



The impact of allergy on asthma in the clinical practice

The relevance of the phenotype

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Dear Editors,

Actually, the link between asthma and allergy, including allergic rhinitis, is a challenge for the allergist, the pulmonologist, and the ear nose throat (ENT) specialist [1]. This topic is very relevant in common practice and deserves careful consideration in the workup of allergy in patients with asthma and rhinitis as suggested by allergic rhinitis and its impact on asthma (ARIA) guidelines [2].

Allergic disorders are characterized by an Immunoglobulin(IgE)-mediated inflammation driven by type 2 immune response [3]. On the other hand, asthma is a multifactorial syndrome and different immunopathological pathways may be involved [4]. In this regard, the assessment of the individual phenotype and endotype allows for personalization of the best adequate therapy for each patient [5].

To stimulate the debate on the current issue, we would like to present our experience in clinical practice. The aim of this study was to identify the impact of allergy, such as allergic rhinitis comorbidity, on some clinical parameters, including age, gender, body

max index (BMI), GINA grading of asthma control, symptoms in the past month, symptom perception by visual analogue scale (VAS), lung function (FVC, FEV1, FEV1/FVC, FEF25-75) FeNO, and asthma control test (ACT) in 735 (436 females) asthmatic patients routinely visited in a real-life setting, such as an outpatient clinic. Allergic rhinitis was diagnosed on the concordance between clinical history of typical nasal symptoms (itching, sneezing, watery rhinorrhea, and congestion) and their occurrence after exposure to the sensitizing allergen as stated by ARIA guidelines [2]. Sensitization was documented by positive skin prick test.

Univariate analysis was performed using the logistic regression model to investigate and screen the association between parameters and rhinitis. The estimated *p*-values were adjusted for multiple comparisons by the Bonferroni correction method and odd ratios associated with rhinitis for each variable were calculated. Data were acquired and analyzed in R 3.3.2 software environment (www.R-project.org).

Table 1 shows the findings: 63% of patients had allergy comorbidity, namely allergic rhinitis. Asthmatics with allergy had better asthma control (graded by GINA), fewer symptoms, lower BMI, and better lung function than patients with asthma alone.

These outcomes could suggest that asthmatic patients without allergic rhinitis, i. e., a nonallergic phenotype, might present a worse asthma feature in comparison with allergic patients. So, nonallergic asthma may be characterized by a more severe profile than allergic asthma. Recently, IL-17 has been proposed as a reliable marker for type 3 endotype, such as a Th17-mediated asthma pathway. Indeed, it was demonstrated that nasal IL-17 expression is associated with asthma severity and asthmatics with frequent exacerbations have bronchial and nasal neutrophilia associated with increased expression of IL-17 [6]. In par-

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Table 1 Contingency tables and output of the univariate multinomial regression models

Characteristics ^a	Group			Logistic regression	
	Total 735	Asthma 273 (36.92%)	Asthma and allergy 462 (63%)	OR (95%CI)	p-value
<i>Gender</i>					1.0000
Male	300 (40.76%)	106 (35.33%)	194 (64.67%)	1	
Female	435 (59.24%)	167 (38.39%)	268 (61.61%)	0.88 (0.65–1.19)	
<i>GINA</i>					0.0001
Well controlled	315 (43.99%)	85 (26.98%)	230 (73.02%)	1	
Partially controlled	325 (45.39%)	148 (45.54%)	177 (54.46%)	0.44 (0.32–0.61)	
Uncontrolled	76 (10.61%)	30 (39.47%)	46 (60.53%)	0.57 (0.34–0.96)	
<i>Symptoms^a</i>					<0.0001
None	168 (22.95%)	56 (33.33%)	112 (66.67%)	1	
Bronchial	140 (19.13%)	86 (61.87%)	53 (38.13%)	0.31 (0.19–0.49)	
Nasal	116 (15.85%)	53 (45.69%)	63 (54.31%)	0.59 (0.36–0.97)	
Bronchial and nasal	308 (42.08%)	72 (23.38%)	236 (76.62%)	1.64 (1.08–2.48)	
<i>Age</i>	40.05 (16.31)	40.68 (18.39)	39.97 (16.02)	1.00 (0.98–1.01)	1.0000
<i>BMI^a</i>	24.99 (5.52)	26.44 (6.61)	23.99 (4.36)	0.91 (0.88–0.94)	<0.0001
<i>VAS</i>	7.16 (1.97)	6.84 (2.38)	7.34 (1.68)	1.14 (1.02–1.27)	0.2001
<i>ACT^a</i>	20.12 (4.29)	19.42 (4.32)	20.38 (4.22)	1.05 (1.01–1.10)	0.1711
<i>FeNO</i>	32.83 (25.19)	35.81 (24.67)	31.49 (25.49)	0.99 (0.98–1.01)	1.0000
<i>FVC (% of predicted)</i>	101.13 (17.73)	97.52 (19.78)	103.2 (16.12)	1.02 (1.01–1.03)	0.0003
<i>FEV₁ (% of predicted)</i>	91.4 (19.69)	84.73 (21.87)	95.22 (17.18)	1.03 (1.02–1.04)	<0.0001
<i>FEV₁/FVC</i>	79 (12.86)	80.09 (15.73)	78.19 (10.58)	0.99 (0.98–1.01)	0.6157
<i>FEF_{25–75} (% of predicted)</i>	71.19 (28.95)	60.4 (28.37)	75.38 (28.02)	1.02 (1.01–1.03)	<0.0001

OR (95% CI) Odd ratios with 95% confidence interval, p-value Likelihood ratio p-value adjusted by using Bonferroni method
GINA Global Initiative for Asthma, BMI Body Mass Index, VAS Visual Analogue Scale, ACT Asthma Control Test, FeNO Fractional exhaled Nitric Oxide, FVC Forced Vital capacity, FEV₁ Forced Expiratory Volume at 1 second, FEF_{25–75} Forced Expiratory Flow between 25% and 75% of FVC
^aCharacteristic: variables taken into account

ticular, IL-17 production has been identified in Th-17 and Tc-17. So, IL-17 may be considered a reliable biomarker for endotyping asthma. On the other hand, it has to be noted that there are subjects with asthma and eosinophilic airways inflammation who are non-allergic.

The present experience has some limitations, including the cross-sectional design and the lack of biomarkers (including type 2 and type 3) assessment. So, we cannot establish the exact pathophysiologic mechanisms involved in our patients.

In conclusion, asthma as well as rhinitis may present different and composite phenotypes and endotypes. Allergy comorbidity may characterize a less severe profile in asthmatics. Allergy workup is clinically relevant mainly concerning the definition of a personalized medicine and should be adequately assessed by the allergist, the pulmonologist, and the ENT specialist in patients with asthma.

Conflict of interest G. Ciprandi, F. Gallo and I. Cirillo declare that they have no competing interests.

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