

Analysis of the impact of allergy and atopy on new onset of uveitis

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ABSTRACT.

Purpose: The inappropriate immune response to harmless foreign and self-antigens is a common feature of allergy, atopy and autoimmune disease. The influence of environmental factors in the initiation of autoimmunity is not well understood. It is conceivable that immune responses to allergens may also serve as a trigger of bystander immune reactions, including autoimmunity such as uveitis. Therefore, we wanted to investigate the prevalence of allergies and atopy in patients with different types of uveitis in comparison to a control cohort.

Methods: In total, 530 consecutive patients with new-onset anterior, intermediate, posterior and panuveitis were compared to a non-uveitis control cohort consisting of 1.060 consecutive new-referral patients who attended our specialized outpatient clinics for other reasons than uveitis. Allergy and atopy status as well as demographic data (age, gender and ethnicity) were obtained by standardized interviewer-assisted questionnaires.

Results: Uveitis case cohort and control cohort did not differ significantly in the allergy status ($p = 0.910$), such as the history of pollen allergy ($p = 0.671$), history of drug allergy ($p = 0.920$), history of food allergy ($p = 0.941$), history of house dust mite allergy ($p = 0.197$) or history of other allergens ($p = 0.593$), nor in the atopy status ($p = 0.802$), such as the history of atopic dermatitis ($p = 0.365$), history of asthma ($p = 0.430$) or history of allergic rhinitis ($p = 0.115$).

Conclusions: Our results argue against a substantial influence of allergies and atopy on the onset of uveitis.

Key words: allergy – atopy – autoimmunity – uveitis

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Introduction

Uveitis is a term to encompass all different kinds of intraocular inflammation and remains a major cause of blindness (Grajewski et al. 2015; Llorenc et al. 2015). Although uveitis can be divided into infectious versus non-infectious aetiologies, the immune system plays a major role in generating the inflammatory reaction in both types of

intraocular inflammation. Generally and in addition to pathogens, harmless antigens such as pollen or food constituents have the potential to incite inflammations that lead to allergic disease. The effective discrimination between harmful and harmless foreign and self-components is a cardinal feature of the immune system. Its failure often leads to inappropriate immune responses to harmless or self-

antigens and can result in allergies or autoimmune diseases such as uveitis, respectively (de Smet et al. 2011). The factors that lead to this kind of inappropriate immunity, which is a feature of both allergies and autoimmune diseases, are under intense investigation. Whereas specific foreign antigens can often be attributed to clinically apparent allergic inflammation, the identification of self-antigens and factors leading to autoimmune diseases turned out to be more difficult. Autoimmune diseases often are preceded by infections that may serve as triggers of immunity through general immune stimulation or by molecular mimicry (Willermain et al. 2012). The influence of other environmental factors in the initiation of autoimmunity is not well understood. It is conceivable that immune reactions to allergens may also serve as a trigger of other bystander immune reactions, including autoimmunity. For example, food allergens have been shown to cross-react with retinal antigens in a rat model of uveitis (Wildner & Diedrichs-Mohring 2003) and to be associated with atopic eczema (Santiago 2015). Atopic dermatitis, asthma and allergic rhinitis represent clinical manifestations of atopy. Whereas an allergy implies an immune response to a specific antigen, an atopy describes a state with increased susceptibility to type 1 allergic reactions (Skaaby et al. 2015). Both may be associated with generally altered immune responses (Valenta et al. 2009). For example, allergy-associated immune responses favour a type 2 helper T response that has a cytokine profile capable of antagonizing type 1

or 17 helper T-cell responses that play a role in the pathogenesis of autoimmune diseases, including uveitis (Grajewski et al. 2006; Amadi-Obi et al. 2007; Luger et al. 2008). Furthermore, antiretinal antibodies have been found more frequently in patients with uveitis when compared to healthy controls (Ten Berge et al. 2016). On another cellular level, mast cells that have important functions in the pathogenesis of allergies also play a role in initiating immune responses against pathogens and possibly self-antigens (Yu et al. 2015). Therefore, we wanted to investigate patients with different types of uveitis regarding a history of allergy and atopy in comparison with an age-matched control cohort.

