EAACI

EUROPEAN ACADEMY OF ALLERGY AND CLINICAL IMMUNOLOGY

Skin Allergy Club 2024

Paris, France

EAACI 8th Skin Allergy Club
28 - 29 November 2024
Paris, France

Thursday, 28 November 2024
Dermatology and Allergy Department
Tenon University Hospital

14:30 – 14:40	**Welcome and introductory remarks** **Annick Barbaud, France** **Pavel Kolkhir, Germany**
14:40 – 16:20	**Topics: Dermatitis and cutaneous adverse reactions** *Five oral presentations by JMs* *(15 minutes each + 5 minutes for discussion with coffee break)*
14:40	"Drug hypersensitivity reactions secondary to HIV pre-exposure prophylaxis medications" **Ky-Lyn Tan, UK**
15:00	"Contact fragrance sensitivity and its association with other chemical allergens in patients with chronic facial skin diseases" **Juste Staikunaite, Lithuania**
15:20	"Atopic dermatitis is associated with Staphylococcal strain growth and metabolic behavior" **Hogan Kok-Fung Wai, UK**
15:40	"Cutaneous adverse reactions in patients with plasma cell neoplasms treated with lenalidomide can be severe and chemotherapy is not always responsible." **Anna Laurier, France**
16:00	"Skin manifestations in progesterone hypersensitivity: case report and literature review" **Denisa Alexandra Baloiu, Romania**
16:20 – 16:40	Coffee break and networking
16:40 – 17:10	**Lecture: "Histaminergic *vs.* bradykinergic angioedema"** **Teresa Caballero, Spain**
17:10 – 17:40	**Lecture: "Update on chronic urticaria treatment"** **Pavel Kolkhir, Germany**
17:40 – 20:00	Free time
20:00	Dinner at Bistro Chantefable (https://chantefable.fr)

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Friday, 29 November 2024
Dermatology and Allergy Department
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07:15 – 08:15	Breakfast at the Hotel Walk to the Tenon University Hospital
09:00 – 09:10	**Welcome and introductory remarks** **Teresa Caballero, Spain** **Polina Pyatilova, Germany**
09:10 – 10:50	**Topics: Angioedema and chronic spontaneous urticaria** *Five oral presentations by JMs* *(15 minutes each + 5 minutes for discussion)*
09:10	"Early Presentation of Hereditary Angioedema Symptoms in 2-year-old Boy" **Justina Sematonyte, Lithuania**
09:30	"Fertility treatments in patients with Bradykinin-Induced Angioedema (BK-AE): a case serie" **Monica Lalesca Colque Bayona, Spain**
09:50	"Omalizumab and chronic spontaneous urticaria: 'one dose does not fit all', an update" **Antonino Marcello Pilia, Italy**
10:10	"Preliminary Insights into the Impact of Elevated Tryptase on Disease Control, Symptoms and Quality of Life in Chronic Spontaneous Urticaria" **Nicole Nojarov, Germany**
10:30	"Chronic urticaria among family members, unmet needs in diagnostic approach, probable clinical role of anti-CCD IgE" **Eralda Lekli, Albania**
10:50 – 11:10	Coffee break and networking
11:10 – 11:30	**Lecture: "Digital health monitoring: MASTHAVE experience"** **Polina Pyatilova (JM), Germany**
11:30 – 12:00	**Lecture: "Which allergy work up for which cutaneous adverse drug reaction"** **Annick Barbaud, France**
12:10 – 13:00	Group Tour to the Dermatology and Allergy department at the Tenon University Hospital (led by Prof. Annick Barbaud)
13:00 – 13:10	**Summary of SAC 2024 and Closing Remarks** **Teresa Caballero, Spain** **Polina Pyatilova, Germany**

EAACI 8th Skin Allergy Club
28 - 29 November 2024
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Table of Contents

Abstract Presentations: Day 1

Topics: Dermatitis and cutaneous adverse reactions

Drug Hypersensitivity Reactions Secondary To HIV Pre-exposure Prophylaxis Medications

Ky-Lyn Tan

Introduction: The use of pre-exposure prophylaxis (PrEP) medication for patients at risk of HIV has been recommended by WHO since 2015. This has become more readily available over recent years. Current available oral PrEP includes a combination of tenofovir disoproxil/emtricitabine or tenofovir alafenamide/emtricitabine with the initial combination being most widely prescribed in the UK. Cabotegravir, lenacapavir and dapivirine are other long-acting options, however they are not widely available in the UK. We have recently noticed an increase in number of patients reporting drug hypersensitivity reactions to PrEP, specifially tenofovir disoproxil/emtricitabine.

