XI congresso nazionale

simeu

ROMA 24-26 MAGGIO 2018

Angioedema Ereditario

Dott.ssa Maria Domenica Guarino
UOC Medicina d'Accattazione e d'Urgenza Fondazione Policlinico Tor Vergata
Centro di rifermento regionale per la malattia rara Angioedema Ereditario Fondazione Policlinico Tor Vergata, UOC Reumatologia,
Gruppo ITACA

DISCLOSURE

- SHIRE, speaker
- CSL BEHRING, speaker

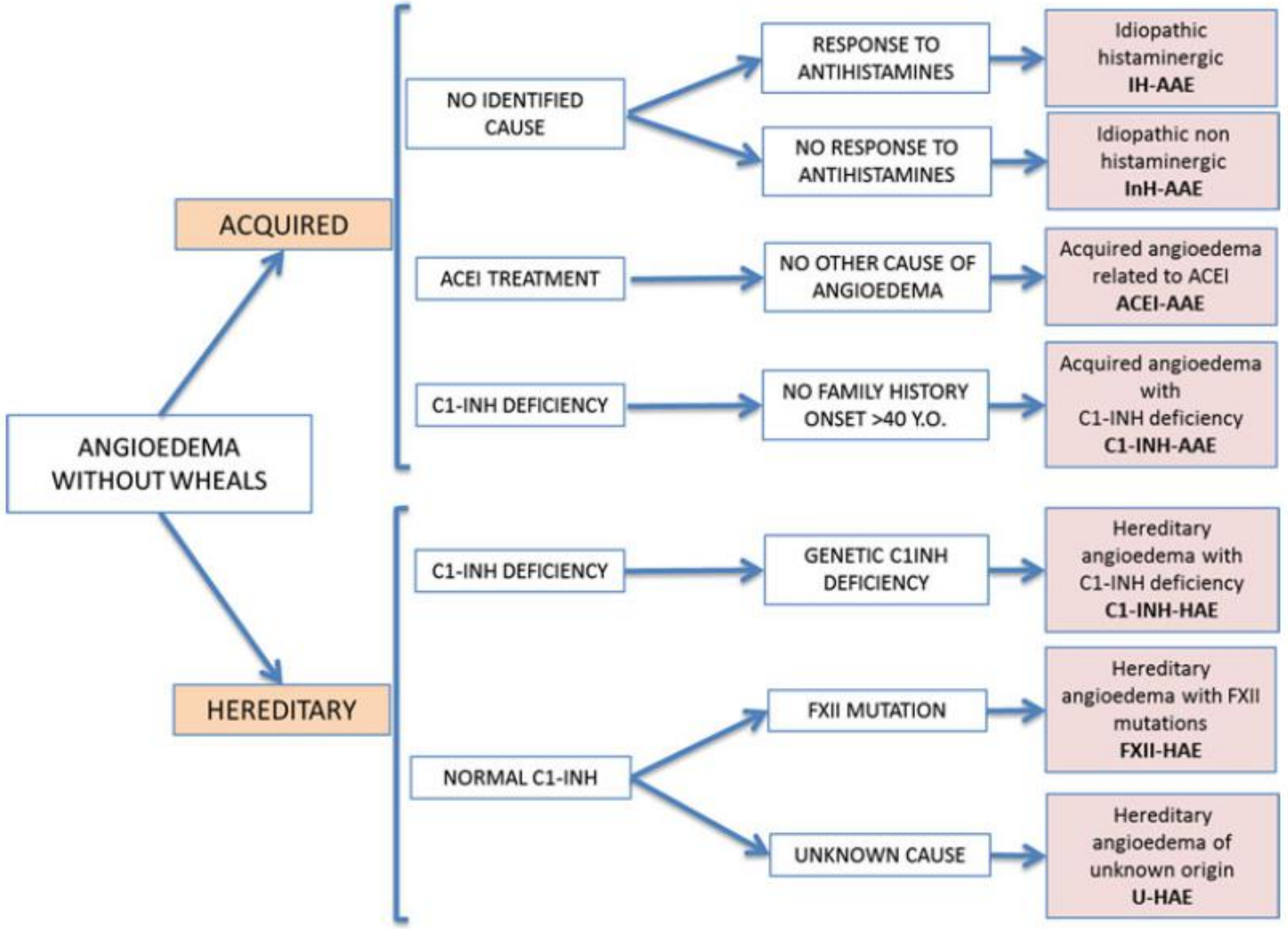
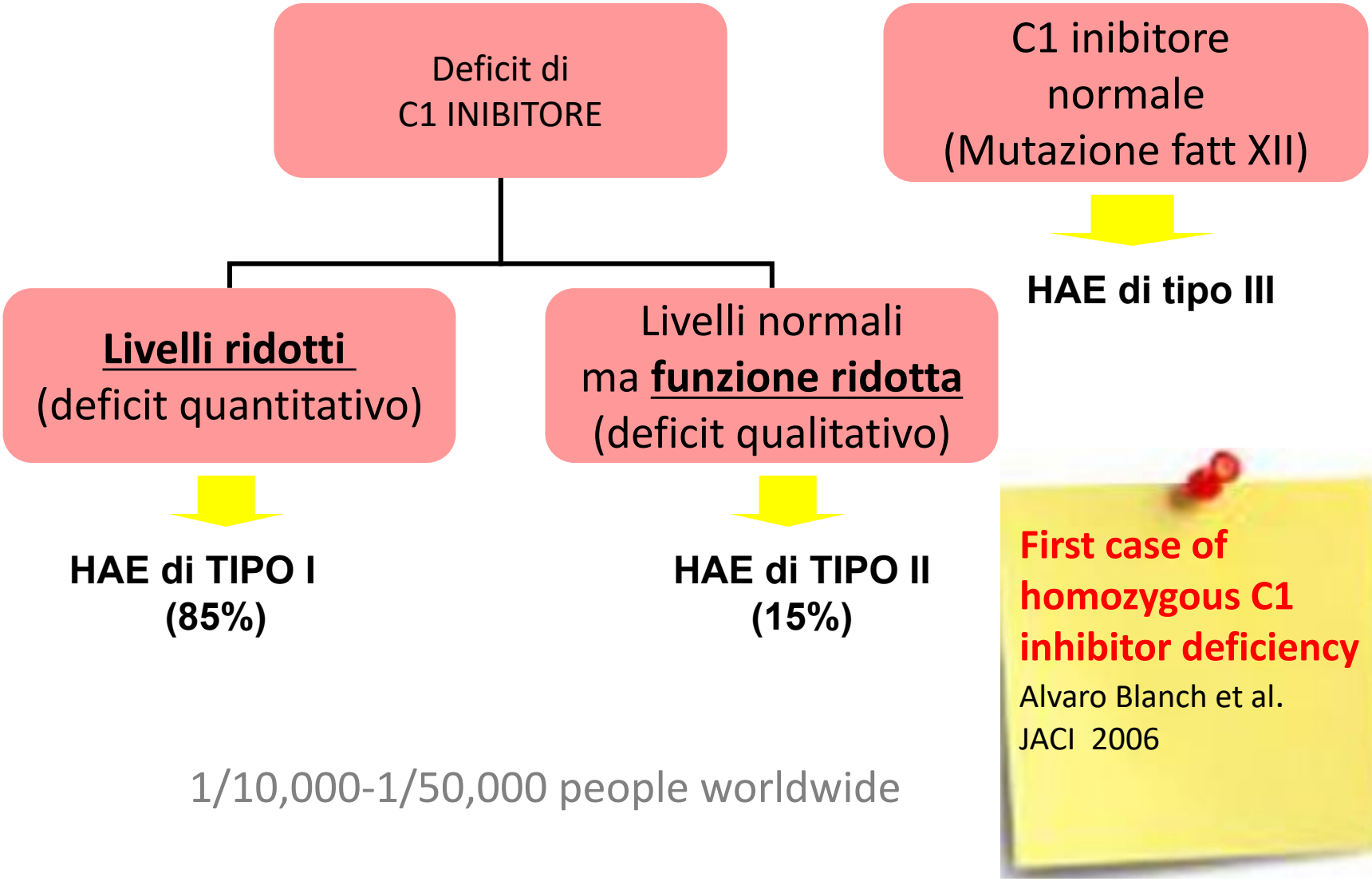


Figure 1 Classification of angioedema without wheals.

M. Cicardi, M. Triggiani et Al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. Allergy 2014


Deficit di
C1 INIBITORE
C1 inibitore
normale
(Mutazione fatt XII)
HAE di tipo III
Livelli ridotti
(deficit quantitativo)
Livelli normali
ma funzione ridotta
(deficit qualitativo)
HAE di TIPO I
(85%)
HAE di TIPO II
(15%)
First case of
homozygous C1
inhibitor deficiency
Alvaro Blanch et al.
JACI 2006
1/10,000-1/50,000 people worldwide

Gonadal mosaicism in hereditary angioedema

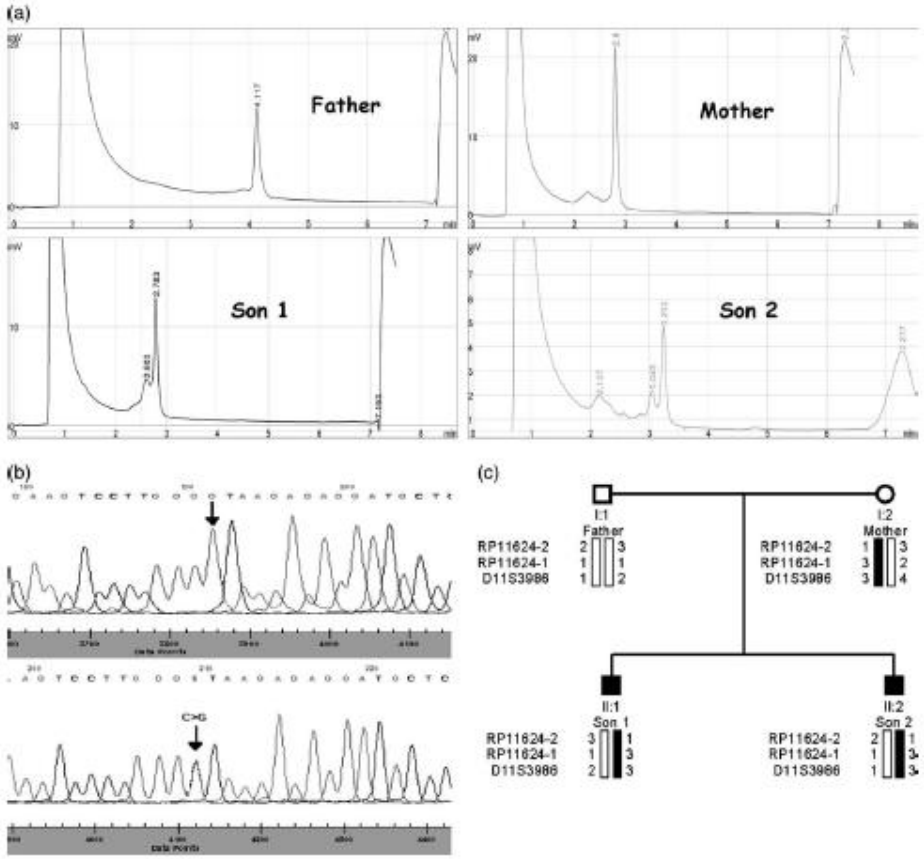
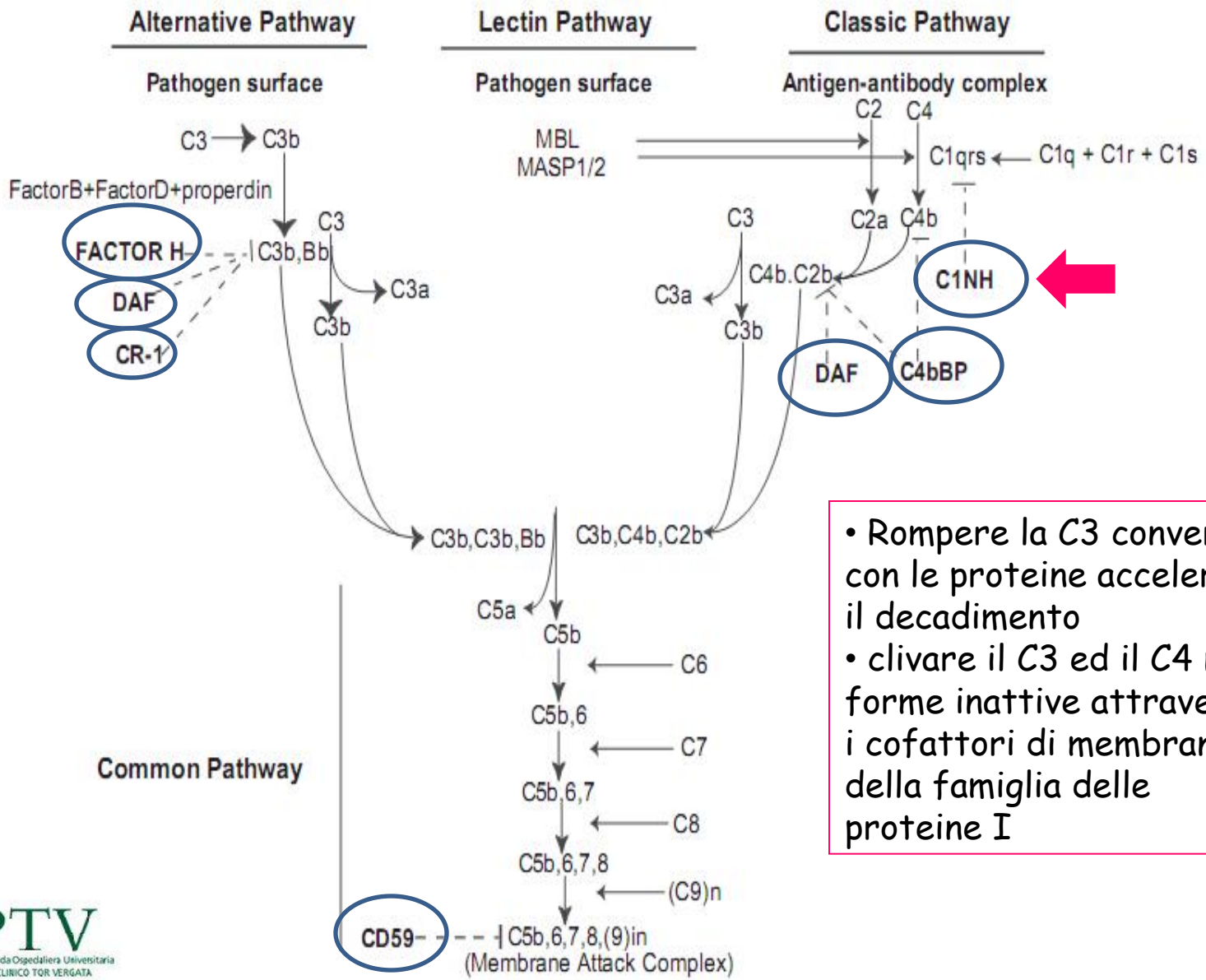