Patients and Methods

This case-control study was performed at the Department of Ophthalmology, University Hospital of Cologne, Cologne, Germany, in conformance with the tenets of the Declaration of Helsinki and was approved by the institutional review board. Written informed consent was obtained from all participants.

Uveitis case cohort

Between 1 January 2012 and 30 April 2014, 594 consecutive patients were referred to the uveitis service of our department. Inclusion criteria were (1) confirmed diagnosis of uni- or bilateral uveitis, and (2) new referral to this German tertiary centre. Patients with isolated keratitis, isolated (epi-)scleritis, isolated retinal vasculitis and isolated optic neuritis were excluded. Altogether, 530 consecutive patients fulfilled these criteria and were enrolled in the uveitis case cohort of the present study.

All patients underwent standardized ophthalmic examination as well as screening for systemic disease associations using a tailored approach as described previously (Grajewski et al. 2015). Standardization of Uveitis Nomenclature (SUN) criteria (Jabs et al. 2005) was used to classify the uveitis patients according to the primary anatomical site of inflammation: anterior uveitis, intermediate uveitis, posterior uveitis and panuveitis. The diagnosis of specific manifestations and aetiologies of uveitis was based on the clinical picture and on classification

according to international criteria (Holland 1994; Rao et al. 2007; Herbert et al. 2009). Therefore, patients were grouped into (1) infectious uveitis, (2) specific clinical entity, (3) uveitis associated with systemic disease and (4) idiopathic uveitis in cases in which a specific diagnosis, either ocular or systemic, could not be made.

Control cohort

The non-uveitis control cohort consisted of 1,060 consecutive new-referral patients who attended our specialized outpatient clinics for other reasons than uveitis, between 1 May 2014 and 15 June 2014.

Allergy and atopy status

Besides demographic data, such as age, gender and ethnicity, the allergy and atopy status were obtained by standardized interviewer-assisted questionnaires. All participants of both the uveitis case cohort and the control cohort were asked for the history of any allergy and/or atopy at or prior to disease onset. Allergy status was categorized according to the triggering allergens: pollen, drug, food, house dust mites and other allergens. Atopy status was grouped into atopic dermatitis, asthma and allergic rhinitis.

Statistical analyses

Commercial software (SPSS version 21.0 for Windows; SPSS, Inc., Chicago, IL, USA) and the statistical programming language R V3.1.1 (R Foundation for Statistical Computing, Vienna, Austria) were used for all statistical analyses. Comparisons between groups or variables were performed using the nonparametric Mann-Whitney *U*-test or the exact Fisher test, and correlations in cross-tables were derived using the Pearson's chi-square test. To examine relationships between uveitis, allergy and atopy status, age, gender and ethnicity, we calculated a logistic regression model and for the subgroups anatomical location of inflammation, ocular involvement, and aetiology three multinomial logistic regression models, and reported odds ratios, confidence intervals and *p* values. A *p* value of less than 0.05 was considered statistically significant.

Results

Demographics and clinical characteristics

The uveitis study group included 530 patients (287 females and 243 males) with a mean $\pm$ SD age of 45 ± 19 years (range, 1–90 years) at onset of uveitis and a European ethnicity in 83% (Table 1). Of the 530 patients, 285 (54%) had anterior uveitis, 102 (19%) had intermediate uveitis, 109 (21%) had posterior uveitis, and 34 (6%) had panuveitis. In total, 56% of the patients suffered from bilateral involvement. Regarding the aetiology of all uveitis cases, we found 15% infectious, 25% specific clinical entities, 17% associated with systemic disease and 43% idiopathic uveitis.

The control group devoid of uveitis consisted of 1060 patients (600 females and 460 males) with a mean $\pm$ SD age of 47 ± 18 years (range, 1–94 years) and a European ethnicity in 84% (Table 1).