Case series presentation: A total of fie patients have been referred for cutaneous reactions secondary to PrEP over the last 18 months across 2 allergy centres. Two confimed positive challenges totenofovir disoproxil/emtricitabine have been observed, both of which were delayed. One case presented as a delayed maculopapular exanthema, while the other presented as symmetrical drug-related intertriginous and flxural exanthema. Ongoing investigations are being conducted to identify the culprit drug and to fid safe alternatives. The remaining three patients report a generalized red rash after taking the same drug, all of which are awaiting further investigation. Of these, two experienced delayed reactions, and one reported a generalized rash occurring within an hour of ingesting the combination drug.

Discussion: There is currently limited evidence in the literature regarding cutaneous drug hypersensitivity reactions to tenofovir and emtricitabine. One case report describes a positive patch test to both drugs, while another reports a lichenoid drug eruption linked to tenofovir. A randomized study comparing emtricitabine and lamivudine in HIV patients showed that 50 out of 294 patients experienced a rash with emtricitabine, though it remains unclear how many of these were due to delayed hypersensitivity. Although tenofovir and emtricitabine are both nucleoside reverse transcriptase inhibitors, their chemical structures diffr. At present, it remains unclear which phenotypes of cutaneous drug hypersensitivity reactions are associated with each antiretroviral.

Conclusion: With the increased use of PrEP medications, we may observe a rise in allergic reactions to these antiretrovirals. Further studies are necessary to better understand the phenotypes of cutaneous manifestations associated with antiretrovirals and their cross-reactivity. This is important to help identify safe alternatives for patients, significantly improving their health and quality of life

EAACI 8th Skin Allergy Club
28 - 29 November 2024
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Contact fragrance sensitivity and its association with other chemical allergens in patients with chronic facial skin diseases

J. Staikunaite[1], G. Rudzikaite-Fergize[2], J. Grigaitiene[3]

[1,3] Vilnius University, Vilnius, Lithuania, [2] Vilnius University, Centre of Dermatovenerology

Background: Daily exposure to chemical compounds puts patients with chronic skin diseases at a higher risk of sensitization due to their damaged skin barrier. The aim of our study was to determine the sensitization pattern to fragrances and its association with other chemical allergens in patients with chronic facial skin diseases.

Methods: A retrospective analysis of the medical records of 158 subjects with chronic facial dermatosis (dermatitis, rosacea, acne), referred to a tertiary Vilnius University Dermatovenerology Centre was conducted. Patch testing with European Baseline Series (S-1000) and Cosmetic Series (C-1000) allergens was performed, results were evaluated according to European guidelines.

Results: Contact sensitivity to at least one tested chemical allergen was confirmed in 132 patients (83.54%). The median age was 39 years; 7 men (5.3%) and 125 women (94.7%). The most common referral diagnosis was allergic contact dermatitis (88, 66.7%). 54 patients (40.9%) tested positive for at least one of ten tested fragrance allergens, with a mean age of 38.5 ± 12.2 years (52 women, 2 men). The most frequent positive reactions were to these fragrances: Myroxylon pereirae (balsam of Peru) (22, 16.7%), sorbitan sesquioleate (15, 11.4%), benzyl salicylate (13, 9.8%), fragrance mix I (12, 9.1%), fragrance mix II (11, 8.3%). Monosensitization was observed in 53.7% of cases, with co-sensitization to fragrance mixes 1 and 2 being the most common combination (5.6%). Exposure to chemical risk factors in the workplace was reported by 10 patients (18.5%). 12 patients (22.2%) with fragrance sensitization also had atopic diseases, with no significant difference between the groups. Fragrance sensitivity was most often associated with sensitization to plant origin allergens (42.1%, p=0.011), metals (63.0%, p=0.024), rubber (14.8%, p=0.04) and pharmaceutical substances (18.5%, p=0.025).

Conclusion: The majority of patients with facial skin diseases were sensitized to chemical compounds, with nearly half to fragrances, most commonly to balsam of Peru. Mixtures of fragrances I and II were the most common combination of fragrances that caused sensitization. No statistically significant difference in sensitization rates were found between age groups, history of atopic diseases and occupational exposure to chemicals. Sensitization to fragrances was statistically significantly associated with sensitization to allergens of plant materials, metals, rubber, pharmaceuticals.

Atopic dermatitis is associated with Staphylococcal strain growth and metabolic behavior

WAI Hogan Kok-Fung, MOYES David, TUN Hein Min

Introduction: It has been established that skin microbes such as Staphylococcus aureus (S. aureus) and Staphylococcus hominis (S. hominis) play a role in the pathophysiology of atopic dermatitis (AD). However, there is an incomplete understanding about the role and interplay of different Staphylococcus species in the disease development. Our study aimed to

determine the growth curves and metabolic activity of Staphylococcus species isolated from the skin of subjects with AD and without atopy.