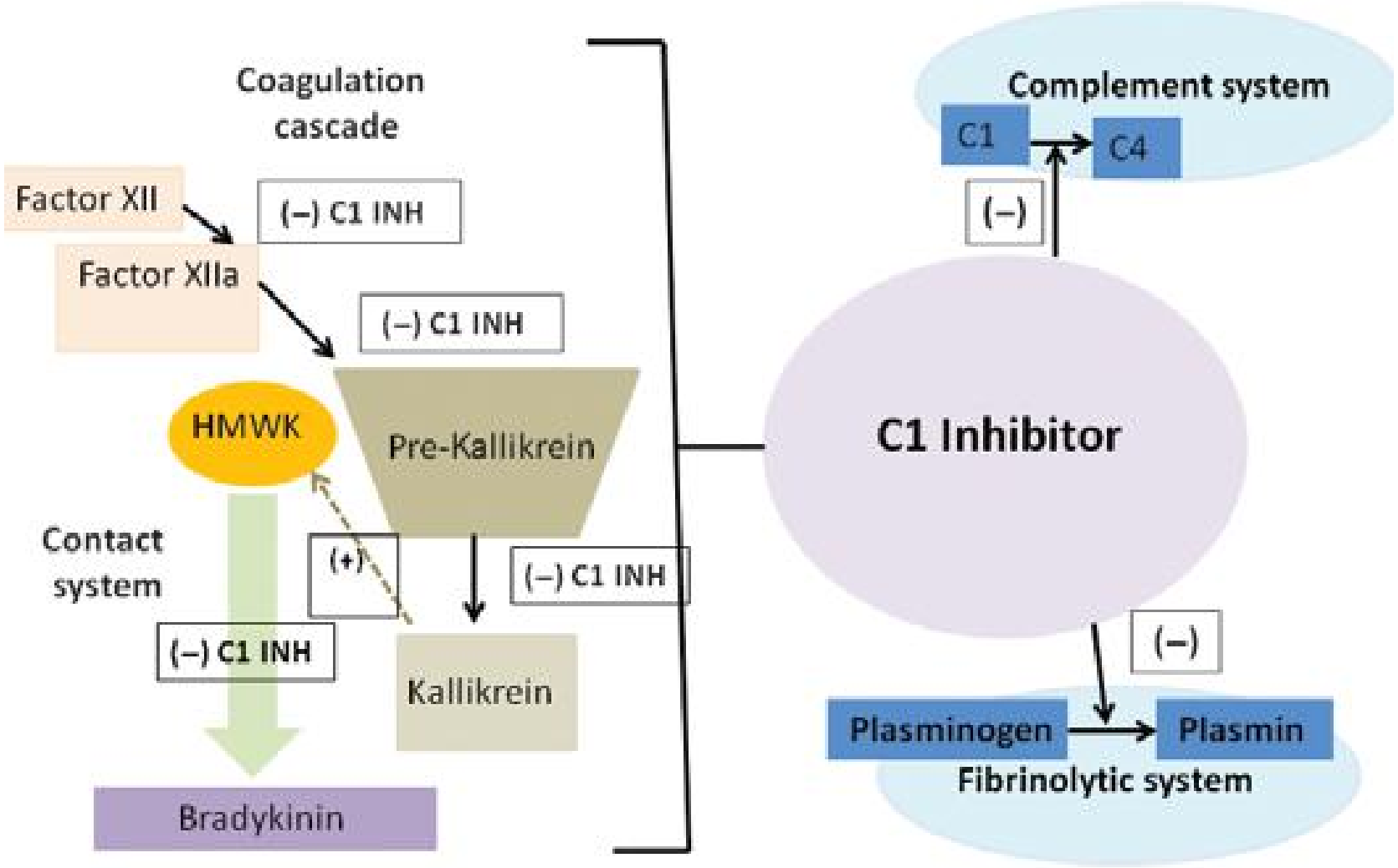
Fig. 1. (a) DHPLC profiles of exon 4 containing fragment derived from the C1-INH gene of the unaffected parents and the affected children. A second lower mobility peak is evident in children's DNA samples but not in DNA derived from parents. (b) DNA sequence analysis of exon 4 containing fragment derived from the C1-INH gene of the unaffected parents and the affected children. A heterozygous c.597C>G transversion (Y199X) in children's DNA samples but not in DNA derived from parents. DNA sequence is in the antisense form. (c) Haplotype analysis revealed that the affected children are concordant for the maternal haplotype 1 3 3 considered associated with the Y199X mutation.

Guarino S. Clin Genet 2006, 70: 83-85

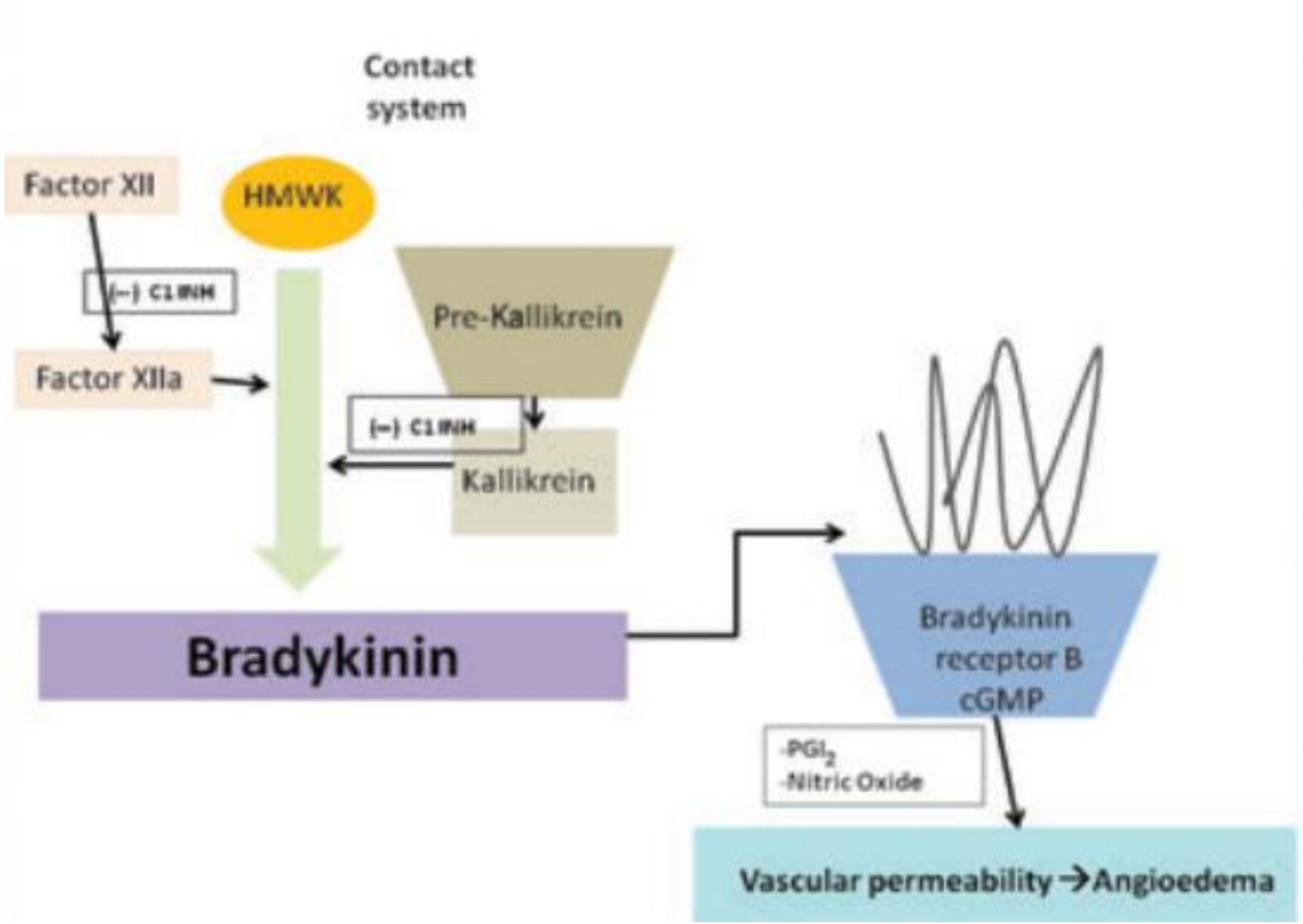


- Rompere la C3 convertasi con le proteine acceleranti il decadimento
- clivare il C3 ed il C4 nelle forme inattive attraverso i cofattori di membrana della famiglia delle proteine I

Biologics: Targets & Therapy 2008:2(4) 671–685


Coagulation cascade
Factor XII
(–) C1 INH
Factor XIIa
(–) C1 INH
HMWK
Pre-Kallikrein
Contact system
(+)
(–) C1 INH
(–) C1 INH
Kallikrein
Bradykinin
Complement system
C1
C4
(–)
C1 Inhibitor
(–)
Plasminogen
Plasmin
Fibrinolytic system

Y.-Y. Xu, 2013


Contact system
Factor XII
HMWK
(–) C1 INH
Factor XIIa
Pre-Kallikrein
(–) C1 INH
Kallikrein
Bradykinin
Bradykinin receptor B cGMP
-PGI2
-Nitric Oxide
Vascular permeability → Angioedema

Y.-Y. Xu, 2013

- ✓ Episodic, localized, nonurticarial, nonpitting, subcutaneous, which usually revert within 48 to 72 hours.
- ✓ About 40-87% of swellings are preceded (by up to 16 h) by prodromal erytema marginatum
- ✓ Mean age at onset of symptoms is about 8-12 years
- ✓ Episodes seem to be more frequent in women, variations in concentrations of sex hormones might all play a part in determining the frequency and severity of swellings

Longhurst, Cicardi, Angioedema, Lancet 2012, Vol 379

- ✓ Episodic swelling can affect face, hands, feet, gastrointestinal tract, genital and upper airway. Attack often occur without a trigger; however precipitating factors can include stress or trauma.

- ✓ From the onset of the clinical symptoms the patients can have symptom-free intervals .

Bork K, Meng G, Staubach P, Hardt J. Hereditary angio-oedema: new findings concerning symptoms, aff ected organs, and course. Am J Med 2006; 119: 267–74.

Trigger factors

- ✓ Trauma (dental manipulations, orotracheal intubation, gastroscopy, minor trauma);
- ✓ psychological stress;
- ✓ drugs (ACE-inhibitors and estrogen-containing drugs) ;
- ✓ hormones (menses, pregnancy, and puberty);
- ✓ infections (upper respiratory tract infections, Helicobacter pylori infection).

Bork K. Am J Med. 2003;114:294-8, Agostoni A. Medicine (Baltimore) 1992;71:206-15, Frank MM. Ann Intern Med.1976;84:580-93, Farkas H. Lancet. 2001;358:1695-6.111, Visy B. Helicobacter. 2007;12:251-7

Cutaneous symptoms

Skin edema is nonpitting and with ill-defined margins. Most often, a single site is affected by an extended edema that grows and then regresses within 2 to 5 days

the attack usually spreads to disfigure the affected site and it can involve multiple sites.

Agostoni, Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond,J Allergy Clin Immunol September 2004, vol 114

Severe headache can be present in the patients, they are not associated with edema episodea at other sites or organs.

The headaches last for 4 hours to 4 days, in most patients for 1 to 2 days.

The headache can be accompanied by various other signs, including feeling of pressure in the head, feeling of pressure in the eyes, visual disturbance, such as double vision, difficulty in focusing and narrowed visual field, ataxia and decrease in physical and mental powers

Bork K, Hereditary angioedema: new findings concerning symptoms, affected organs, and course. The American Journal of Medicine 2006, 119, 267-274

Abdominal symptoms

Recurrent abdominal pain is reported by 70% to 80% of patients with HAE, it presents with symptoms that may vary from mild discomfort to severe, intractable pain accompained by vomiting and /or diarrhea

The absence of fever can afford to put a differential diagnosis with surgical emergencies

Hemoconcentration with an increase in RBC, hematocrit, platelet count, hemoglobin, white blood cell increases and decreases in coagulation time.

Ultrasonography usually shows a small peritoneal effusion.

Radiology: Volume 253: Number 2—November 2009, Cohen N, Hereditary angioneurotic edema with severe hypovolemic shock. J Clin Gastroenterol. 1993 Apr;16(3):237-9

Abdominal symptoms

Hypovolemia can result from a combination of fluid loss, plasma extravasation, and vasodilatation and can progress to hypovolemic shock and ascites

Cohen N, Hereditary angioneurotic edema with severe hypovolemic shock. J Clin Gastroenterol. 1993 Apr;16(3):237-9, Bork K. Hypovolemic shock caused by ascites in hereditary angioedema. Med Klin 1998;93:554

Laryngeal Edema

About half of the patients experienced a laryngeal angioedema during their lifetime. Mortality by asphyxiation is described to be nearly 30% in patients with undiagnosed hereditary angioedema.

The clinical signs can be voice changes, dyspnea, dysphagia and the sensation of a lump or a tightness in the throat.

Laryngeal edema may occur at any age, although young adults are at greatest risk.

Bork K. Transfus Apher Sci 2003, 29:235–238, Bork K. Arch Intern Med. 2003 May 26;163(10):1229-35, Bork K. J Allergy Clin Immunol. 2012 Sep;130(3):692-7.

Differential Diagnosis

- ✓ angioedema with sporadic-acquired C1 inhibitor deficiency;
- ✓ hereditary angioedema with normal C1 inhibitor;
- ✓ ACE-inhibitors related angioedema;
- ✓ sporadic angioedema with normal C1 inhibitor non responsive to anti-histamine;
- ✓ angioedema of unknown origin responsive to anti-histamine;
- ✓ angioedema related to other diseaes (infections or autoimmune diseases).

Zingale LC. CMAJ. 2006 Oct 24;175(9):1065-70, Cicardi M. Allergy Asthma Clin Immunol. 2010 Jul 28;6(1):14, Beltrami L. J Hypertens. 2011 Nov;29(11):2273-7, Zuraw BL. Allergy Asthma Proc. 2012 Dec 13Madsen F. Acta Derm Venereol 2012 Sep;92(5):475-9.