The uveitis case cohort and control cohort differed significantly in age ($p = 0.017$), whereas gender ($p = 0.353$) and ethnicity ($p = 0.596$) did not vary significantly.

Allergy and atopy status

In the uveitis case cohort, 178 patients (34%) revealed a positive history of allergy: pollen allergy was reported by 65 patients (12%), drug allergy was reported by 78 patients (15%), food allergy was reported by 32 patients (6%), house dust mite allergy was reported by 25 patients (5%), and other allergens were reported by 43 patients (8%; Table 1). The history of atopy was positive in 45 uveitis patients (9%): atopic dermatitis was described by 16 patients (3%), asthma was described by 31 patients (6%), and allergic rhinitis was described by seven patients (1%; Table 1). Comparing the anatomical location of inflammation, no significant differences could be seen regarding allergy ($p = 0.810$) as well as atopy status ($p = 0.196$), although none of the 34 panuveitis patients reported positive history of atopy. Furthermore, the history of allergy and atopy did not vary significantly regarding ocular involvement ($p = 0.794$ and $p = 0.503$, respectively) and underlying aetiology ($p = 0.121$ and $p = 0.305$, respectively).

Table 1. Baseline characteristics of the uveitis case cohort and the control cohort.

	Uveitis					Controls (n = 1060)
	Total (n = 530)	Anterior uveitis (n = 285)	Intermediate uveitis (n = 102)	Posterior uveitis (n = 109)	Panuveitis (n = 34)	
Age at onset (years)						
Mean ± SD (range)	45 ± 19 (1–90)	45 ± 19 (1–90)	44 ± 19 (6–85)	43 ± 18 (6–87)	52 ± 17 (18–83)	47 ± 18 (1–94)
0–15, n (%)	33 (6)	22 (8)	8 (8)	3 (3)	–	58 (6)
16–24, n (%)	36 (7)	16 (6)	6 (6)	13 (12)	1 (3)	71 (7)
25–44, n (%)	196 (37)	100 (35)	41 (40)	43 (39)	12 (35)	323 (31)
45–64, n (%)	177 (33)	100 (35)	30 (29)	36 (33)	11 (32)	428 (40)
≥65, n (%)	88 (17)	47 (17)	17 (17)	14 (13)	10 (29)	180 (17)
Gender						
Female, n (%)	287 (54)	158 (55)	57 (56)	59 (54)	13 (38)	600 (57)
Male, n (%)	243 (46)	127 (45)	45 (44)	50 (46)	21 (62)	460 (43)
Ethnicity						
European, n (%)	441 (83)	233 (82)	92 (90)	89 (82)	27 (79)	893 (84)
Mediterranean Ancestry, n (%)	42 (8)	25 (9)	5 (5)	12 (11)	–	86 (8)
Middle East, n (%)	22 (4)	12 (4)	3 (3)	4 (4)	3 (9)	46 (4)
Black, n (%)	14 (3)	10 (4)	–	3 (3)	1 (3)	19 (2)
Indian, n (%)	8 (2)	3 (1)	1 (1)	1 (1)	3 (9)	10 (1)
Asian-Pacific-Islander, n (%)	2 (0.4)	2 (1)	–	–	–	3 (0.3)
Hispanic, n (%)	1 (0.2)	–	1 (1)	–	–	3 (0.3)
History of allergy, n (%)	178 (34)	96 (34)	31 (30)	40 (37)	11 (32)	353 (33)
Pollen allergy, n (%)	65 (12)	40 (14)	7 (7)	17 (16)	1 (3)	138 (13)
Drug allergy, n (%)	78 (15)	38 (13)	17 (17)	19 (17)	4 (12)	154 (15)
Food allergy, n (%)	32 (6)	17 (6)	3 (3)	10 (9)	2 (6)	65 (6)
House dust mite allergy, n (%)	25 (5)	12 (4)	8 (8)	4 (4)	1 (3)	67 (6)
Other allergens, n (%)	43 (8)	20 (7)	10 (10)	8 (7)	5 (15)	78 (7)
History of atopy, n (%)	45 (9)	23 (8)	12 (12)	10 (9)	–	94 (9)
Atopic dermatitis, n (%)	16 (3)	6 (2)	4 (4)	6 (6)	–	24 (2)
Asthma, n (%)	31 (6)	15 (5)	8 (8)	8 (7)	–	73 (7)
Allergic rhinitis, n (%)	7 (1)	4 (1)	1 (1)	2 (2)	–	6 (1)