Methods: In this cross-sectional study, 23 AD subjects and 22 healthy controls were recruited. Premoistened swabbing was conducted to isolate bacteria from a lesional and non-lesional area of each subject's body. Growth curves from 35 S. aureus and 12 S. hominis strains were generated by measuring the optical density of each strain for 24 hours. A tetrazolium-based XTT assay was used as a proxy to measure the metabolic output of each Staphylococcal strain.

Results: Compared to healthy non-atopic controls, S. aureus was positively associated with AD children and S. hominis was negatively associated with AD children ($p < 0.01$). There was an inverse relationship ($\rho = -0.723$; $p < 0.01$) between the growth rate of S. aureus strains and the absolute amount of growth of the S. aureus strains. Notably, S. aureus strains isolated from severe AD patients tended to have higher absolute amounts of growth and slower growth rates than strains isolated from less severe AD patients. No discernable relationship could be observed for S. hominis strains in terms of their growth dynamics. When looking at the metabolic behavior of the Staphylococcal strains, S. hominis strains isolated from lesional skin exhibited lower metabolic activity than those from non-lesional skin ($p < 0.05$). The opposite held true for S. aureus strains.

Conclusions: These findings suggest that there is a key difference in the Staphylococcal strains found on the skin of AD subjects and healthy controls, with AD strains growing slower but to a higher burden. The inverse metabolic outputs of Staphylococcal strains based on lesion status provides initial evidence for the interaction of strains present on the skin of patients with AD. Further investigation is needed to elucidate whether this could result in higher levels of Staphylococcus metabolites that could drive the more severe manifestations of disease

Cutaneous adverse reactions in patients with plasma cell neoplasms treated with lenalidomide can be severe and chemotherapy is not always responsible.

Anna Laurier, Annick Barbaud, Angèle Soria

AP-HP Sorbonne Universite, Tenon Hopital, Department of Dermatology and Allergology, Paris, France

Background: Since 2007, plasma cell neoplasms (PCN) have been treated with lenalidomide, an immunomodulator drug that can be combined with a proteasome inhibitor (bortezomib) or an anti-CD38 monoclonal antibody (daratumumab). Corticosteroids and many anti-infectives are often used in combination. Lenalidomide causes rash in 44.4% of cases. Although a few cases of lenalidomide-induced drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported, they have not been confirmed by positive allergy tests. The aim of this retrospective analysis of 5 cases is to evaluate whether chemotherapeutic agents or other drugs were the cause of severe cutaneous adverse reactions in PCN patients treated with lenalidomide and other drugs.

Methods: Five patients with PCN developed serious cutaneous adverse reactions, two with DRESS and three with maculopapular exanthema (MPE) accompanied by systemic symptoms. Suspected drugs, including chemotherapeutic agents in only some patients, were tested by patch testing, intradermal testing (IDT), and drug challenge (DC) when skin tests were negative.

Results: In both cases of DRESS, multi-sensitization was demonstrated by positive patch tests to anti-infective drugs (Table 1). Although lenalidomide and cotrimoxazole tested negative, the drug challenge with cotrimoxazole induced a mild rash in both patients. Lenalidomide was reintroduced in only one patient, who developed a mild rash. In two of the three MPE cases, skin tests were negative to all tested drugs. One of the MPE cases had a positive IDT to bortezomib (0,025mg/ml and 0,25mg/ml).

Conclusion: Lenalidomide can induce rash, but in two cases of DRESS, patients were multi-sensitized to other drug classes. The sensitivity of skin tests to lenalidomide remains to be defined, as in one case the skin tests were negative but the DC to lenalidomide was positive. The specificity of IDT for bortezomib needs to be confirmed. Severe MPE or DRESS in PCN seems to be increasingly common in our allergy center. As in cladribine treated hairy cell leukemias, we emphasize that in DRESS occurring in PCN treated with lenalidomide, a breakdown of drug tolerance may occur leading to severe CADRs with multiple sensitizations, especially to anti-infectives which need to be tested.

Table 1.