IT J ALLERGY CLIN IMMUNOL 2008;18:114-122

CONSENSUS DOCUMENT

Angioedema ereditario da carenza di C1 inibitore *Consensus Document* italiano per la diagnosi e la terapia

Italian Consensus Document for the diagnosis and the therapy of hereditary angioedema

F. ARCOLEO[1], M. BOVA[2], M. CANCIAN[3], M. CICARDI[4], E. CILLARI[1], C. DE CAROLIS[5], M. DE MARCHI[6], B. FERLAZZO[7], L. FONTANA[8], M.D. GUARINO[5], G. MARONE[2], V. MONTINARO[9], S. NERI[10], R. PERRICONE[5], S. PUCCI[11], M. TRIGGIANI[12], A. ZANICHELLI[4], G. ZANIERATO[12], L.C. ZINGALE[4]

[1] Unità Operativa di Patologia Clinica, Ospedale "V. Cervello", Università di Palermo; [2] Dipartimento di Medicina Interna, Scienze Cardiovascolari ed Immunologiche, Università di Napoli Federico II; [3] Dipartimento di Scienze Mediche e Chirurgiche, Università di Padova; [4] Dipartimento di Medicina Interna, Ospedale "L. Sacco", Università di Milano; [5] Dipartimento di Medicina Interna, Reumatologia, Allergologia ed Immunologia Clinica, Università di Roma "Tor Vergata"; [6] Dipartimento di Scienze Cliniche e Biologiche, Università di Torino; [7] Dipartimento di Patologia Umana, Unità Operativa di Allergologia e Immunologia Clinica, Policlinico Universitario di Messina; [8] Dipartimento di Medicina Interna e Clinica Medica, Università di Roma "Tor Vergata"; [9] Dipartimento di Nefrologia, Azienda Ospedaliera "Policlinico Consorziale" di Bari; [10] Unità Operativa di Medicina Interna, Policlinico Universitario di Catania; [11] Unità Operativa di Allergologia, Presidio Ospedaliero di Civitanova Marche; [12] Unità Operativa di Pneumologia, Ospedale degli Infermi, ASL 12, Biella

Diagnosis

Clinical criteria

(1) Self-limiting, non inflammatory subcutaneous angioedema without major urticarial rash, often recurrent and often lasting more than 12 hours

(2) Self-remitting abdominal pain without clear organic etiology, often recurrent and often lasting more than 6 hours

(3) Recurrent laryngeal edema

(4) Family history of recurrent angioedema and/or abdominal pain and/or laryngeal edema due to C1 inhibitor deficiency

Diagnosis

Correct treatment of samples to be analyzed is critically important in order to obtain reliable results

Laboratory criteria

(1)C1 inhibitor antigenic levels <50% of normal at 2 separate determinations with patient in basal condition and after the first year of age

(2) C1 inhibitor functional levels <50% of normal at 2 separate determinations with patient in basal condition and after the first year of age

(3) Mutation in C1 inhibitor gene altering protein synthesis and/or function

Diagnosis can be established in presence of 1 clinical criterion and 1 laboratory criterion

Denaturing HPLC in laboratory diagnosis of hereditary angioedema

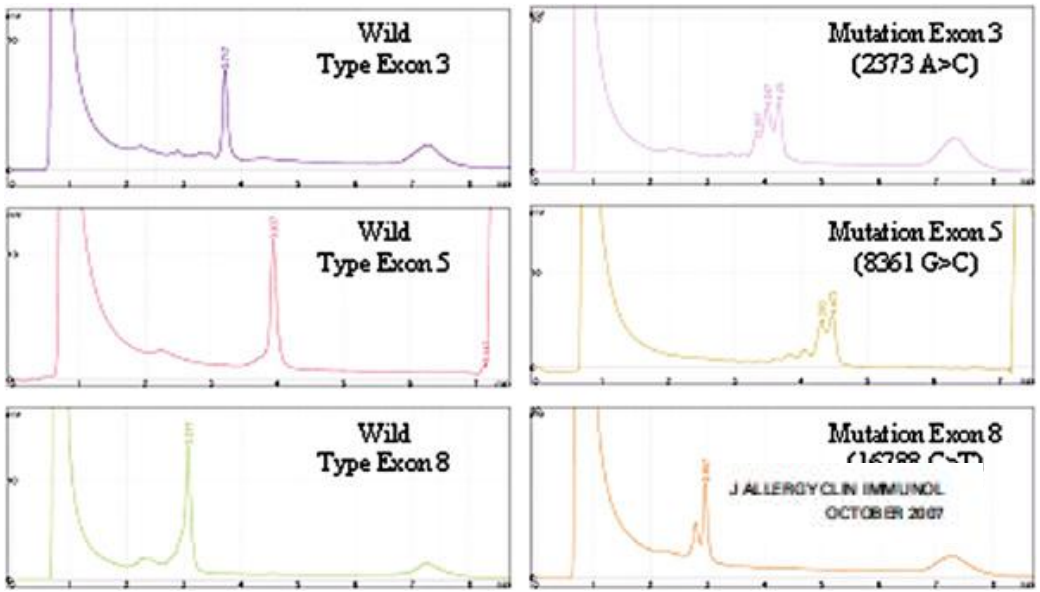


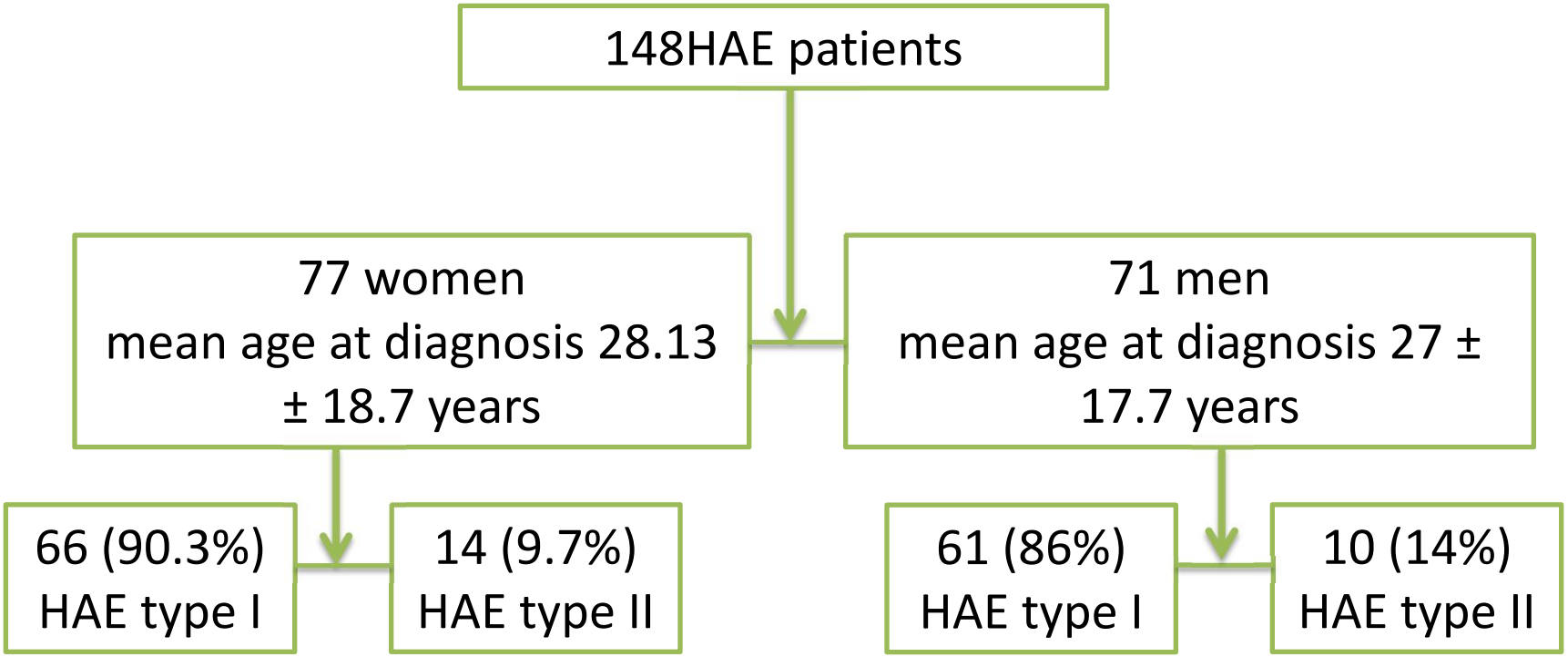
TABLE I. C1INH mutations and polymorphisms identified by DHPLC

Family no.	Patient no.	Intron/exon	Traditional DNA numbering*	Predicted effect on protein or splicing alteration: Traditional numbering	Predicted effect on protein or splicing alteration: Systematic numbering	Type
Sporadic	1	Exon 3	2373 A>C	Lys55Gln	Lys77Gln	Missense
1	2-5	Exon 3	2558 C>T	Ser115Ter	Ser137Ter	Nonsense
1	4	Exon 8	16655 T>C	Phe399Phe	Phe421Phe	Polymorphism
2	6-9	Exon 3	2586 G>T	Asp126Tyr	Asp148Tyr	Missense
3	10-12	Exon 4	4390 T>A	Leu175His	Leu197His	Missense
Germinal mosaicism	13,14	Exon 4	4397 C>G	Tyr177Ter	Tyr199Ter	Nonsense
4	15,16	Exon 5	8361 G>C	Arg219Pro	Arg241Pro	Missense
5	17,18	Exon 5	8424 T>G	Ile240Ser	Ile262Ser	Missense
6	19-21	Exon 8	16662 G>T	Asp402Tyr	Asp424Tyr	Missense
6	19	Exon 8	16830 G>A	Val458Met	Val480Met	Polymorphism
Sporadic	22	Exon 8	16672 T>C	Leu405Pro	Leu427Pro	Missense
Sporadic†	23	Exon 8	16788 C>T[6]	Arg444Cys	Arg466Cys	Missense
Sporadic†	23	Exon 6	8488 C>T	Ser261Ser	Ser283Ser	Polymorphism
7	24,25	Exon 8	16823 C>A	Phe455Leu	Phe477Leu	Missense
Sporadic	26	Exon 8	16834 T>C[7]	Leu459Pro	Leu481Pro	Missense
8	27-29	Exon 8	16870 delG	Frameshift471	Frameshift493	Nonsense
9	30-35	Exon 8	16872 C>T[7]	Arg472Ter	Arg492Ter	Nonsense
10	36-51	Intronic	4350 (c.551-1 G>A) G>A	Donor splicing site?	Donor splicing site?	Splicing

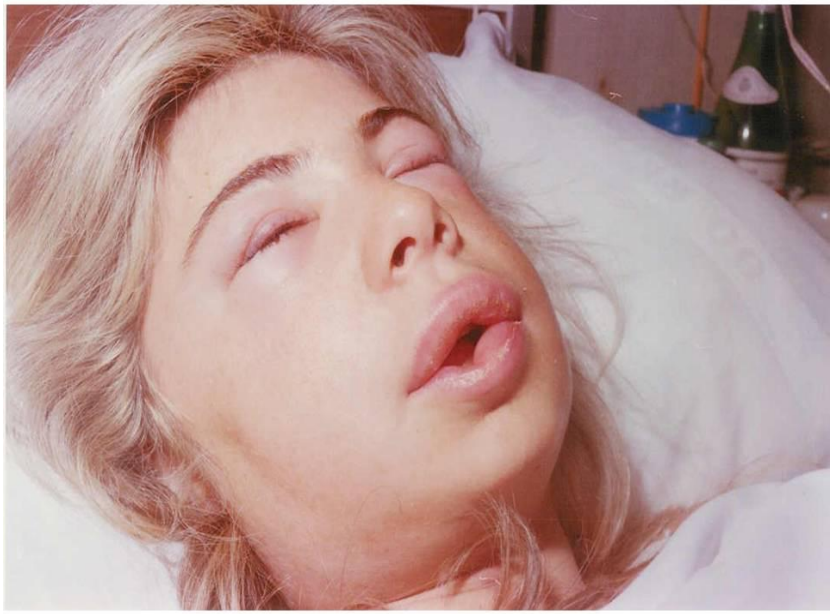
*The traditional genomic DNA nomenclature follows the numbering currently used in the hereditary angioedema database.[8] For amino acids, both traditional and systematic numberings are shown.[9]
†HAE type II.