SD = standard deviation.

In the control cohort devoid of uveitis, 353 patients (33%) revealed a positive history of allergy: pollen allergy was reported by 138 patients (13%), drug allergy was reported by 154 patients (15%), food allergy was reported by 65 patients (6%), house dust mite allergy was reported by 67 patients (6%), and other allergens were reported by 78 patients (7%; Table 1). The history of atopy was positive in 94 patients (9%): atopic dermatitis was described by 24 patients (2%), asthma was described by 73 patients (7%), and allergic rhinitis was described by six patients (1%; Table 1).

Uveitis case cohort and control cohort did not differ significantly in the allergy status ($p = 0.910$), such as the history of pollen allergy ($p = 0.671$), history of drug allergy ($p = 0.920$), history of food allergy ($p = 0.941$), history of house dust mite allergy ($p = 0.197$) or history of other allergens ($p = 0.593$) nor in the atopy status ($p = 0.802$), such as the history of atopic dermatitis ($p = 0.365$), history of asthma ($p = 0.430$) or history of

Table 2. Multivariate logistic regression analyses predicting new onset of uveitis by allergy and atopy status.

	Odds ratio (95% CI)	p value
History of allergy (yes)	1.27 (0.78–2.06)	0.340
Pollen allergy (yes)	0.80 (0.51–1.25)	0.337
Drug allergy (yes)	0.87 (0.55–1.36)	0.545
Food allergy (yes)	0.91 (0.54–1.49)	0.701
House dust mite allergy (yes)	0.62 (0.35–1.05)	0.082
Other allergens (yes)	1.09 (0.68–1.74)	0.708
History of atopy (yes)	0.65 (0.18–2.22)	0.494
Atopic dermatitis (yes)	1.74 (0.60–5.07)	0.306
Asthma (yes)	1.23 (0.37–4.24)	0.732
Allergic rhinitis (yes)	3.59 (0.93–14.92)	0.066
Age	0.99 (0.99–1.00)	0.040
Gender (male)	1.12 (0.91–1.39)	0.290
Ethnicity (non-European)	1.04 (0.78–1.39)	0.775

CI = confidence interval.

allergic rhinitis ($p = 0.115$). European patients had significantly higher rates of allergies ($p = 0.007$ and $p = 0.009$ in the uveitis and the control group, respectively) but similar rates of atopies ($p = 0.677$ and $p = 0.301$ in the uveitis and the control group, respectively) when compared to the non-European group.

Association of allergy and atopy with uveitis

Using multivariate logistic regression analyses, neither the positive history of allergy ($p = 0.340$) nor the positive history of atopy ($p = 0.494$) was significant predictors of developing uveitis (Table 2). Younger patients' age was

significantly associated with the new onset of uveitis ($p = 0.040$).

Comparing the anatomical locations of inflammation, multinomial regression analyses revealed no significant association between the positive history of allergy as well as atopy and the new onset of anterior uveitis ($p = 0.247$ and $p = 0.650$, respectively), intermediate uveitis ($p = 0.355$ and $p = 0.517$, respectively) as well as posterior uveitis ($p = 0.855$ and $p = 0.050$, respectively; Table 3). In panuveitis, allergy was no significant predictor ($p = 0.228$), but atopy was a significant predictor of disease onset ($p < 0.001$), as none of our panuveitis patients suffered from any atopy.