Patient	1	2	3	4	5
Sex	M	F	M	M	F
Age (years) (Median age=62)	59	55	62	85	64
Pathology	Multiple Myeloma	Plasmocytoma	MGUS	Multiple Myeloma	Multiple Myeloma
Manifestation	DRESS (regiScar 7)	DRESS (regiScar 4)	mini-DRESS/severe EMP with systemic symptoms	EMP with systemic symptoms	EMP with systemic symptoms
Immunomodulator	Lenalidomide	Lenalidomide	Lenalidomide	Lenalidomide	Lenalidomide
Proteasome inhibitor	Bortezomib	-	-	-	Bortezomib
Anti CD38 monoclonal antibody	Daratumumab	-	Daratumumab	Daratumumab	-
Corticosteroid	Dexamethasone	Dexamethasone	Prednisone	Dexamethasone	Dexamethasone
Chronologically suspected drugs	Lenalidomide Dexamethasone Cotrimoxazole Valaciclovir Alaciclovir Entecavir Cefazoline Cefepime Ceftriaxone, **Clindamycin** Apixaban Esomeprazole Acide folinique Teicoplanin	Lenalidomide Dexamethasone Cotrimoxazole **Valaciclovir**, **Amoxicillin** Apixaban	Lenalidomide Prednisone Cotrimoxazole Oracilline Apixaban Acide folinique	Lenalidomide Dexamethasone	Lenalidomide **Bortezomib** Dexamethasone
Skin Test positive	Yes: Clindamycin (patch)	Yes: Amoxicillin (patch) Valaciclovir (patch) Dicloxacillin (patch) Tazocillin (patch + and IDT)	No	No	Yes: Bortezomib (IDT)
Oral challenge positive	Yes: Cotrimoxazole, Lenalidomide	Yes: Cotrimoxazole	No	Scheduled	-
Co-sensitization	Yes	Yes	No	No	No
Cotrimoxazole oral challenge	Positive	Positive	-	Scheduled	-
Reintroduced and tolerated drugs	Daratumumab, Valaciclovir, Folic acid, Esomeprazole	Dexamethasone, Apixaban	Valaciclovir, Apixaban, Oracilline	Bortezomib	Dexamethasone
Treatment and outcome after allergic investigations	Carfilzomib, Daratumumab, Autologus Stem Cell Transplant	Remission	Unknown	Dexamethasone, Bortezomib, Daratumumab	Cyclophosphamide, Autologus Stem Cell Transplant, Reccurence in 2023 treated with Carfilzomib, Dexamethasone

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28 - 29 November 2024
Paris, France

Skin manifestations in progesterone hypersensitivity: case report and literature review

Denisa-Alexandra Băloiu1 ,2, Selda Ali1,2, Mihaela Ruxandra Udrea1 ,2, Roxana Silvia Bumbăcea1,2

1. Carol Davila University of Medicine and Pharmacy, Bucharest
2. Department of Allergy and Clinical Immunology, “Dr. Carol Davila” Nephrology Hospital, Bucharest

RATIONALE: Progesterone hypersensitivity (PH) is an uncommon condition that can arise from exposure to both exogenous and endogenous sources of progesterone. The clinical presentations of PH are diverse, encompassing a broad spectrum of dermatological manifestations such as urticaria, erythema multiforme, eczema, and fixed drug eruptions, which contribute to the complexity and challenges in its diagnosis. In some cases, the skin lesions are associated with a systemic, anaphylactic reaction.

METHODS: We report a case of PH and conducted a literature review, using PubMed database, to better classify the full spectrum of dermatological manifestations associated with this condition.

RESULTS: A 45-year-old woman, with primary infertility, developed a pruritic maculopapular exanthema during her first in-vitro fertilization (IVF) cycle, several weeks after receiving various forms of exogenous progesterone (oral, intravaginal, and subcutaneous). PH was suspected, leading to the discontinuation of progesterone and a subsequent spontaneous abortion. Allergy workup confirmed PH with positive patch and intradermal tests to injectable progesterone. Two successful intravaginal progesterone desensitizations for two other subsequent IVF cycles were necessary, as one resulted in early pregnancy loss, and the other one failed to achieve implantation. The review of the literature yielded 131 publications documenting 196 patients with PH involving skin and/or mucosal symptoms. The mean age of onset was 28.7 years (range: 12–55 years). The most common cutaneous manifestations were urticaria in 90 patients (46%), erythema multiforme in 32 (16%), and eczema in 18 (9%). While angioedema occurred in 39 patients (20%), lesions of the oral/vaginal mucosa were reported in 16 patients (8%). Anaphylaxis was documented in 25 patients, with 72% of episodes triggered by endogenous progesterone and the remaining 28% were linked to exogenous progesterone administration. Diagnosis was confirmed with an intradermal progesterone sensitivity test in 118 patients (60%) and 22 patients (11%) required progesterone desensitization.

CONCLUSION: PH is a challenging condition to diagnose due to its variable clinical presentations. For cases with endogenous trigger, it is crucial to consider PH in any recurrent rash in females. In the context of infertility, where luteal support is necessary, PH can present significant challenges, necessitating the consideration of desensitization protocols.