Guarino MD et al.
J Allergy Clin Immun oct 2007

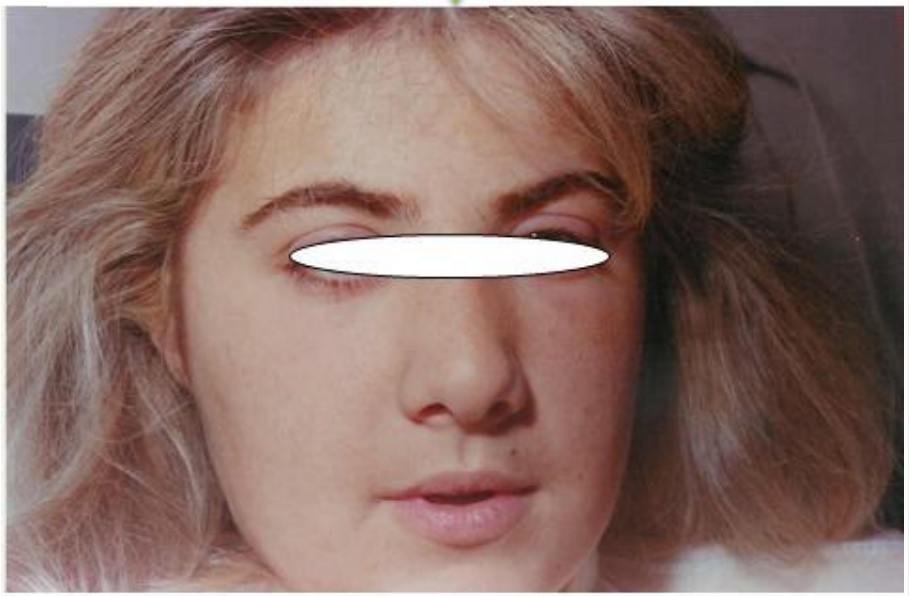
HAE
data from our Division

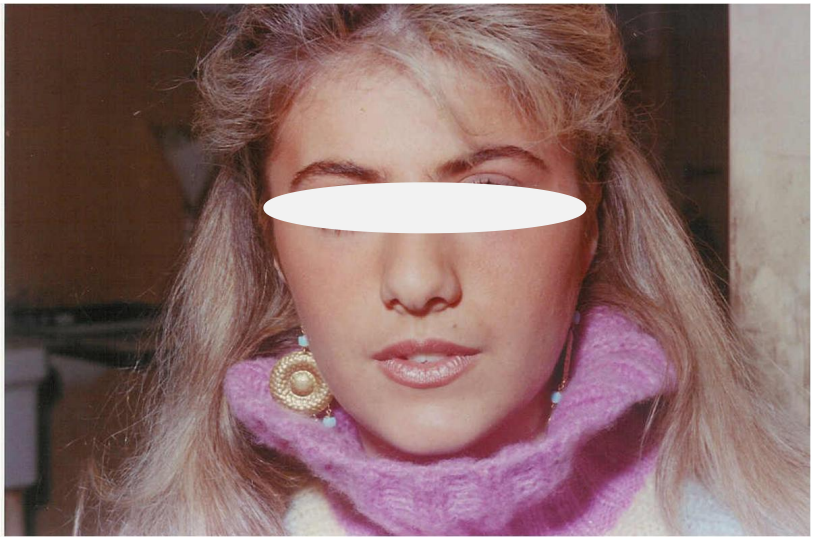


8 of them were diagnosed in the emergency departement



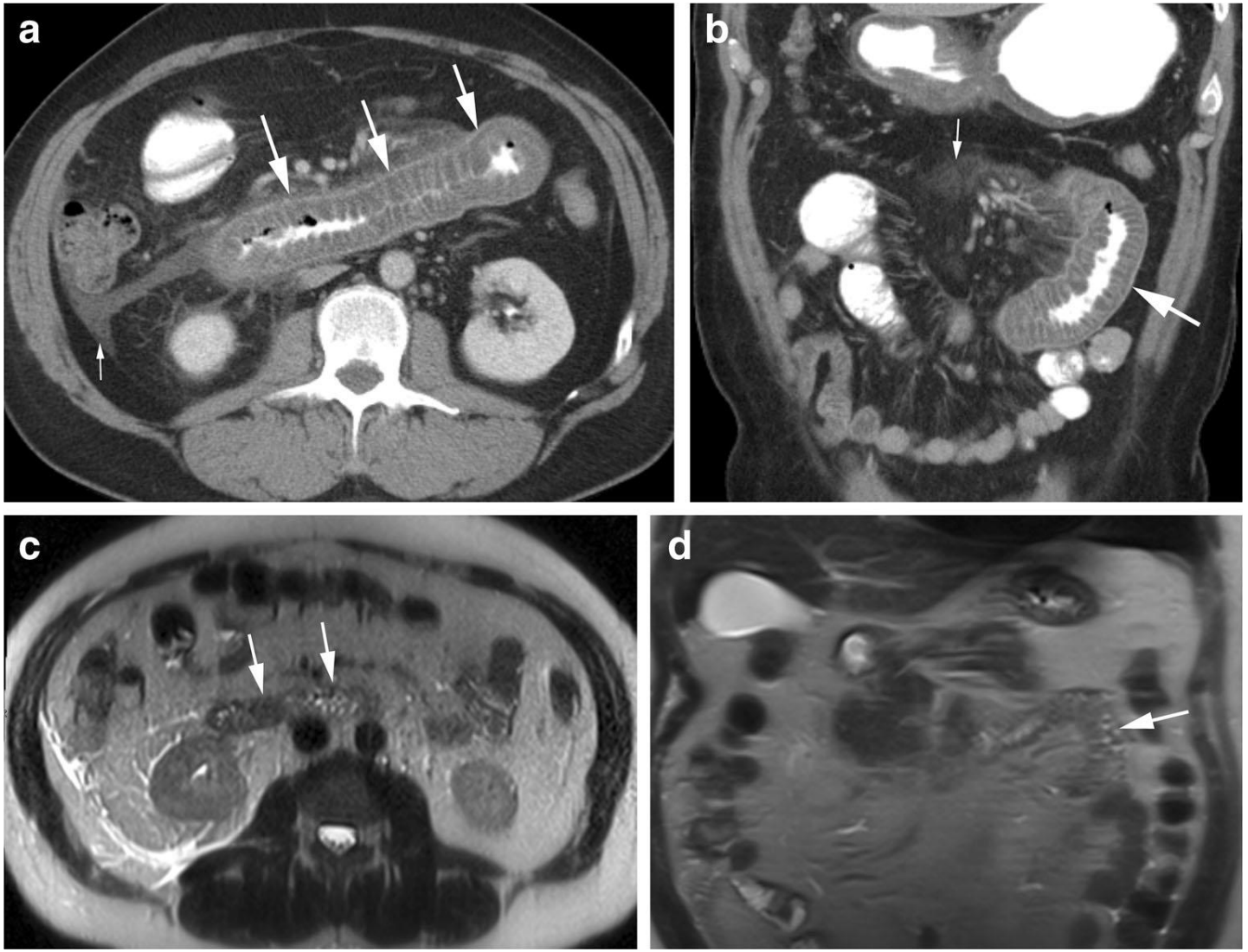
4-6 hours after the treatment





20-24 hours after the treatment

Casistica del centro

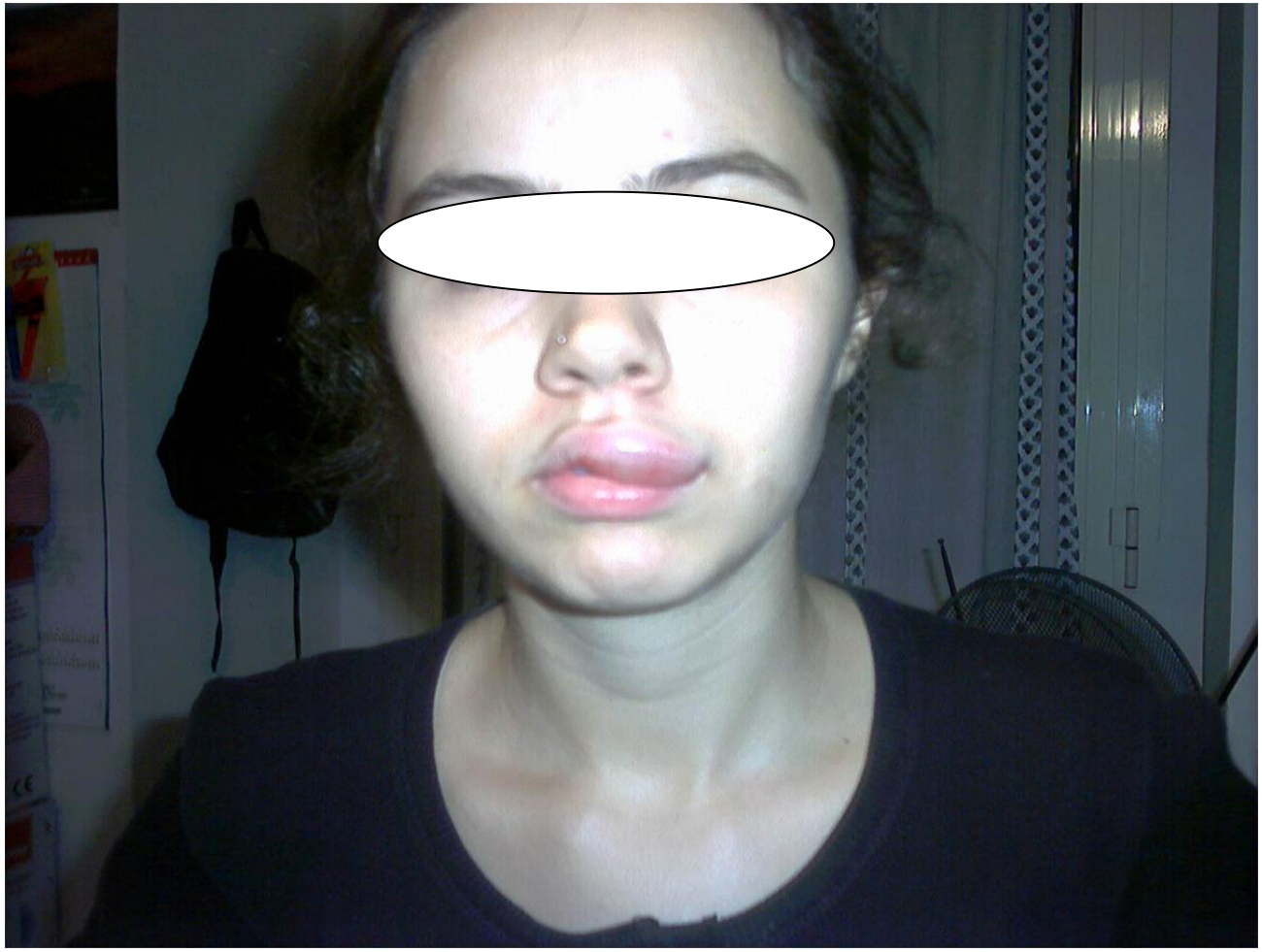


Emerg Radiol
DOI 10.1007/s10140-014-1242-0

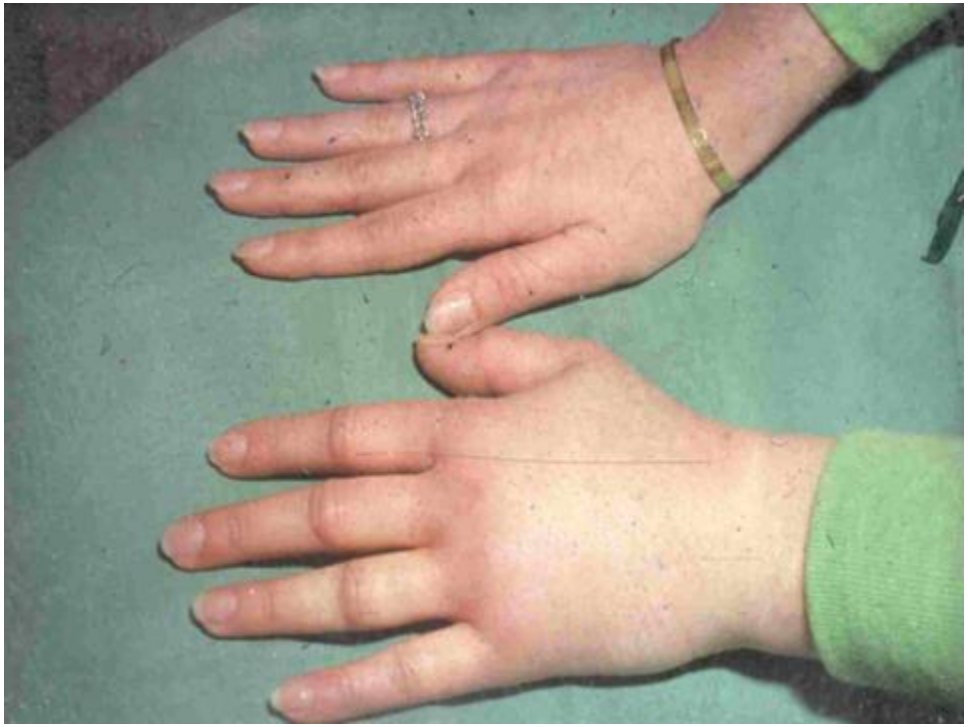
PICTORIAL ESSAY

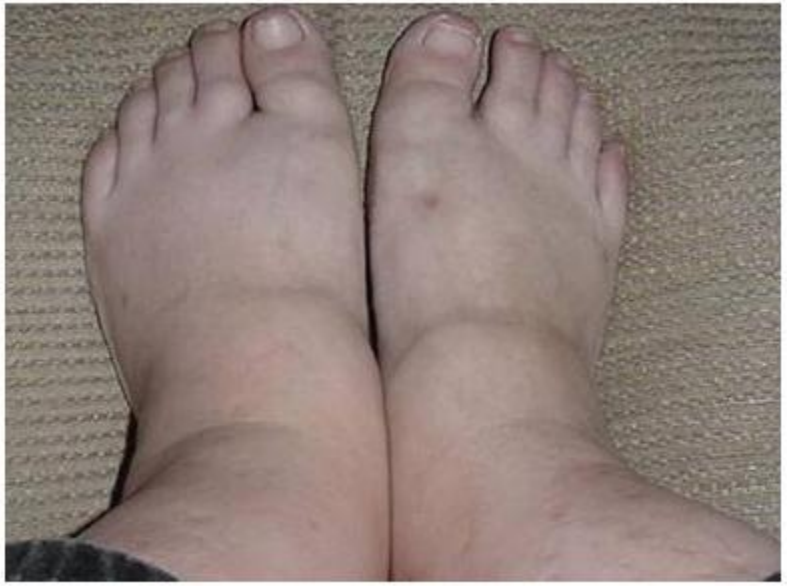
Hereditary angioedema: imaging manifestations and clinical management