For the subgroup analysis of unilateral and bilateral uveitis, neither a positive allergy status ($p = 0.694$ and $p = 0.334$, respectively) nor a positive atopy status ($p = 0.339$ and $p = 0.999$, respectively) was significant predictors of developing uveitis (Table 4).

Comparing the aetiology of uveitis, multinomial regression analyses revealed no significant association between the positive history of allergy as well as atopy and the new onset of infectious uveitis ($p = 0.267$ and $p = 0.809$, respectively), specific clinical entity of uveitis ($p = 0.342$ and $p = 0.088$, respectively), uveitis associated with systemic disease ($p = 0.112$ and $p = 0.526$, respectively) as well as idiopathic uveitis ($p = 0.698$ and $p = 0.856$, respectively; Table 5).

Discussion

This study revealed similar rates of allergy and atopy in new-onset uveitis in comparison with a control cohort with ophthalmic diseases other than uveitis. The potential relationship between these clinical conditions is an important issue, as they can substantially influence the immune system that in turn is responsible for onset of autoimmune diseases, such as uveitis. Furthermore, regulatory T cells (Treg) that can suppress autoimmune responses might play a role in the regulation of both allergies and autoimmune diseases. In line with this,

children simultaneously suffering from both diseases had the most polymorphisms of the FoxP3 gene, the master transcription factor of Tregs (Pacheco-Gonzalez et al. 2015). The precise mechanisms that trigger autoimmunity are still incompletely understood. Environmental factors include various types of antigens such as microbial products, pollen, metals, food, dust mite, drugs and air pollutants including smoking (Yuen et al. 2015). While all of these antigens can result in allergies, some are believed to influence autoimmune responses, especially microbial products, either directly by molecular mimicry or indirectly by

Table 4. Multivariate multinomial regression analyses predicting new onset of uveitis (in dependence of ocular involvement) by allergy and atopy status.

	Unilateral uveitis		Bilateral uveitis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
History of allergy (yes)	1.14 (0.59–2.19)	0.694	1.35 (0.74–2.47)	0.334
Pollen allergy (yes)	0.94 (0.52–1.71)	0.844	0.70 (0.40–1.25)	0.231
Drug allergy (yes)	1.05 (0.57–1.93)	0.868	0.76 (0.43–1.34)	0.334
Food allergy (yes)	1.14 (0.61–2.16)	0.680	0.73 (0.37–1.42)	0.350
House dust mite allergy (yes)	0.60 (0.28–1.30)	0.195	0.63 (0.32–1.24)	0.182
Other allergens (yes)	0.72 (0.36–1.42)	0.341	1.43 (0.82–2.50)	0.212
History of atopy (yes)	0.48 (0.11–2.16)	0.339	1.00 (0.20–5.04)	0.999
Atopic dermatitis (yes)	2.45 (0.71–8.38)	0.155	1.07 (0.26–4.47)	0.926
Asthma (yes)	1.80 (0.42–7.59)	0.426	0.74 (0.15–3.70)	0.715
Allergic rhinitis (yes)	3.05 (0.57–16.20)	0.191	3.44 (0.64–18.48)	0.149
Age	1.00 (0.99–1.00)	0.213	0.99 (0.99–1.00)	0.062
Gender (male)	1.03 (0.77–1.38)	0.826	1.20 (0.92–1.56)	0.182
Ethnicity (non-European)	0.91 (0.61–1.37)	0.662	1.15 (0.81–1.63)	0.427

CI = confidence interval.

Table 3. Multivariate multinomial regression analyses predicting new onset of uveitis (in dependence of anatomical location of inflammation) by allergy and atopy status.