EAACI 8th Skin Allergy Club
28 - 29 November 2024
Paris, France

Abstract Presentations: Day 2

Topics: Angioedema and chronic spontaneous urticaria

Early Presentation of Hereditary Angioedema Symptoms in 2-year-old Boy

Sematonyte J[1], Staikunaite J[2], Staikuniene-Kozonis J[1]

[1] Department of Immunology and Allergology, Lithuanian University of Health Sciences, Kaunas, Lithuania

[2] Faculty of Medicine, Vilnius University, Lithuania

Background: Hereditary angioedema (HAE) is a rare autosomal dominant disease that is caused by deficiency or dysfunction of the C1 inhibitor (C1-INH). There are three types of HAE. Type I (low level of C1-INH) and type II (dysfunction of C1-INH) are caused by a mutation in the SERPING1 gene which makes the C1 inhibitor protein, while type III (normal level of C1-INH) is often due to a mutation in the F12 gene. HAE clinically manifests with intermittent attacks of swelling of the subcutaneous tissue or submucosal layers of the respiratory or gastrointestinal tracts which were triggered by precipitating factors such as emotional stress, traumas, hormonal influences, infections, surgery or dental procedures. Symptoms often begin in puberty and occur by age 20 in the most patients but attacks are uncommon among pediatric patients. We present a 2-year-old boy with HAE who had recurrent episodes of swelling of the extremities and face without urticaria and pruritus.

Methods: The patients was consulted by allergologist – clinical immunologist in a tertiary university hospital for reccurent peripheral oedema attacks. Complement C3, C4, C1 inhibitor levels were measured in serum. Genetical testing for suspected HAE was performed. HAE was diagnosed for patient‘s father after 8 years from the disease onset and the diagnosis was confirmed by de novo SERPING1 gene mutation.

Results: A 2-year-old male had experienced attacks of painfull swelling on his face and upper extremities which were triggered by a minor trauma or viral infections. The symptoms were not associated with urticaria or pruritus. The level of serum C4 was 0.07 g/l (normal: 0.16-0.38), C3 was 0.78 g/l. (normal: 0.79-1.52). The level of C1 inhibitor was 0.05 g/l (normal: 0.15-0.35). SERPING1 gene mutation was identified and HAE Type 1 due to C1-INH deficiency was confirmed. Plasma-derived C1 esterase inhibitors concentrates were prescribed during acute attacks. Symptoms usually stabilized within 30 minutes.

Conclusion: The presented clinical case confirms that there is a tendency to transmit this disease among other family members. As far as we know, this is the first pediatric case with particularly early onset with typical clinical symptoms of HAE due to C1 esterase inhibitor deficiency in Lithuania.

EAACI 8th Skin Allergy Club
28 - 29 November 2024
Paris, France

Fertility treatments in patients with Bradykinin-Induced Angioedema (BK-AE): a case series

M Colque-Bayona1, T Navarro-Cascales1,2, M Goyanes-Malumbres 1,2, T Caballero1,2,3

1. Department of Allergy, La Paz University Hospital, Madrid, Spain.
2. La Paz Institute for Health Research (IdiPAZ), Madrid, Spain.
3. Center for Biomedical Research Network on Rare Diseases (CIBERER U754), Madrid, Spain.

Introduction: Increased estrogen levels are recognized as a trigger of angioedema (AE) attacks in BK-AE. Assisted reproductive techniques (ARTs) encompass administration of hormones, resulting in an increase in estrogen levels.

Aim: to describe a case series of female patients with BK-AE who underwent ARTs.

Methods: A retrospective, descriptive study was performed. The clinical records of female patients with BK-AE were reviewed. The study was approved by the Ethics Committee (HULP-PI 4598).

Results: We included 10 patients with BK-AE who underwent a total of 30 ART procedures (Table I, II). Long-term prophylaxis with intravenous plasma derived C1INH 1,000 IU twice weekly starting at least one week before the procedure (LTP) was recommended for in vitro fertilization (IVF).
-Artificial insemination (n=6): No LTP was administered. Five procedures were well tolerated without AE attacks, while one resulted in increased AE attacks. One procedure resulted in a pregnancy.
-IVF with egg donation (n=6): Two procedures were performed using LTP. These procedures did not lead to any worsening of disease activity. Four procedures were carried out without LTP; three led to an increase in AE attacks, while one did not. Two of the procedures without LTP were successful. One procedure ended in miscarriage.
-IVF with own egg (n=18): Eight procedures were performed with LTP; no AE attacks occurred during five of these, while three maintained the same attack rate. Of the seven procedures without
LTP, all experienced an increase in attack frequency. Four procedures resulted in successful pregnancies, two ended in miscarriage and one in an anembryonic pregnancy.

Pre-implantation genetic diagnosis was performed in five cases, with one successful outcome, leading to the birth of a girl without HAE-C1INH. In one case, an embryo was transferred, but the patient experienced a miscarriage. In another case, the embryo was not implanted due to the presence of a SERPING1 gene mutation, and in another, the embryos were non-viable. One patient is still under study, and oocyte cryopreservation was performed.