Mandip S. Gakhal · Gregory V. Marcotte



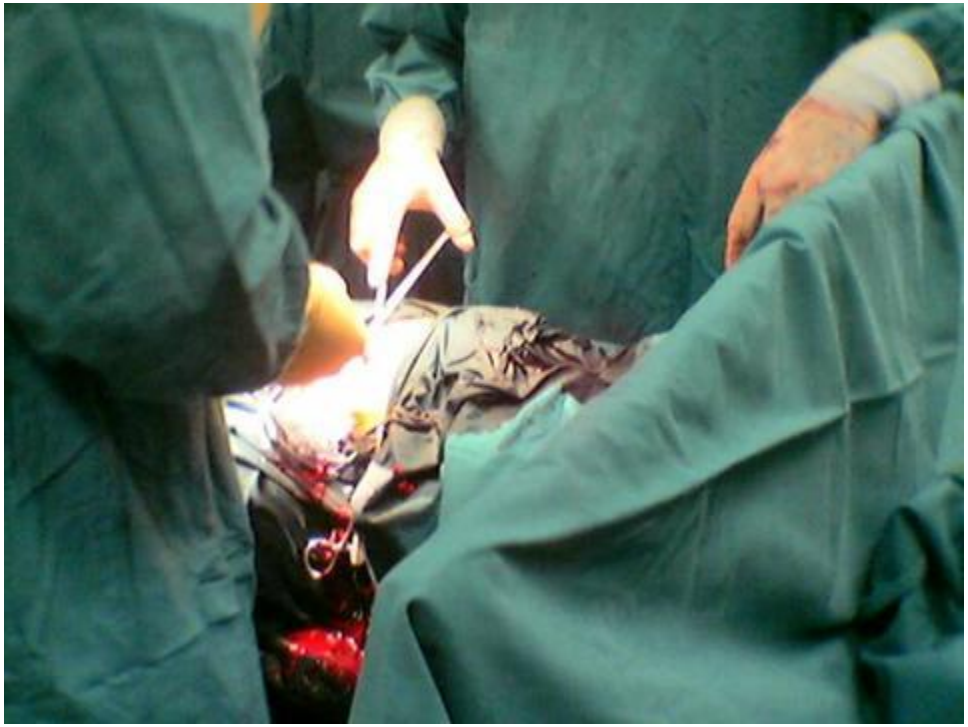
Casistica del centro





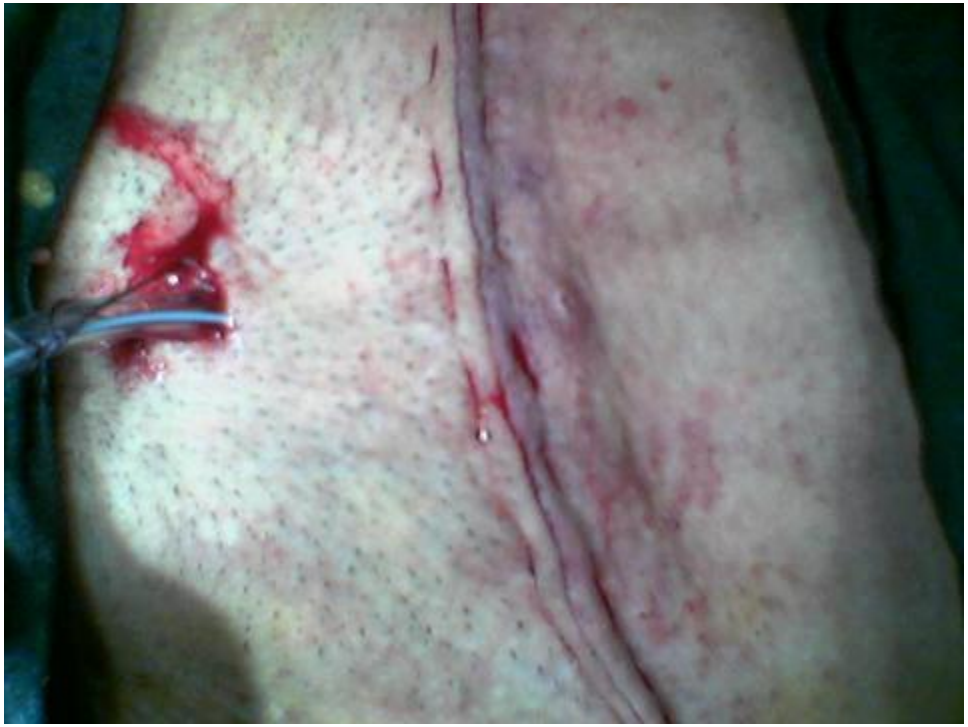
Azienda Ospedaliera Universitaria
POLICLINICO TOR VERGATA

Casistica del centro



Azienda Ospedaliera Universitaria
POLICLINICO TOR VERGATA

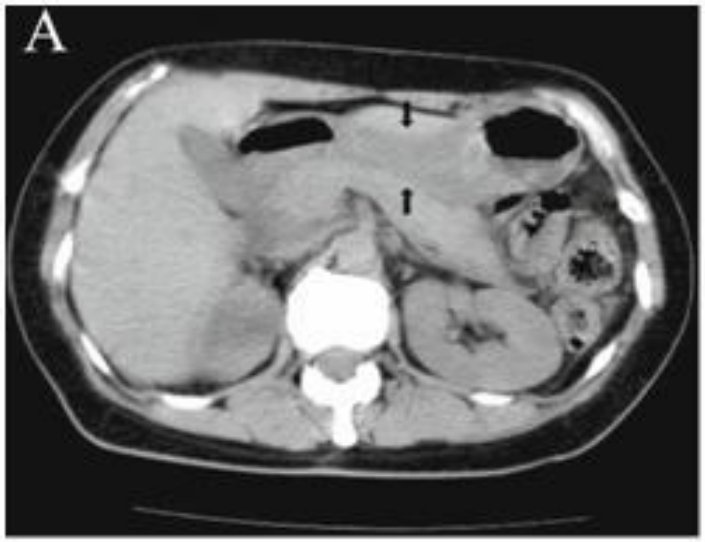
Casistica del centro



Azienda Ospedaliera Universitaria
POLICLINICO TOR VERGATA

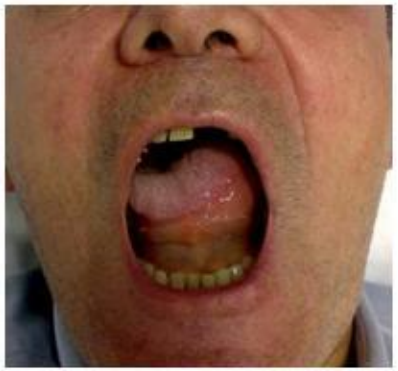
Casistica del centro

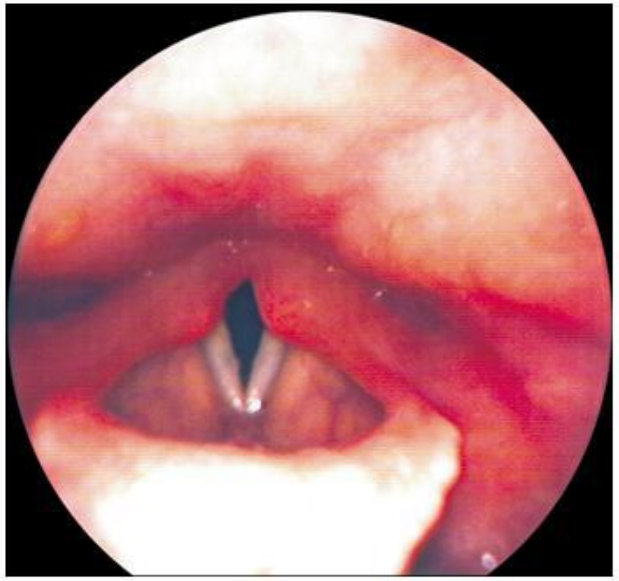
Donna di 51 anni



Radiat Med (2008) 26:618–621

PTV
Azienda Ospedaliera Universitaria
POLICLINICO TOR VERGATA





Courtesy of Prof Cicardi

CURRENT OPINION

Diagnostic and therapeutic management of hereditary angioedema due to C1-inhibitor deficiency: the Italian experience

Table 2. Drugs currently available in Europe for specific management of C1-INH-HAE

Drug	Characteristics	Indication	Dose	Potential side-effects and limitations
Berinert	Plasma-derived C1-INH concentrate	Acute treatment; short-term prophylaxis	20 U/kg body weight intravenous for acute treatment. 1000 U for STP	Theoretical transmission of blood-borne infectious agents
Cinryze	Plasma-derived C1-INH concentrate	Acute treatment; short-term prophylaxis; long-term prophylaxis	1000 U intravenous for acute treatment and STP. 1000 U q3–4 days for LTP	Theoretical transmission of blood-borne infectious agents. Avoid indwelling catheters for LTP (potential risk of thrombosis)
Ruconest (Rhucin)	Human recombinant C1-INH concentrate	Acute treatment	50 U/kg intravenous up to 84 kg body weight. 4200 U for heavier patients	Potential anaphylaxis (rule out rabbit allergy before administration). Not authorized under 18 years of age nor for pregnant and breast-feeding women. Self-administration not allowed
Icatibant (Firazyr)	Synthetic Bradykinin- B2 receptor antagonist	Acute treatment	30 mg subcutaneous injection	Negligible pain and swelling at injection site. Theoretical risk of exacerbating coronary heart disease. Not authorized under 18 years of age nor for pregnant and breast-feeding women

LTP, long-term prophylaxis; STP, short-term prophylaxis.

Cancian M, Guarino MD et al Curr Opinion Vol 15, num 4 August 2015

C1INH DEFICIENCY: ON DEMAND TREATMENT

- ✓ Prevent mortality
- ✓ Treat morbidity
- ✓ Improve QL
- ✓ Reduce social cost

Long-term prophylaxis (LTP)

is a chronic and continuous treatment aimed at reducing frequency, severity and duration of angioedema attacks in those patients presenting a more severe disease and is based on periodic administration of drugs in absence of HAE symptoms. LTP is not recommended to all HAE patients but is generally considered when the on-demand treatment does not achieve a significant improvement of quality of life in suffering patients

Long-term Prophylactic Therapy

Defined as a routine and regular scheduled dose C1 esterase inhibitor (C1-INH) to the patient:

- Cinryze®, C1 esterase inhibitor (C1-INH),
- Attenuated androgens (eg, Danazol)
- Tranexamic acid
- Coming soon… C1 inhibitor s.c

SHORT TERM PROPHYLAXIS :

- ✓ Minor or major surgical interventions
- ✓ Medical or dental interventions including endoscopies
- ✓ Dental manipulations
- ✓ Stressful events (eg. Exam times, busy work periods, major family events)
- ✓ Hormonal changes in women (eg. At delivery, Menstrual cycle)

Acute Therapy

The administration of treatment to manage attack symptoms:

Berinert®, C1 esterase inhibitor (C1-INH), CSL Behring

Firazyr® (icatibant, bradykinin 2 receptor antagonist), Shire (licensed in Europe)

Cinryze®, C1 esterase inhibitor (C1-INH), Shire

Ruconest®,

BERINERT P®

- E’ un C1 inattivatore emoderivato altamente purificato, liofilizzato per uso endovenoso, utilizzato per la prima volta in germania nel 1985.
- Un’unità di C1 inattivatore Berinert P® è equivalente ad 1 ml di C1 inibitore presente nel plasma umano. Ha un’emivita di circa 5.62±5.02 giorni.
- Viene prodotto dalla purificazione di un pool di plasma fresco umano di donatori che vengono testati singolarmente per HBV, HCV, HIV 1-2, HAV.
- Il C1 inibitore viene separato dal plasma umano fresco attraverso crioprecipitazione, stadi di precipitazione ed adsorbimento e viene quindi successivamente pastorizzato.
- Quindi viene purificato attraverso precipitazione e cromatografia, filtrato in ambiente sterile e liofilizzato in assenza di conservanti.

(Transfusion and Apheresis Science 29 2003 247-254)

Icatibant (Firazyr®)

Antagonista altamente selettivo del recettore B2 per la bradichinina (affinità per il recettore B1 100 volte più bassa);

Attività di agonista per B2 solo per alte concentrazioni (>3,2 mg/KG)

1 somministrazione s.c (30 mg/3ml) lenta

ripetibile in caso di necessità dopo 6 ore (fino a 3 dosi in 24 ore)

Indicazione: trattamento attacco acuto di angioedema ereditario I e II tipo

Rapido assorbimento (20’-30’ min)
Durata d’azione: non dose dipendente
Emivita: 1,2-1,5 ore

- Metabolizzazione epatica (non attraverso CYP450); escrezione urinaria
- Non aggiustamenti posologici in insufficienza epatica e renale
- Controindicato in pazienti con eventi ischemici
- Studi non disponibili in gravidanza e allattamento

10% dei pazienti necessita di una seconda dose, generalmente dopo 10-27 h dalla prima somministrazione (la breve emivita dell’icatibant potrebbe essere la causa)

Il paziente deve avere sempre a disposizione **2 siringhe**

Effetti indesiderati

LOCALI Insorgono dopo circa 10’ e regrediscono entro 4 h

Eritema

Edema

Dolore

Orticaria

Prurito

SISTEMICI

- Cefalea
- Nausea
- Vertigini
- Piressia
- Aumento delle transaminasi

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 23, 2017 VOL. 376 NO. 8

Inhibiting Plasma Kallikrein for Hereditary Angioedema Prophylaxis

A. Banerji, P. Busse, M. Shennak, W. Lumry, M. Davis-Lorton, H.J. Wedner, J. Jacobs, J. Baker, J.A. Bernstein, R. Lockey, H.H. Li, T. Craig, M. Cicardi, M. Riedl, A. Al-Ghazawi, C. Soo, R. Iarrobino, D.J. Sexton, C. TenHoor, J.A. Kenniston, R. Faucette, J.G. Still, H. Kushner, R. Mensah, C. Stevens, J.C. Biedenkapp, Y. Chyung, and B. Adelman

Conclusions: Lanadelumab provided sustained protection against angioedema attacks during the 26-week treatment period, regardless of baseline attack frequency. Together with its safety profile, lanadelumab may offer patients a novel therapeutic option for HAE prophylaxis.

RESEARCH Open Access

A nationwide survey of hereditary angioedema due to C1 inhibitor deficiency in Italy

Andrea Zanichelli[1*], Francesco Arcoleo[2], Maria Pina Barca[3], Paolo Borrelli[4], Maria Bova[5], Mauro Cancian[6], Marco Cicardi[1], Enrico Cillari[2], Caterina De Carolis[7], Tiziana De Pasquale[8], Isabella Del Corso[9], Paola Cesinaro Di Rocco[10], Maria Domenica Guarino[11], Ilaria Massaro[12], Paola Minale[13], Vincenzo Montinaro[14], Sergio Neri[15], Roberto Perricone[11], Stefano Pucci[8], Paolina Quattrocchi[16], Oliviero Rossi[17], Massimo Triggiani[18], Giuseppina Zanierato[19] and Alessandra Zoli[20]

Table 1 Demographic characteristics and laboratory assessments of Italian C1-INH-HAE patients

	Type I	Type II	Total
Patients (%)	859 (87%)	124 (13%)	983
Gender (M/F)	407/452	55/69	462/521
Median age (years)	44	45	45
Median age at diagnosis (years)	25	31	26
Antigenic C1-INH, median value (%)	21 (IR 13-25)	96 (IR 64-150)	24 (IR 14-31)
Funcitional C1-INH, median value (%)	20 (IR 10-30)	19 (IR 10-30)	20 (IR 10-30)
Antigenic C4, median value (%)	20 (IR 10-25)	21(IR 12-30)	20 (IR 11-26)

Difficulties encountered in the emergency department by patients with hereditary angioedema experiencing acute attacks

Ramazan Ucar, M.D.,[1] Sevket Arslan, M.D.,[1] Mehmet Baran, M.D.,[2] and Ahmet Zafer Caliskaner, M.D.[1]

Allergy and Asthma Proceedings

S. B 12 y

13-02-2012 facial swelling, abdominal pain

No allergic diseases

No familiarity for HAE

Treatment Corticosteroid and anthystamines

WBC 11.50 *mila/µL*

Neutrofili % 93.5 ** *%*

Linfociti % 8 ***%* -

Monociti % .1 *%*

Eosinofili % 0

Basofili % 0.00

C4 4 mg/dl

C1 inhibitor 20 U/l

After 5-6 h onset of relief

Num. Richiesta:

