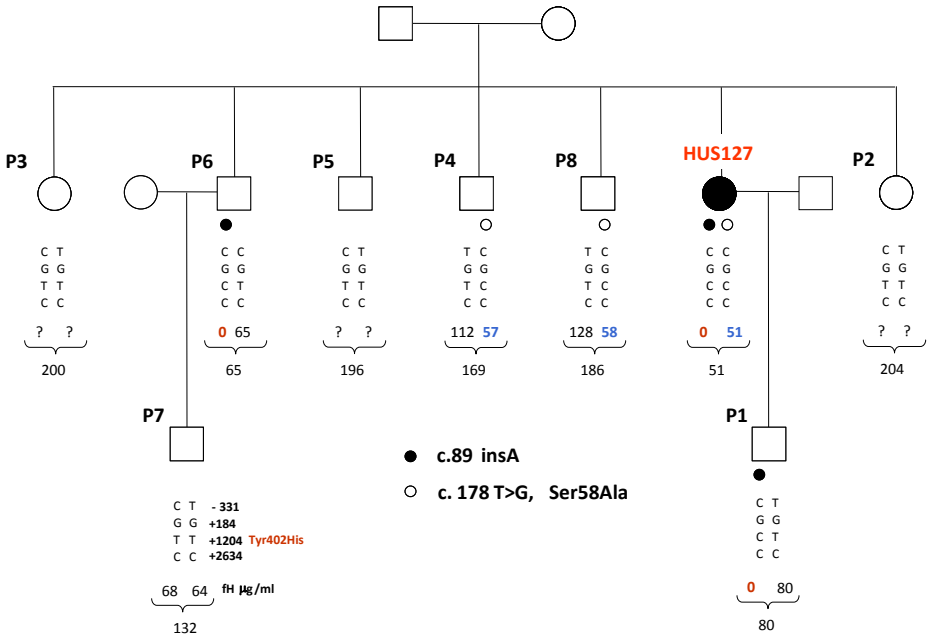
http://www.revistanefrologia.com

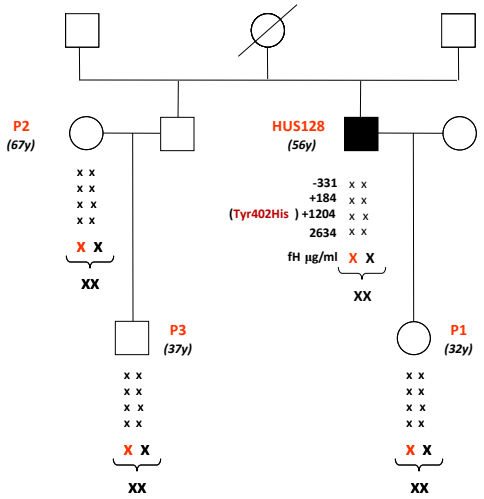
artículo especial

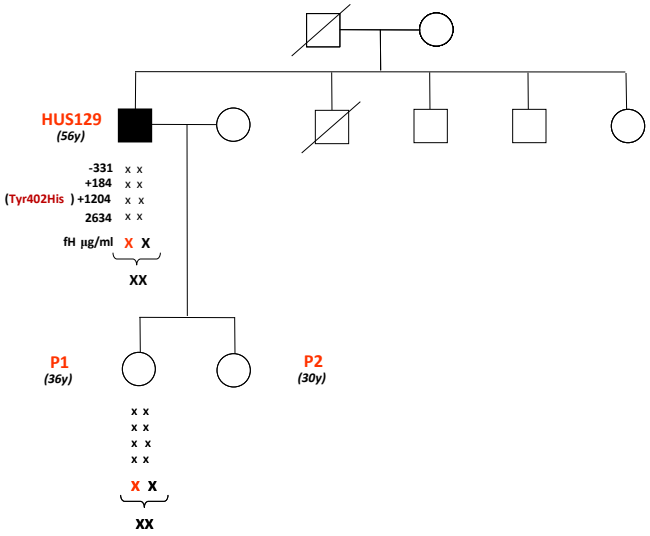
Actualización en síndrome hemolítico urémico atípico: diagnóstico y tratamiento. Documento de consenso

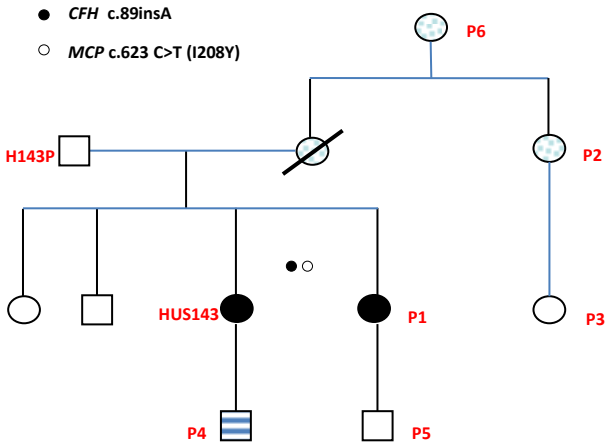
Josep M. Campistol[1], Manuel Arias[2], Gema Ariceta[3], Miguel Blasco[1], Mario Espinosa[4], Josep M. Grinyó[5], Manuel Praga[6], Roser Torra[7], Ramón Vilalta[3], Santiago Rodríguez de Córdoba[8]

Nefrologia 2013;33(1):27-45
doi:10.3265/Nefrologia.pre2012.Nov.11781


P3
P6
P5
P4
P8
HUS127
P2
P7
P1
C T
G G
T T
C C
? ?
200
C C
G G
C T
C C
0 65
65
C T
G G
T T
C C
? ?
196
T C
G G
T C
C C
112 57
169
T C
G G
T C
C C
128 58
186
C C
G G
C C
C C
0 51
51
C T
G G
T T
C C
? ?
204
C T - 331
G G +184
T T +1204 Tyr402His
C C +2634
68 64 fH µg/ml
132
C T
G G
C T
C C
0 80
80
c.89 insA
c. 178 T>G, Ser58Ala


P2
(67y)
HUS128
(56y)
x x
x x
x x
x x
X X
XX
-331 x x
+184 x x
(Tyr402His) +1204 x x
2634 x x
fH µg/ml X X
XX
P3
(37y)
P1
(32y)
x x
x x
x x
x x
X X
XX


HUS129
(56y)
-331 x x
+184 x x
(Tyr402His) +1204 x x
2634 x x
fH µg/ml X X
XX
P1
(36y)
P2
(30y)
x x
x x
x x
x x
X X
XX


CFH c.89insA
MCP c.623 C>T (I208Y)
P6
H143P
P2
HUS143
P1
P3
P4
P5