Conclusion: ARTs can be performed in patients with BK-AE, though these procedures are associated with increased estrogen levels, which may raise the risk of more frequent and severe AE attacks.

Table I

Number of patients with BK-AE		10
HAE-C1INH type I		7
AAE-C1INH		2
HAE-FXII		1
Number of ARTs performed		30
AI		6
IVF		24
IVF with egg donation		6
IVF with own egg		18
Long term prophylaxis with IV pdC1INH used in the procedures		
AI		0
IVF with egg donation		2
IVF with own egg		8
ART performed according to angioedema type		
HAE-C1INH type I	AI	3
	IVF with oocyte donation	4
	IVF with own egg	7
AAE-C1INH	AI	3
	IVF with oocyte donation	2
	IVF with own egg	10
HAE-FXII	AI	0
	IVF with oocyte donation	0
	IVF with own egg	1
Successful procedures[a]		
AI	Boys	1
	Girls	0
	Twins	0
IVF with egg donation	Boys	0
	Girls	1
	Twins (2 boys)	1
IVF with own egg	Boys	2
	Girls	2
	Twins	0
Gynecologic/obstetric complications		
Artificial insemination	Pelvic inflammatory disease with tubo-ovarian abscess	1
IVF with egg donation	Miscarriage	1
	Endometrioma, salpingo-oophorectomy	1
IVF with own egg	Miscarriage	2
	Anembryonic gestation	1

Abbreviations: BK-AE, Bradykinin-Induced Angioedema; HAE-C1INH, hereditary angioedema due to C1 inhibitor deficiency; AAE-C1INH, acquired angioedema due C1 inhibitor deficiency; HAE-FXII, hereditary angioedema due to *F12* gene mutation; ARTs, assisted reproductive techniques; AI, artificial insemination; IVF, in vitro fertilization.

[a] Pregnancy with delivery

Table II

	Age[a]	Diagnosis	ARTs	LTP[b]	AE activity during ARTs	Pregnancy	Delivery	PGD	Child sex	BK-AE diagnosis of the child	Gynecologic/obstetric complications
1	35	HAE-C1INH type I	IVF OE	Yes	No change	Yes	No	Yes	--	--	Miscarriage
			IVF ED	Yes	No change	No	--	No	--	--	
			IVF ED	Yes	No change	No	--	No	--	--	Endometrioma, salpingo-oophorectomy
			IVF ED	No	No change	No	--	No	--	--	
			IVF ED	No	Increase	Yes	Yes	No	Girl	No	
2	34	HAE-C1INH type I	AI	No	Increase	Yes	Yes	No	Boy	No	
3	36	HAE-C1INH type I	AI	No	No attacks	No	--	--	--	--	Pelvic inflammatory disease with tubo-ovarian abscess
4	37	HAE-C1INH type I	IVF OE	Yes	No attacks	Yes	Yes	Yes	Girl	No	
5	38	HAE-C1INH type I	IVF OE	Yes	No attacks	No	--	Yes[c]	--	--	
			IVF OE	Yes	No attacks	No	--	Yes[d]	--	--	
			IVF OE	Yes	No attacks	No	--	Yes[e]	--	--	
6	21	HAE-C1INH type I	AI	No	No attacks	No	--	--	--	--	
			IVF OE	Yes	No attacks	No	--	No	--	--	
7	32	HAE-C1INH type I	IVF OE	Yes	No change	Yes	Yes	No	Boy	No	
8	45	AAE-C1INH	IVF OE	No	Increase	--	--	--	--	--	
			IVF OE	No	Increase	--	--	--	--	--	
			IVF OE	No	Increase	Yes	No	No	--	--	Miscarriage
			IVF OE	No	Increase	Yes	Yes	No	Girl	No	
			IVF OE	Yes	No change	Yes	Yes	No	Boy	No	
			IVF OE	ND	ND	--	--	--	--	--	
			IVF OE	ND	ND	--	--	--	--	--	
			IVF OE	ND	ND	--	--	--	--	--	
9	38	AAE-C1INH	AI	No	No attacks	No	--	--	--	--	
			AI	No	No attacks	No	--	--	--	--	
			AI	No	No attacks	No	--	--	--	--	
			IVF OE	No	Increase	No	--	--	--	--	
			IVF OE	No	Increase	No	--	--	--	--	
			IVF ED	No	Increase	Yes	No	No	--	--	Miscarriage
			IVF ED	No	Increase	Yes	Yes	No	Twins	No	
10	33	HAE-FXII	IVF OE	No	Increase	Yes	No	No	--	--	Anembryonic gestation

Abbreviations: ARTs, assisted reproductive techniques; LTP, Long-term prophylaxis; PGD, pre-implantation genetic diagnosis; BK-AE, Bradykinin-Induced angioedema; AAEC1INH, acquired angioedema due C1 inhibitor deficiency; HAE-FXII, hereditary angioedema due to F12 gene mutation; AI, artificial insemination; IVF OE, in vitro fertilization
with own egg; IVF ED, in vitro fertilization with egg donation; ND, no data.
a Age at the first assisted reproductive technique.
b IV pdC1INH 1,000 twice weekly at least 1 week before the procedure.
c Embryo not implanted because ofSERPING1 gene mutation.
d Embryos non-viable.
e Patient still under study, oocyte cryopreservation was performed.