UOC BIOCHIMICA CLINICA
Direttore Prof. Sergio Bernardini

EMATOLOGIA
Resp.: Prof. Renato Massoud

EMOCROMO

Globuli Rossi	4.74		*milioni/µL*	4.40 - 6.00
Emoglobina	**11.90**	**	*g/dL*	13.00 - 16.00
Ematocrito	38.00		%	34.50 - 52.00
Volume Globulare Medio	80.2		*fL*	77.0 - 95.0
MCH	25.1		*pg*	25.0 - 35.0
MCHC	**31.3**	**	*g/dl*	32.0 - 36.0
RDW-CV	12.8		%	11.0 - 16.0

CH 50	**25.40**	**	%	51.00 - 150.00
C1 Inibitore (Immunodiffusione Radiale)	**36.50**	**	*mg/dL*	15.40 - 35.10
C1INH funzionale	**24.30**	**	%	70.00 - 130.00
C1Q (Immunodiffusione Radiale)	70.50		*mg/L*	50.00 - 250.00

Neutrofili %	53.3		%	38.0 - 74.0
Linfociti %	39.2		%	28.0 - 48.0
Monociti %	4.0		%	3.4 - 11.0
Eosinofili %	3.1		%	0 - 7
Basofili %	0.40		%	0.00 - 1.50

Referto Validato da: Dott.ssa Veronica Botteri

Hereditary Angioedema confirmed also for his mother

Fattore del Complemento C3	90.10		*mg/dL*	90.00 - 180.00
Fattore del Complemento C4	**4.35**	**	*mg/dL*	10.00 - 40.00

M. L 73 y

10.10.2014 facial and tongue swelling

No allergic diseases

No familiarity for HAE

Treatment Corticosteroid and anthystamines

C1 inhibitor 20 U/I

After 5-6 h onset of relief

17.10.14

Medical history: 3 facial attacks in the last 2 months

Physical examination: splenomegaly

Direttore Prof. Sergio Bernardini

EMATOLOGIA
Resp.: Prof. Renato Massoud

EMOCROMO

Globuli Rossi	4.91		milioni/µL	4.30 - 10.80	
Emoglobina	13.50		g/dL		
Ematocrito	42.10		%		
Volume Globulare Medio	85.7		fL		
MCH	27.5		pg		
MCHC	32.1		g/dl		
RDW-CV	15.5		%		
Piastrine	90	**	mila/µL		
Globuli Bianchi	4.42		mila/µL		
Neutrofili #	2.86		mila/µL		
Linfociti #					
Monociti #					
Eosinofili #					
Basofili #					
Neutrofili %					
Linfociti %					
Monociti %					
Eosinofili %	0.9		%	0 - 7	
Basofili %	0.20		%	0.00 - 1.50	
Velocità di Eritrosedimentazione (VES)	32	**	mm/h	2 - 30	

Lattico Deidrogenasi - LDH	253.00	**	U/L	85.00 - 245.00
Sideremia	61.00		µg/dl	50.00 - 170.00
Ferritina	36.40		ng/ml	10.00 - 291.00
Colesterolo Totale	146.00		mg/dl	110.00 - 200.00
Colesterolo HDL	30.00	**	mg/dl	35.00 - 60.00
Proteina C Reattiva	8.42	**	mg/L	0.00 - 3.00
Fattore del Complemento C3	127.00		mg/dL	90.00 - 180.00
Fattore del Complemento C4	2.17	**	mg/dL	10.00 - 40.00

Beta2 Microglobulina siero	0.47	**	mg/dL	0.07 - 0.18
Immuglobuline Classe A	39.80	**	mg/dL	70.00 - 400.00
Immuglobuline Classe G	568.00	**	mg/dL	700.00 - 1500.00
Immuglobuline Classe M	31.20	**	mg/dL	40.00 - 230.00

Ab anti ds-DNA (CLIA) *CLIA*	3.05	*IU/ml*	<25 >25	Negativo Positivo

Ab Anti Jo1 qualitativo Negativo

Metodo Analitico:
dot blot

Ab anti La (SS-B) qualitativo Negativo

Metodo Analitico:
dot blot

Ab Anti PM-Scl Negativo

Metodo Analitico:
dot blot

Ab anti Scl 70 qualitativo Negativo

Metodo Analitico:
dot blot

Ab Anti Sm qualitativo Negativo

Metodo Analitico:
dot blot

Ab Anti Sm-RNP qualitativo Negativo

Metodo Analitico:
dot blot

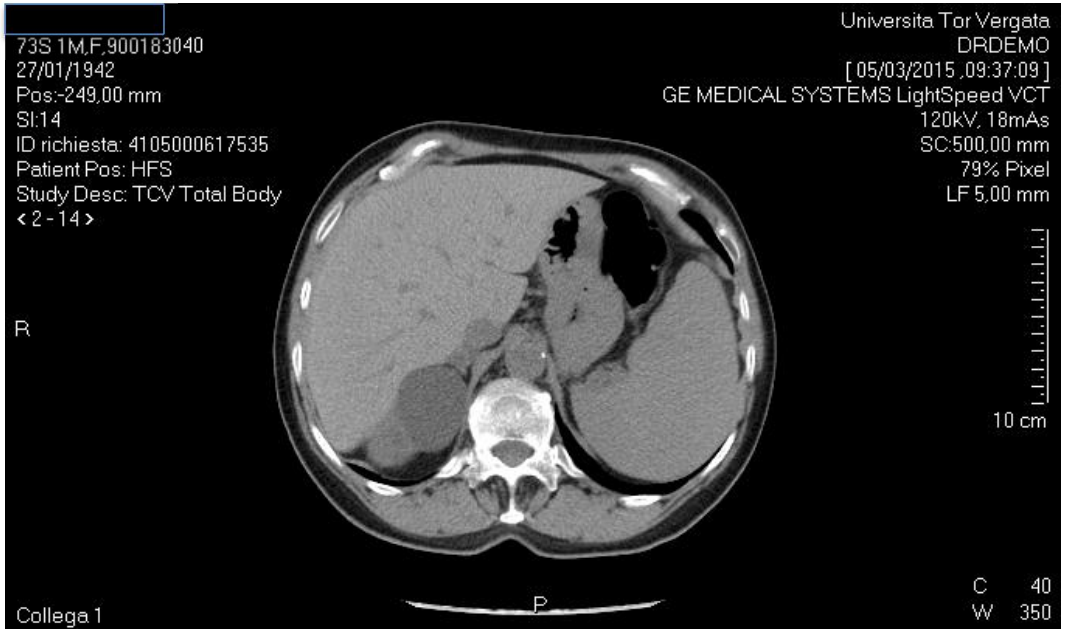
Anti CENP-A/B qualitativo Negativo

Metodo Analitico:
dot blot

Ab anti-Ro (SS-A 60 Kd) qualitativo Negativo

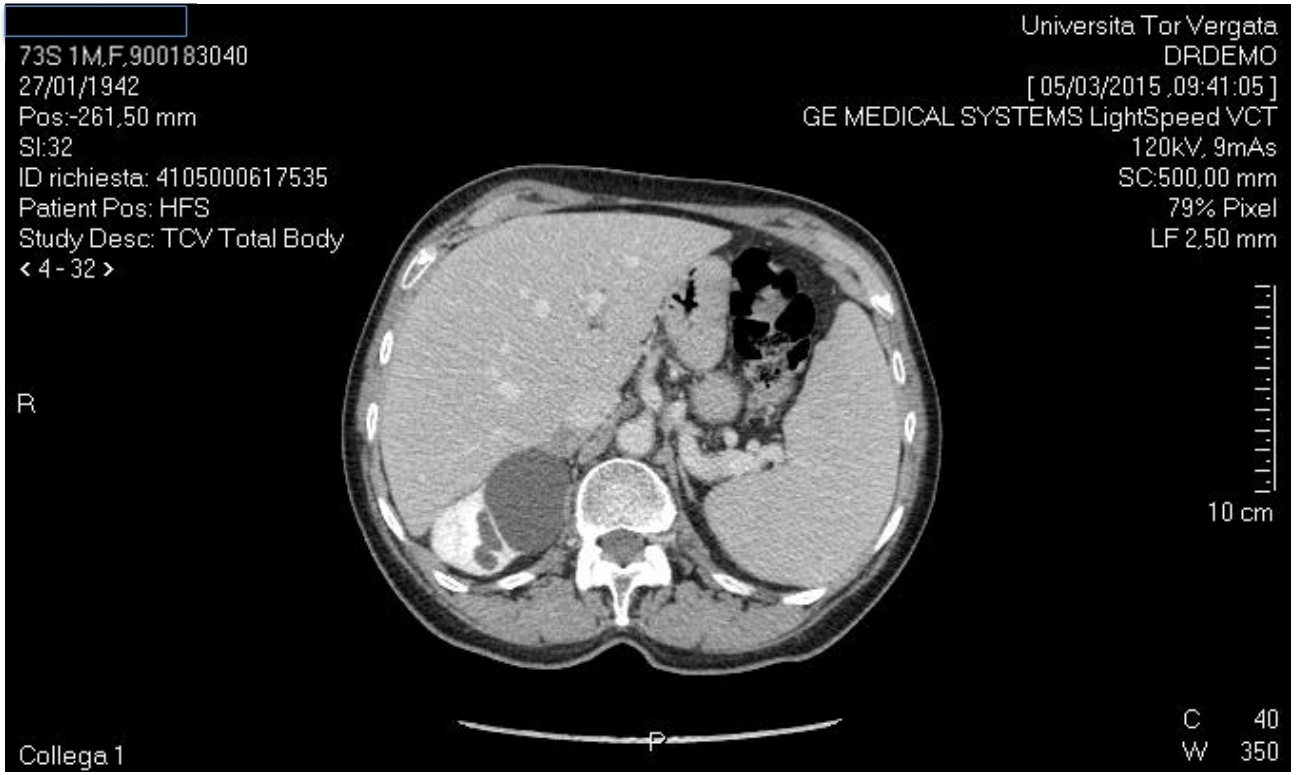
CH 50	25.00	**	%	51.00	-	150.00
C1 Inibitore (Immunodiffusione Radiale)	16.40		*mg/dL*	15.40	-	35.10
C1INH funzionale	58.00	**	%	70.00	-	130.00
C1Q (Immunodiffusione Radiale)	128.00		*mg/L*	50.00	-	250.00
Ab anti Nucleo (IFA) diluizione di screeing 1:80	Negativo					

TC/PET



Casistica del centro

TC/PET



Casistica del centro

Splenic marginal zone lymphoma

CTX started in november 2014

No more angioedema attacks

S. R 48 y

27.01.2016 coliche addominali con nausea e vomito da circa 8 ore

No familiarità per HAE

Nell'infanzia mal di pancia ricorrenti, epatopatia HCV relata

EMATOLOGIA
Resp.: Prof. Renato Massoud

EMOCROMO

Globuli Rossi	4.08		milioni/µL	3.50	-	5.20
Emoglobina	12.90		g/dL	12.00	-	16.00
Ematocrito	38.10		%	34.50	-	52.00
Volume Globulare Medio	93.4		fL	80.0	-	100.0
MCH	31.6		pg	25.0	-	35.0
MCHC	33.9		g/dl	32.0	-	36.0
RDW-CV	12.2		%	11.0	-	16.0
Piastrine	135	**	mila/µL	150	-	450
Globuli Bianchi	6.26		mila/µL	4.30	-	10.80
Neutrofili #	3.33		mila/µL			
Linfociti #	2.34		mila/µL			
Monociti #	0.54		mila/µL			
Eosinofili #	0.05		mila/µL			
Basofili #	0.00		mila/µL			
Neutrofili %	53.2		%	40.0	-	75.0
Linfociti %	37.4		%	20.0	-	45.0
Monociti %	8.6		%	3.4	-	11.0
Eosinofili %	0.8		%	0	-	7
Basofili %	0.00		%	0.00	-	1.50

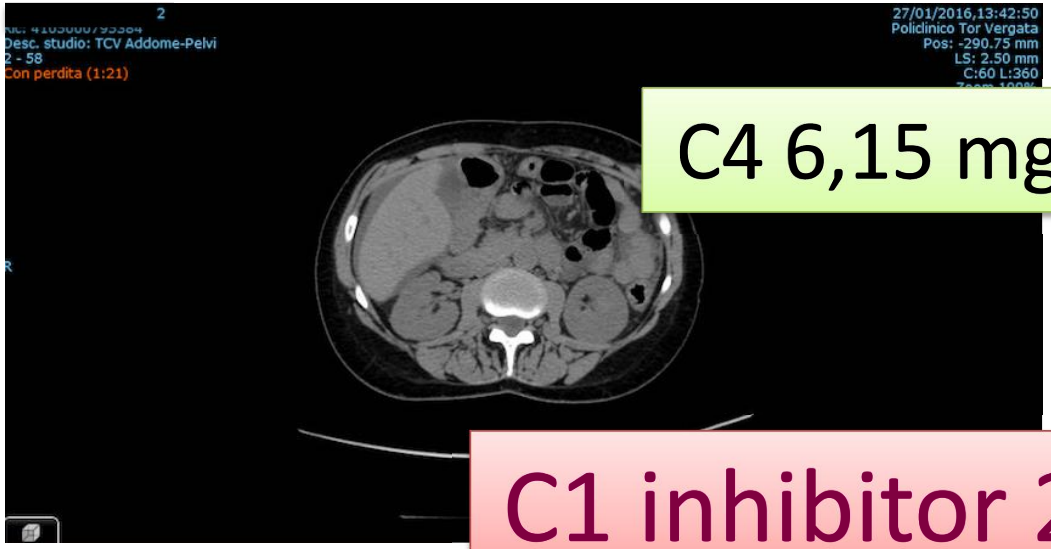
Referto Validato da: Dott.ssa Lorenza Bellincampi