	Anterior uveitis		Intermediate uveitis		Posterior uveitis		Panuveitis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
History of allergy (yes)	1.44 (0.78–2.67)	0.247	0.62 (0.23–1.71)	0.355	1.09 (0.45–2.63)	0.855	3.12 (0.49–19.75)	0.228
Pollen allergy (yes)	0.91 (0.51–1.61)	0.743	0.52 (0.19–1.38)	0.187	1.08 (0.48–2.44)	0.851	0.13 (0.01–1.46)	0.099
Drug allergy (yes)	0.72 (0.40–1.28)	0.263	1.67 (0.65–4.30)	0.287	1.18 (0.53–2.63)	0.688	0.36 (0.06–2.05)	0.252
Food allergy (yes)	0.86 (0.46–1.63)	0.651	0.60 (0.17–2.11)	0.427	1.29 (0.56–2.96)	0.557	0.71 (0.10–4.92)	0.726
House dust mite allergy (yes)	0.50 (0.24–1.01)	0.054	1.95 (0.71–5.34)	0.194	0.46 (0.14–1.47)	0.190	0.30 (0.03–3.28)	0.324
Other allergens (yes)	0.89 (0.48–1.64)	0.708	1.53 (0.65–3.58)	0.328	1.07 (0.44–2.59)	0.881	1.74 (0.33–9.12)	0.512
History of atopy (yes)	1.53 (0.24–9.75)	0.650	2.35 (0.18–31.08)	0.517	0.13 (0.02–1.00)	0.050	0.00 (0.00–0.00)	<0.001
Atopic dermatitis (yes)	0.65 (0.12–3.40)	0.611	0.99 (0.10–10.03)	0.990	6.38 (1.39–29.24)	0.017	0.02 (0.02–0.02)	<0.001
Asthma (yes)	0.52 (0.08–3.25)	0.485	0.51 (0.04–6.37)	0.604	5.08 (0.73–35.14)	0.099	0.00 (0.00–0.00)	<0.001
Allergic rhinitis (yes)	2.29 (0.35–14.87)	0.384	1.57 (0.10–24.94)	0.748	4.68 (0.52–42.50)	0.170	0.27 (0.27–0.27)	<0.001
Age	1.00 (0.99–1.00)	0.211	0.99 (0.98–1.00)	0.055	0.99 (0.98–1.00)	0.028	1.02 (1.00–1.04)	0.078
Gender (male)	1.05 (0.80–1.37)	0.727	1.03 (0.67–1.56)	0.908	1.14 (0.76–1.71)	0.539	2.39 (1.15–4.96)	0.019
Ethnicity (non-European)	1.17 (0.82–1.66)	0.387	0.53 (0.26–1.04)	0.066	1.12 (0.66–1.92)	0.673	1.66 (0.69–4.00)	0.257

CI = confidence interval.

Table 5. Multivariate multinomial regression analyses predicting new onset of uveitis (in dependence of aetiology) by allergy and atopy status.