OMALIZUMAB and chronic spontaneous urticaria: ‘one dose does not fit all’, an update

Pilia A.M. 1 Vivarelli E. 1 Rossi O. 2 Di Agosta E. 2 Cosmi L. 1,2 Salvati G. 3 Liotta F. 1,3 Parronchi P. 1,3 Matucci A.2 Vultaggio A. 1,2

1. Department of Experimental and Clinical Medicine, University of Florence

2. Immunoallergology Unit, Careggi University Hospital, Florence

3. Immunology and Cell Therapy Unit, Careggi University Hospital, Florence

Background: Omalizumab represents the second line treatment for chronic spontaneous urticaria (CSU). It is indicated in subjects who are non-responsive to antihistamine therapy.

Recommended dose is 300 mg every 4 weeks, independently from the total serum IgE (TSIgE) level and body weight (BW). Our study evaluated the efficacy of omalizumab in CSU at the standard dose and at the calculated dose, basing on TSIgE values and BW as in severe allergic asthma and chronic rhinosinusitis with nasal polyps.

Methods: Retrospective analysis of 120 patients with CSU who were treated with at least one 6 months-long omalizumab cycle at Careggi University Hospital from 2014 to June 2024. Patients who reached full remission after one cycle were defined as responders. Among relapsers who underwent two cycles or more, heavy relapsers were treated with more than four cycles. A ratio between the omalizumab calculated dose on TSIgE and BW and the standard dose for CSU was calculated for each patient. Mann-Whitney U test and chi-squared test were used for the comparison of continuous and categorical variables, respectively. Correlations were analysed with Spearman's rho and Kendall's tau.

Results: More than two third of our cohort was female (82/120), 39±15 years old at diagnosis with 8±8.1 years of disease. Most of patients had an association of angioedema and urticaria (76/120) and were treated with daily (46/120) or as needed (57/120) oral corticosteroids (OCS). Baseline eosinophil count was 1 71 ±1 83 cells/μL and TSIgE were 222.2±188.4 kU/L. No statistical difference was observed in terms of sex, age of onset, years of disease, baseline TSIgE, UAS7 and eosinophils, access to emergency department and presence of angioedema between responders (32/120) and relapsers (88/120). Among heavy relapsers a lower baseline eosinophil count (172±123 vs 190±201, $p<0.01$) and a positive correlation between the number of omalizumab cycles and TSIgE ($r=0.31$, $p<0.05$) emerged. Normalizing the omalizumab calculated dose on TSIgE and BW with standard dose for CSU (300 mg/4 weeks) a ratio = 1, < 1, > 1 e ≥ 2 in 45 (37.5%), 33 (27.5%), 42 (35.0%) and 25 (20.8%) patients resulted, respectively. In the heavy relapser group, such ratio positively correlated with the number of omalizumab cycles (Kendall Tau correlation coefficient 0.33, $p<0.05$).

Conclusion: The analysis of our data confirmed that a higher dose of omalizumab may prevent relapses and therefore reduce the number of drug cycles in heavy relapsers.

Preliminary Insights into the Impact of Elevated Tryptase on Disease Control, Symptoms and Quality of Life in Chronic Spontaneous Urticaria

Nicole Nojarov [1,2], Pascale Salameh [1,3], Frank Siebenhaar [1,2]

[1]Institute of Allergology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Berlin, Germany.

[2]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Immunology and Allergology IFA, Berlin, Germany.

[3]Department of Primary Care and Population Health, University of Nicosia Medical School, Nicosia, Cyprus; School of Medicine, Lebanese American University, Lebanon; Institut National de Santé Publique, Epidémiologie Clinique et Toxicologie (INSPECT-LB), Lebanon.

Objective: Hereditary Alpha-Tryptasemia (HαT) is an autosomal dominant disorder with a prevalence of 4-6% in the Western population. It is caused by an increased copy number of the TPSAB1 gene, which encodes the α-tryptase, resulting in persistently elevated serum tryptase levels (≥ 8 ng/ml). Previous studies have already shown that HαT has a higher prevalence in patients with mastocytosis, which is associated with an increased risk of

anaphylaxis. HαT symptoms resemble mast cell-mediated responses, suggesting that HαT may play a key role in modifying other mast cell-related diseases such as urticaria. In order to provide an initial impression of the potential frequency of HαT in urticaria patients, this study investigated the prevalence of elevated tryptase levels in patients with chronic spontaneous urticaria (CSU). The aim was to identify possible correlations between elevated tryptase levels, disease control, symptoms and their impact on disease progression and quality of life.