CHIMICA CLINICA
Resp.: Prof. Sergio Bernardini

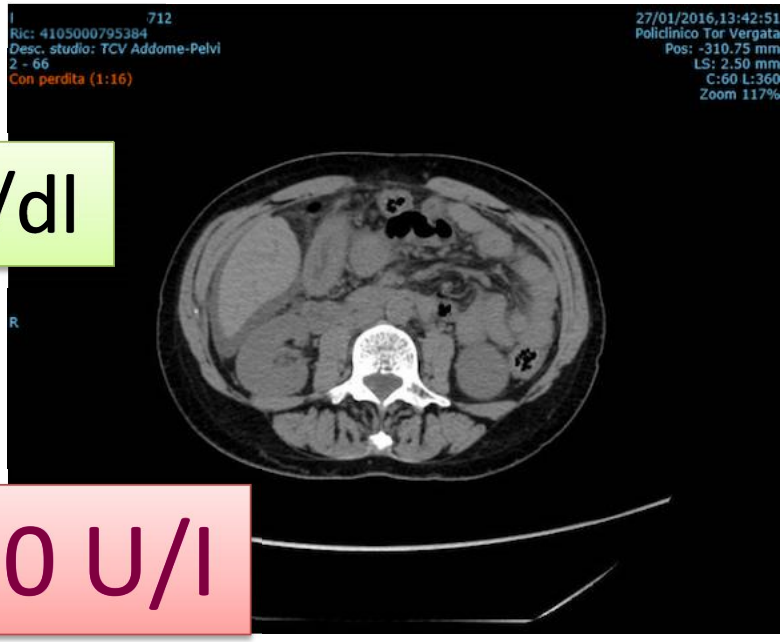
Glicemia	112	**	mg/dl	65	-	100
Azotemia	25.00		mg/dl	15.00	-	50.00
Creatinina nel siero	0.70		mg/dl	0.44	-	1.10
Uricemia	3.40		mg/dl	2.40	-	5.70
Calcio	9.00		mg/dl	8.40	-	10.20

Fosforo Inorganico	3.10	mg/dl	2.70	-	4.50
Sodio nel Siero	136	mEq/L	133	-	145
Potassio nel Siero	4.30	mEq/L	3.30	-	5.10
Magnesio	1.91	mg/dl	1.58	-	2.55
Cloro	101	mEq/L	96	-	110
Proteine Totali	7.20	g/dL	6.40	-	8.20
ALBUMINA	4.00	gr/dl	3.40	-	4.80
GOT/AST	14.00	U/L	6.00	-	24.00
GPT /ALT	27.00	U/L	13.00	-	45.00
Bilirubina Totale	0.23	mg/dl	0.20	-	1.10
Bilirubina Diretta	0.10	mg/dl	0.01	-	0.20
Gamma GT	16.00	U/L	5.00	-	55.00
Fosfatasi Alcalina	56.00	U/L	35.00	-	120.00
Colinesterasi (CHE)	8403	U/L	7000	-	19000

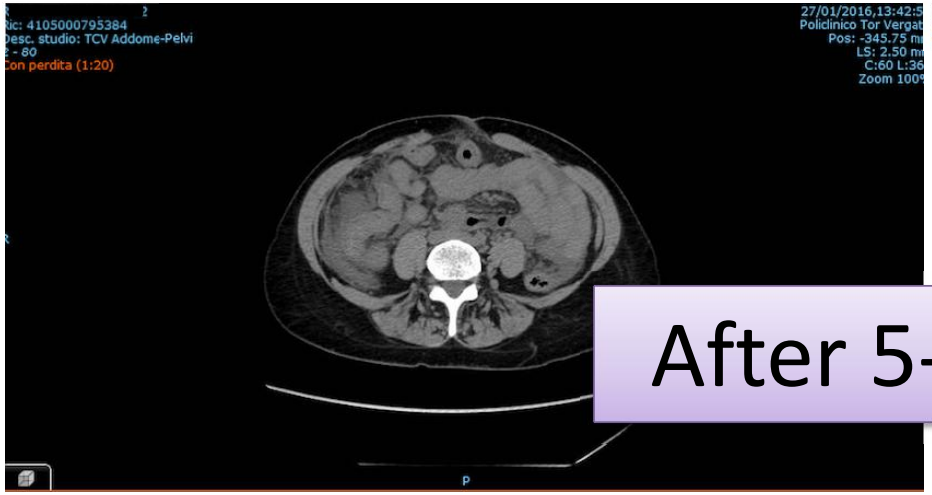
Ect: falda di versamento fluido in sede periepatica, a livello del recesso del Morrison a livello dello spazio perisplenico lungo le docce parietocoliche e nello scavo del Douglas