	Infectious uveitis		Specific clinical entity		Uveitis associated with systemic disease		Idiopathic uveitis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
History of allergy (yes)	0.54 (0.18–1.61)	0.267	1.47 (0.67–3.24)	0.342	2.22 (0.83–5.96)	0.112	1.15 (0.57–2.34)	0.698
Pollen allergy (yes)	0.91 (0.32–2.63)	0.868	0.93 (0.45–1.93)	0.849	0.72 (0.28–1.83)	0.491	0.70 (0.36–1.36)	0.296
Drug allergy (yes)	1.74 (0.64–4.74)	0.282	0.61 (0.29–1.29)	0.197	0.69 (0.28–1.73)	0.430	0.98 (0.50–1.92)	0.954
Food allergy (yes)	1.79 (0.64–5.06)	0.270	1.37 (0.64–2.90)	0.418	0.33 (0.09–1.19)	0.091	0.75 (0.35–1.63)	0.468
House dust mite allergy (yes)	0.68 (0.17–2.69)	0.586	0.63 (0.25–1.57)	0.321	0.39 (0.12–1.24)	0.111	0.75 (0.34–1.63)	0.465
Other allergens (yes)	1.33 (0.45–3.94)	0.606	1.32 (0.62–2.80)	0.476	1.10 (0.45–2.69)	0.840	0.87 (0.43–1.74)	0.690
History of atopy (yes)	1.31 (0.14–12.03)	0.809	0.18 (0.03–1.29)	0.088	0.38 (0.02–7.73)	0.526	1.19 (0.18–7.66)	0.856
Atopic dermatitis (yes)	1.26 (0.19–8.45)	0.810	5.66 (1.16–27.72)	0.032	0.66 (0.07–6.77)	0.729	1.11 (0.21–6.01)	0.903
Asthma (yes)	0.86 (0.10–7.61)	0.893	2.42 (0.41–14.33)	0.331	4.64 (0.22–96.42)	0.322	0.44 (0.07–2.84)	0.389
Allergic rhinitis (yes)	4.63 (0.53–40.30)	0.165	2.24 (0.19–26.00)	0.519	5.71 (0.29–112.64)	0.253	2.85 (0.44–18.61)	0.274
Age	1.01 (1.00–1.02)	0.202	0.98 (0.97–0.99)	<0.001	1.00 (0.99–1.01)	0.873	1.00 (0.99–1.00)	0.208
Gender (male)	1.58 (0.99–2.53)	0.055	0.93 (0.63–1.36)	0.703	0.96 (0.62–1.50)	0.865	1.17 (0.88–1.57)	0.289
Ethnicity (non-European)	1.26 (0.68–2.33)	0.471	0.51 (0.27–0.93)	0.029	1.73 (1.02–2.95)	0.044	1.10 (0.75–1.62)	0.628

CI = confidence interval.

induction of proinflammatory cytokine production and cellular responses. Indeed, a recent study demonstrated an association between atopy and herpetic eye disease, showing that immune dysregulation in atopic patients leads to increased susceptibility to herpetic eye infections (Borkar et al. 2014). On the other hand, autoimmune diseases are frequently treated by immunomodulatory regimens such as glucocorticoids and immunosuppressive drugs that could potentially conceal concurrent allergic or atopic symptoms, leading to underestimation of their incidence.

Therefore, in this study, we performed a thorough analysis of patients with new onset of uveitis before subsequent immunomodulatory treatment. This revealed a similar prevalence of positive history for allergies and atopy in uveitis and control patients, comparable with another recent study that focused on atopy and possible associations with Crohn's disease, multiple sclerosis, polymyalgia rheumatica, psoriasis vulgaris, rheumatoid arthritis and thyrotoxicosis (Skaaby et al. 2015) as well as the association of atopy with a subtype of uveitis, iridocyclitis, with negative result. The present study investigated the prevalence of atopy and allergy in all forms of uveitis. Previous studies suggested that the prevalence of the allergic disease in Germany's population is 33% to 40% (Augustin et al. 2013), comparable with our uveitis (34%) and control

group (33%). Furthermore, the types of allergies were similar in both the uveitis and the control group and reflected the same pattern as has been found within the normal population in Germany (Augustin et al. 2013). Interestingly, no patient with panuveitis reported a history of atopy in our study, but despite statistical significance, the low number of patients does not allow drawing general conclusions. Limitations of the present study include that the diagnosis of allergy and atopy was based on questionnaires alone, without definitive confirmation by laboratory testing. Furthermore, the age distribution of our uveitis study group (mean age 45 ± 17 years, range 1–90 years) was very similar to our control group (mean age 47 ± 18 years, range 1–94 years), but not strictly age-matched. In our study, European (Caucasian) patients represented the largest group and had significantly higher rates of allergies but similar rates of atopies, when compared to the non-European group. However, due to the limited number of non-European patients in our study, conclusions regarding the influence of ethnicity on allergy and atopy rates in uveitis patients have to be proven in larger international multicenter studies.

Taken together, our results argue against a substantial influence of allergies and atopy on the onset of uveitis. It still needs to be determined whether the course and complication types and

rates in uveitis are affected by these conditions.

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