Methods: The tryptase values of 95 CSU patients from the outpatient clinic of the Institute of Allergology at Charité Universitätsmedizin Berlin were analyzed. The tryptase value was defined as elevated if it was ≥ 11.4 ng/ml, while values < 11.4 ng/ml were considered normal. For the analysis, the group with elevated tryptase levels was compared to a control group in terms of their disease symptoms, disease activity, and quality of life. The collected parameters included urticaria symptoms such as wheals and/or angioedema, the need for antihistamines or omalizumab and Patient-Reported Outcome Measures (PROMs) such as the Urticaria Control Test (UCT) and the Chronic Urticaria Quality of Life Questionnaire (CU-QoL).

Results: The examined patient cohort consisted of 44 patients with elevated tryptase and 51 patients with normal tryptase levels. For patients with elevated tryptase levels, the mean was 16.5 ng/ml, compared to 4.4 ng/ml in the control group. In the group with elevated tryptase levels no significantly more frequent occurrence of wheals or angioedema or simultaneous existence of wheals and angioedema was observed compared to the control group. The need for antihistamines was also comparable between the groups, but the group with increased tryptase tended to have a higher need for omalizumab (43.2% vs. 27.5%), without reaching statistical significance. The mean UCT value was lower in the group with elevated tryptase levels (5.83 vs. 6.57), which could indicate poorer disease control, but no statistical significance was detectable here either. In contrast, the mean CU-QoL value showed a significantly poorer quality of life in the group with elevated tryptase levels (48.56 vs. 38.91), which indicates a greater impairment of quality of life.

Outlook: The presented data are the first findings of an ongoing study. Due to the small patient group analyzed so far, continued ongoing data collection with additional clinical parameters and laboratory values in a larger patient cohort is necessary. Future analyses will therefore also include longer observation periods in order to be able to assess long-term changes, such as the response to omalizumab therapy.

Chronic urticaria among family members, unmet needs in diagnosis approach, probable clinical role of anti-CCD IgE.

Eralda Lekli1,2, Mehmet Hoxha1

1.University of Medicine, Tirana, Albania; Service of Allergology Mother Teresa UHC

2. Salus Hospital Tirana, Albania

Introduction: Genetics role in Chronic Urticaria(CU) has been investigated in several studies reporting higher ratios of HLA class I antigens in CSU patients(HLA-B*44[1,2], HLA-B*50,[3] HLA-B*14[4] and higher HLA class II antigens(HLA-DRB1*04 allele[2,5] both HLA-DRB1*04 and HLA-DQB1*0302 (DQ8)[6] HLA-DRB1*12 and HLA-DRB1*0901 [7] HLA-DRB1*01 and HLA-DRB1*15[1], HLA-DQ1[8]. Along with Chronic Inducible urticaria, two endotypes of

chronic spontaneous urticaria associated with mast cell-activating autoantibodies are described, autoallergic chronic spontaneous urticaria (with IgE-anti-autoallergens) and autoimmune chronic spontaneous urticaria (with IgG-anti-high-affinity receptor for the Fc region of immunoglobulin E [FcεRI]/IgE).[9] Some studies have demonstrated that IgE to CCD can in a few cases induce basophil activation that correlates with clinical symptoms [10].

Case report: We present a family case of Chronic Urticaria, grandmother 68 years, 23 years of CU(no remission), Father 39 years old, 12 years of CU(with 2-3 years remission periods), daughter 7 years(5 months CU and then remission since one year), son 11 years (8 months CU and then remission since 3 months). No history of known autoimmunity, ANA, Ant TPO negative, Total IgE more 100 UI/ml. In extracts based sIgE positivity for several pollens and food class I-III, with IgE ant CCD class 3, without respiratory symptoms or clinically food allergy susception. Negative for HBV and HCV. Normal blood count, ALT, AST, azotemia, creatinine, abdominal ultrasound. Positivity for Giardia lambia in feces, symptoms not improved after treatment. Elevated ESR, suboptimal vitamin D levels. Autologous serum test was not performed. Disease was controlled with 2-3 fold second generation AH in all cases. No diagnostic test available for IgE or IgG ant [FcεRI]/IgE.

Conclusions: Investigation of autoallergy and autoimmunity is an unmet need in our clinical setting which could be genetically predisposed and furthermore a possible clinical role of ant CCD IgE should be investigated in researches for Chronic Urticaria.

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