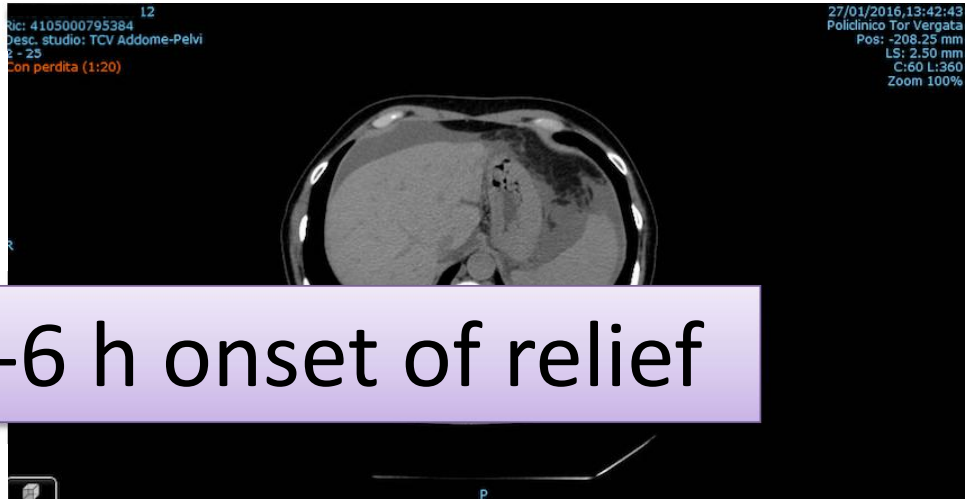


C4 6,15 mg/dl



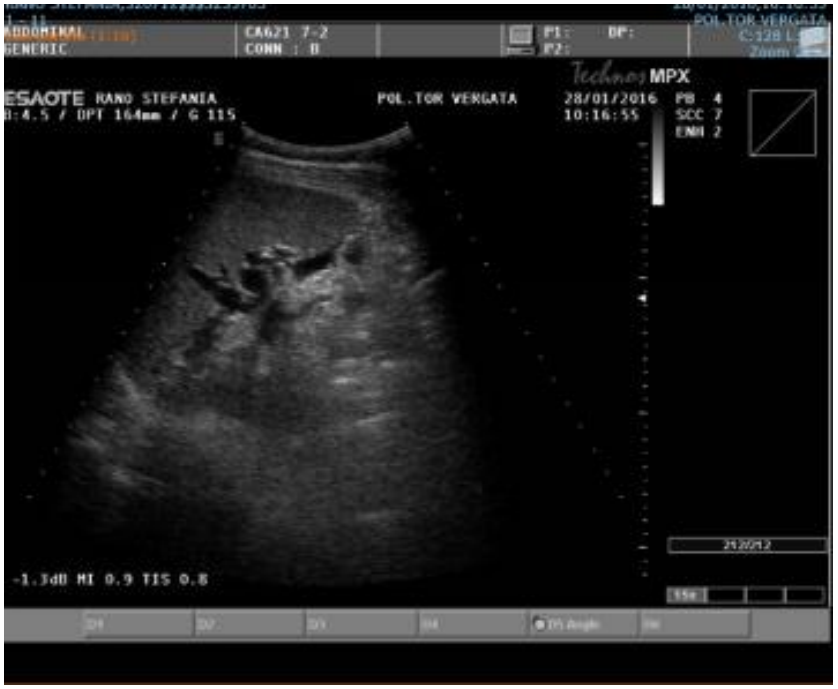
C1 inhibitor 20 U/l

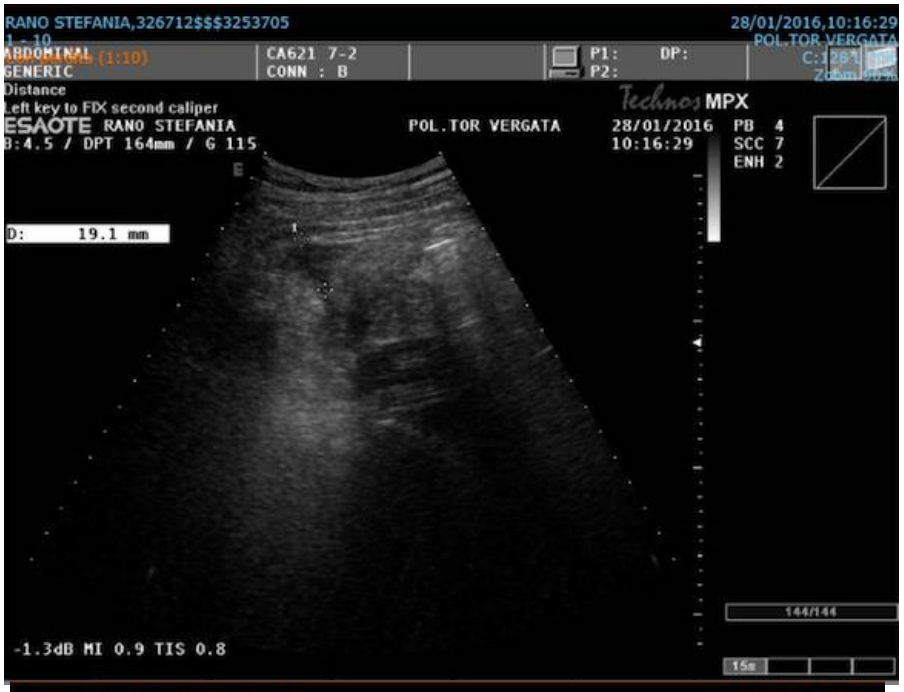


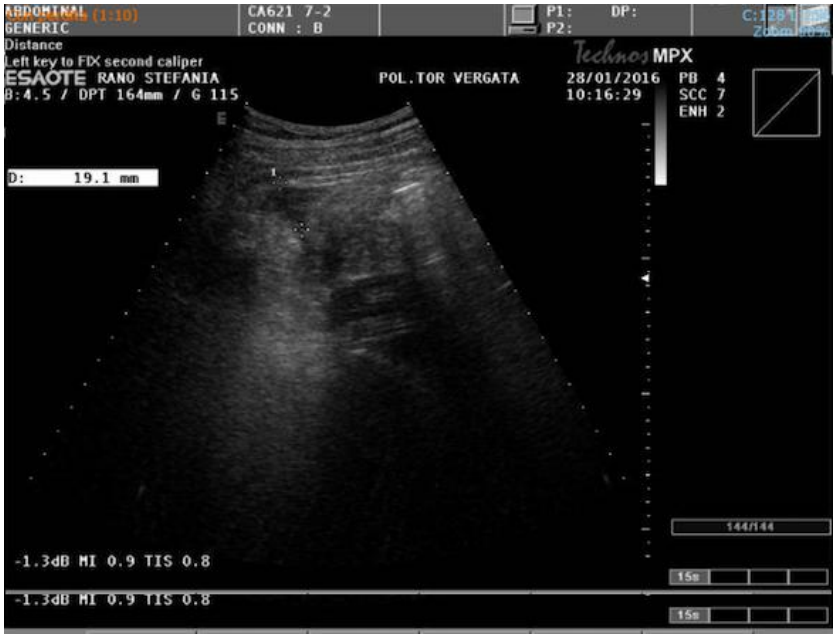


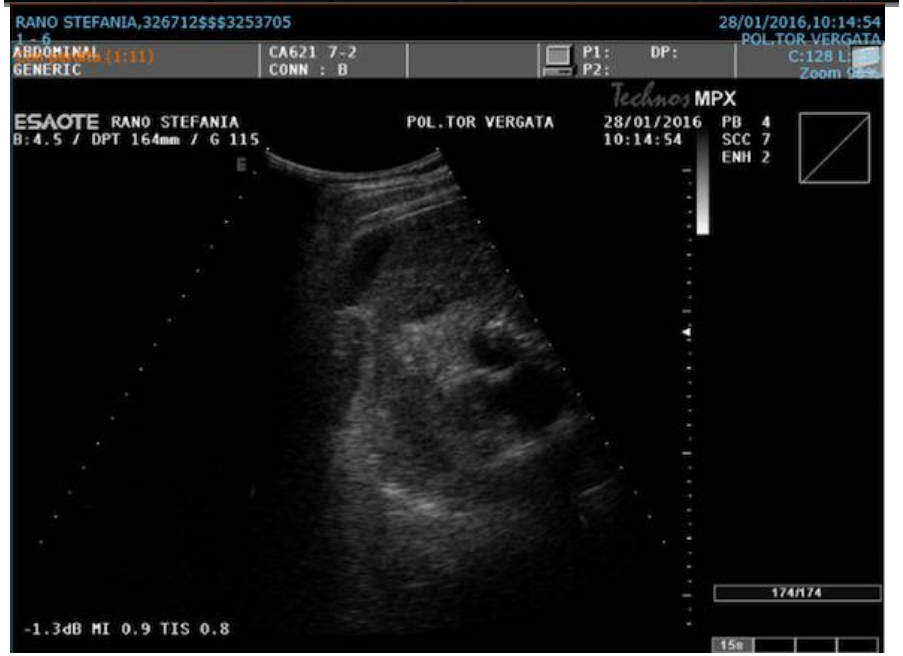
After 5-6 h onset of relief

Casistica del centro

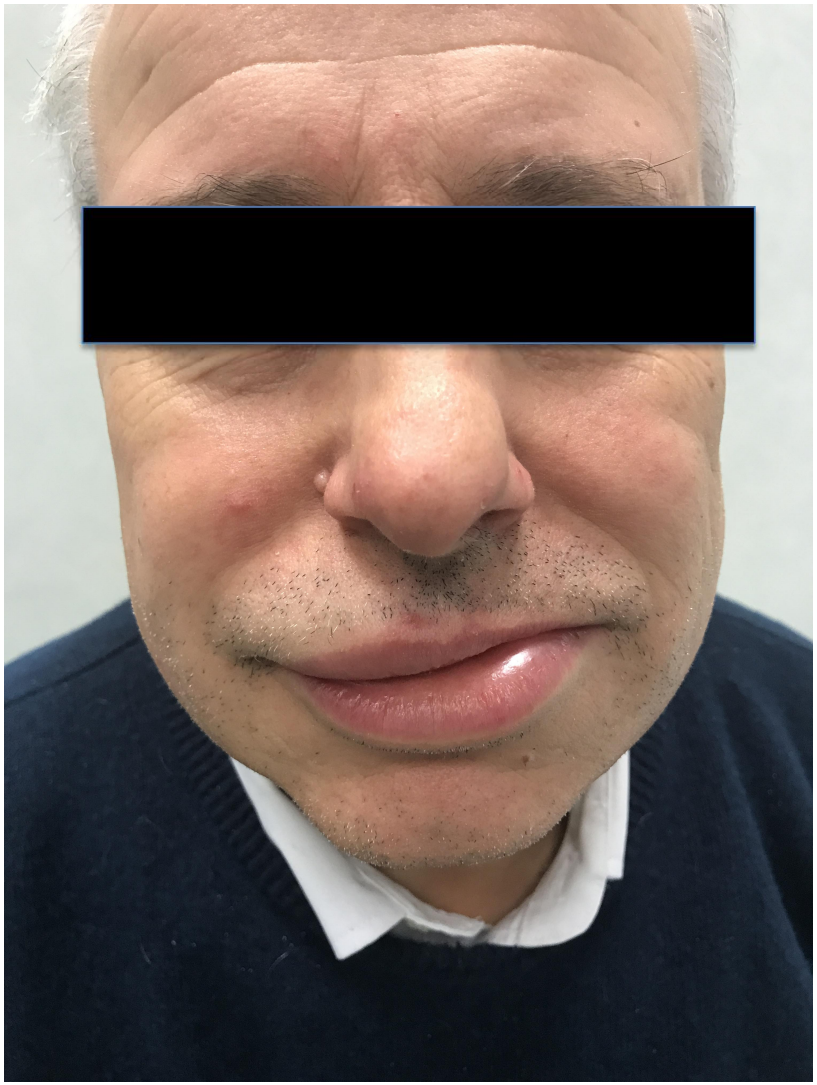




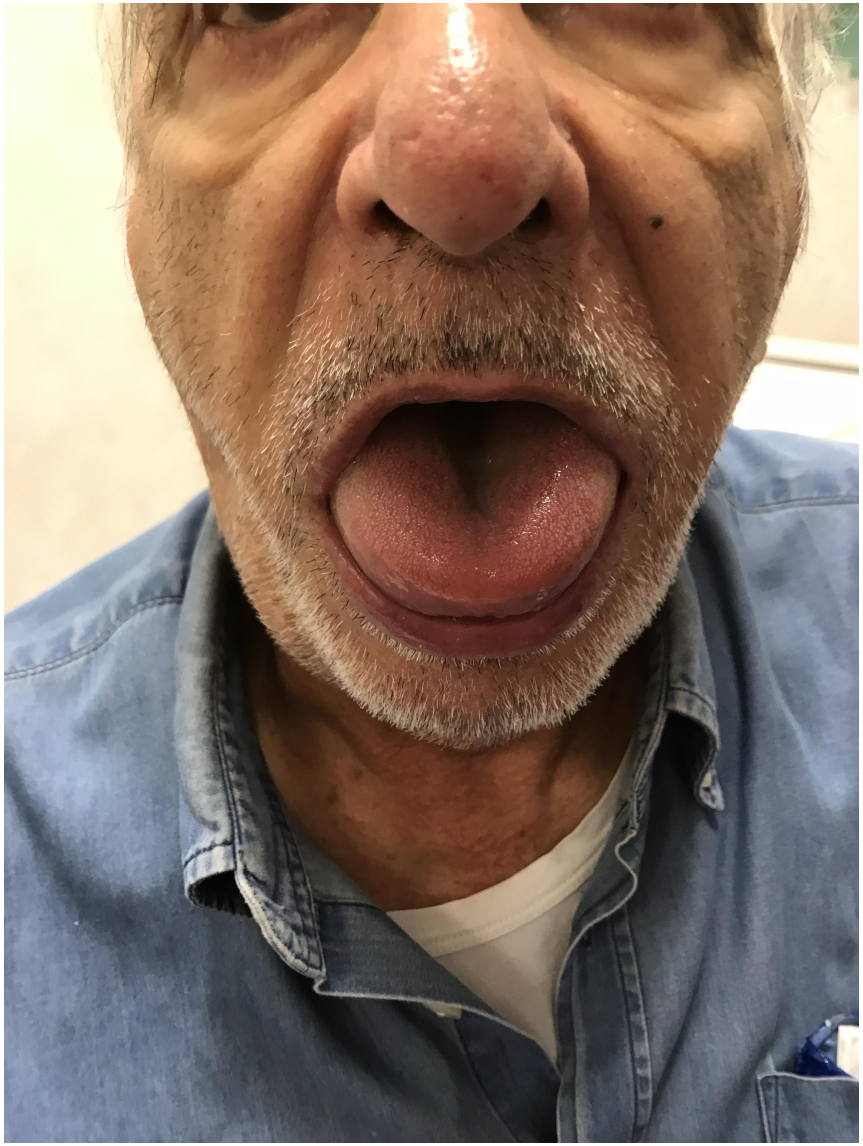




Casistica del centro



Casistica del centro



Casistica del centro

Intern Emerg Med (2014) 9:455–462
DOI 10.1007/s11739-013-1007-x

EM - ORIGINAL

Drug-induced angioedema: experience of Italian emergency departments

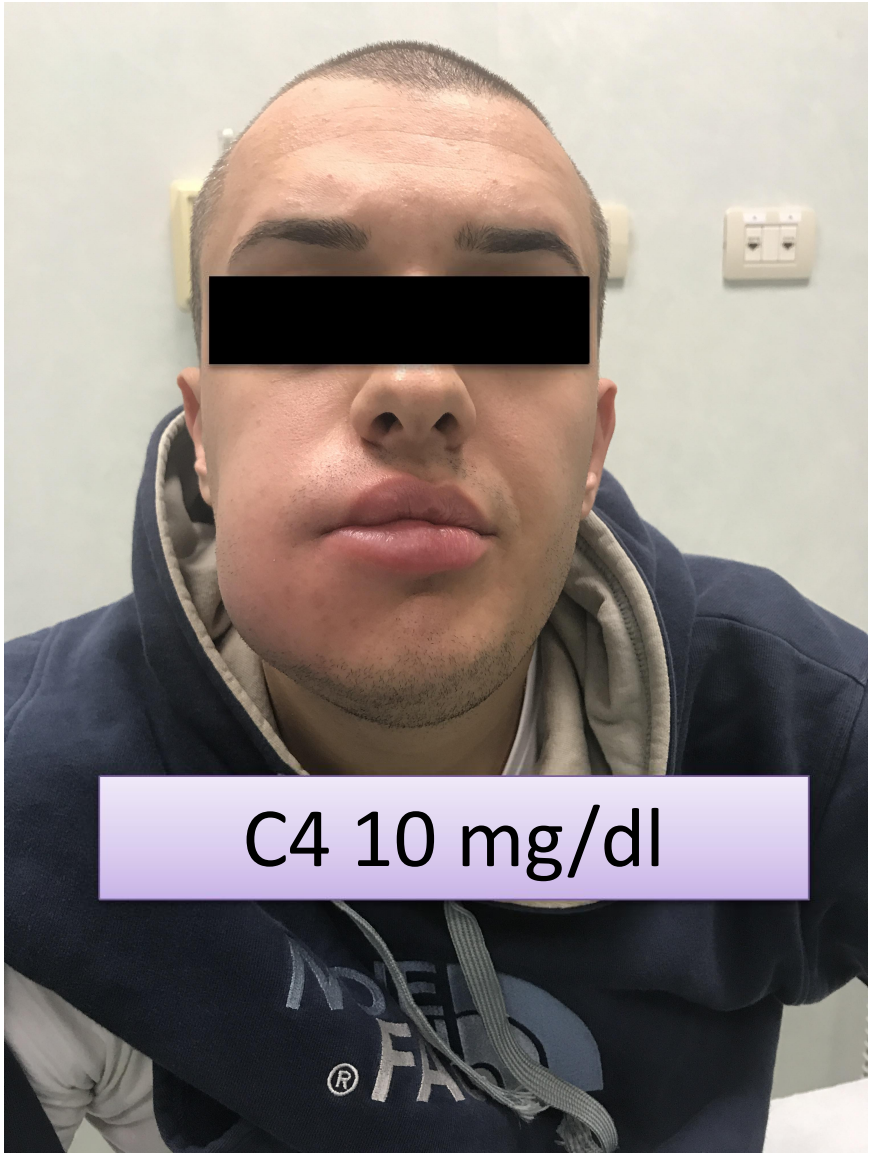
G. Bertazzoni · M. T. Spina · M. G. Scarpellini · F. Buccelletti · M. De Simone · M. Gregori · V. Valeriano · FR Pugliese · M. P. Ruggieri · M. Magnanti · B. Susi · L. Minetola · L. Zulli · F. D'Ambrogio

European Review for Medical and Pharmacological Sciences 2015; 19: 149-153

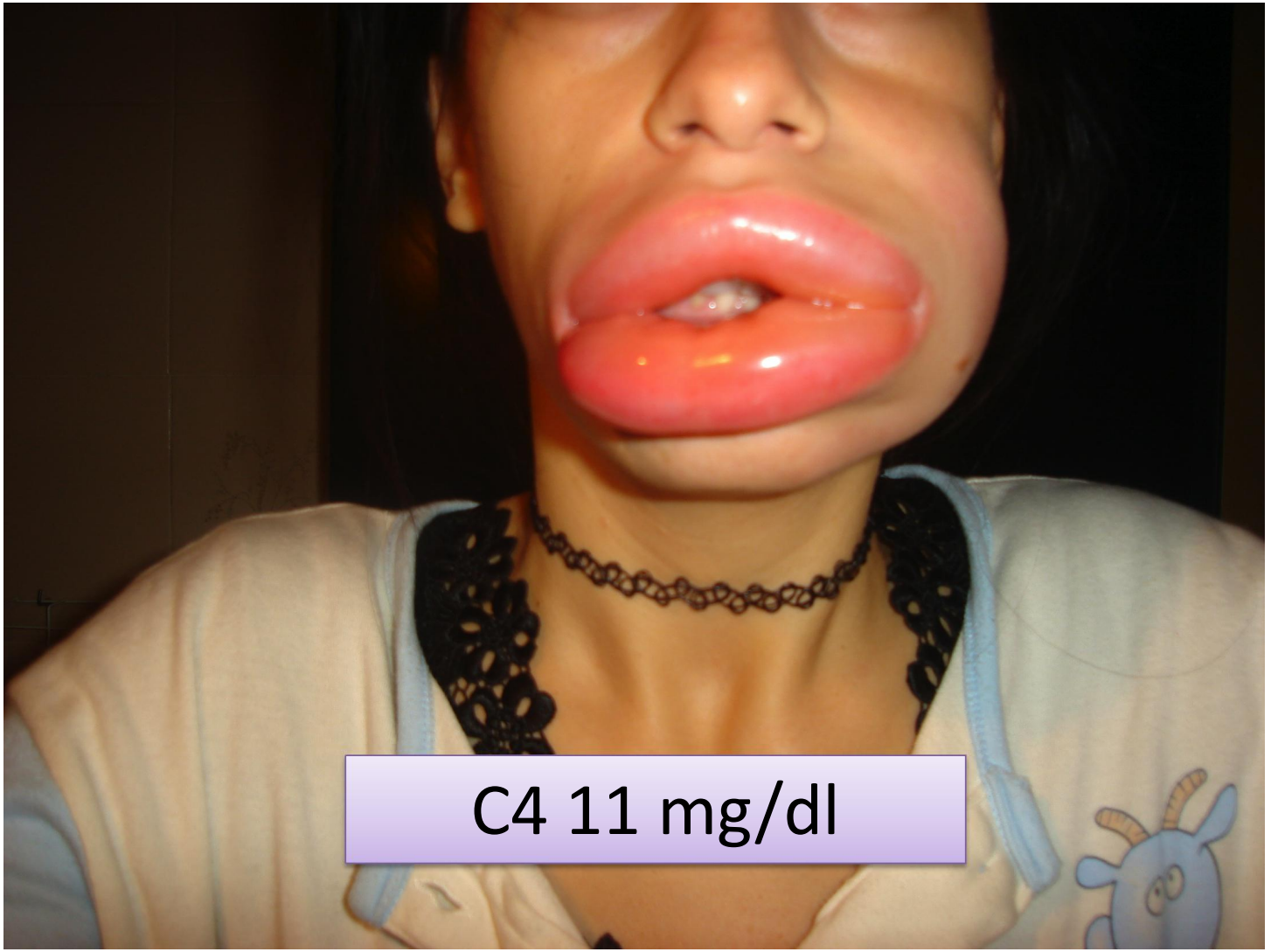
Treatment with icatibant in the management of drug induced angioedema

G. BERTAZZONI, E. BRESCIANI[1], L. CIPOLLONE[1], E. FANTE[1], R. GALANDRINI

Research Center on Evaluation and Promotion of Quality in Medicine (CEQUAM), "Sapienza" University of Rome, Rome, Italy
Emergency Medicine Unit, "Sapienza" University of Rome, Umberto I Polyclinic, Rome, Italy



Casistica del centro



Casistica del centro

LINEE GUIDA PS

il triage segue le stesse regole del triage avanzato Regione Lazio con in aggiunta

Codice Rosso: presenza di edema del volto, edema della glottide, edema del collo, con una delle seguenti condizioni
- disfonia
- stridore laringeo
- tirage
- distress respiratorio
- ipossiemia

il triage segue le stesse regole del triage avanzato Regione Lazio con in aggiunta

Codice Giallo: edema delle labbra, edema delle palpebre, edema lieve del volto, dolori addominali con nausea, diarrea e/o vomito, sensazione di corpo estraneo a livello della gola non obiettivabile come edema della glottide, edema dei genitali

il triage segue le stesse regole del triage avanzato Regione Lazio con in aggiunta

Codice Verde: edema delle estremità, arti superiori, arti inferiori

Esame obiettivo ed anamnesi con particolare attenzione alla frequenza degli attacchi ed alla localizzazione, in caso di pazienti senza diagnosi di angioedema ereditario e/o acquisito chiedere anche se presente familiarità, anamnesi farmacologica

Esami di laboratorio da eseguire in caso si attacco acuto di angioedema ereditario: Emocromo, crasi epatica e renale, coagulazione (**senza il D dimero che nei casi di attacchi acuti può essere aumentato in maniera aspecifica**)

Esami strumentali da eseguire, in caso dei edema del volto e del collo: videat ORL con fibrolaringosopia; nei pazienti con attacchi localizzati all'addome, eseguire ecografia addominale ed eventualamente Tc addome per escludere cause organiche di addome acuto.

ALLERGY,
CLINICAL IMMUNOLOGY
RHEUMATOLOGY
R. PERRICONE

Francesca Cedola
Paola Triggianese

reumatologia@ptvonline.it

EMERGENCY DEPARTEMENT
B. SUSI J.M. LEGRAMANTE

ALIVERNINI
BEVILACQUA
BRANDI
CANONACO
CLEMENTE
BURATTI
DELLE ROSE
DI LECCE
DE VITO
DI VINCENZO
FATTORE
FERRANNINI

M. ROMANI… G. DE ANDREIS

CIROTTI…. COMPAGNONI….
MARCHINI… BOTTARDI…..
CALVITTI…

CARE

MORAZZINI