

Clinical course of rhinitis and changes in vivo and in vitro of allergic parameters in elderly patients: a long-term follow-up study

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Received: 27 August 2011 / Accepted: 8 January 2012
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Abstract Changes in rhinitis symptom severity tend to decrease with aging, but whether the decrease is associated with allergic skin test reactivity, serum total and specific IgE, and nasal eosinophils or determined only by aging is poorly understood. The aim of the study was to analyze sensitivity in vivo and in vitro some 15 years after primary testing, skin prick test (SPT), serum total and specific IgE, ratio sIgE/tIgE, and nasal eosinophils in order to evaluate changes due to age and changes due to the severity of rhinitis symptoms. One hundred and eight rhinitis patients who had been investigated in 1995 were re-interviewed and their current allergy re-assessed after a follow-up of 15 years. All patients were SPT with eight common allergens in the area of Palermo (Italy). Rhinitis symptoms tended, on average, to have become milder at the follow-up. All parameters examined showed a decreasing trend in older age groups over the period between the two investigations. Rhinitis symptoms tend to become milder and the

allergic parameters both in vivo and in vitro usually decrease in the long run; however, the changes in rhinitis symptoms appear to be related to changes in the nasal eosinophils, independently of SPT and serum-specific IgE.

Keywords Aging · Allergic rhinitis · Serum total IgE · Serum-specific IgE · Eosinophil in nasal fluid · Symptom score

Abbreviations

AR	Allergic rhinitis
SPT	Skin prick test
tIgE	Total IgE
sIgE	Specific IgE
VAS	Visual analog scale
nEOS	Nasal eosinophil

Introduction

Rhinitis is an inflammation of nasal mucosa resulting in nasal secretions that are non-purulent and watery. Non-infectious rhinitis includes both allergic rhinitis (AR) and non-allergic rhinitis (NAR). AR is further divided into two groups: seasonal and perennial. An alternative classification system based on the severity of the nasal symptoms and frequency was proposed in the Allergic Rhinitis and Its Impact on Asthma (ARIA) trial [1]. The increasing prevalence of allergic respiratory diseases is well documented. Allergic rhinitis has the highest prevalence, affecting an average of 24% of the European population [2]. Although assuming its peak incidence in young adulthood, it continues to be an important health issue in the elderly. The occurrence of the allergic disease in the elderly is particularly important and is

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receiving increasing attention for several reasons. First, in the last 10 years, the population over the age of 65 has been the fastest growing group. Individuals over 65 in 1994 comprised 12.6% of the total population, but it is estimated that between 2010 and 2030, this figure will increase by 75% [3]. Second, the elderly continue to be consumers of approximately one-third of total health care resources. Third, diseases associated with chronic airflow obstruction are very common in the elderly and are projected to increase as a consequence of continued exposure to tobacco smoke and other indoor and outdoor inhaled allergens [4].

The incidence of the onset of allergic symptoms, as well as their severity, seems to decrease with age [5]. However, in studies of rhinitis patients, the influence of age has usually been neglected. There are not many reports on the natural course of AR in middle-aged subjects. Numerous reports performed in the 1960s and 1970s described the results of questionnaire studies in children and young adults. In a study of 638 high-school students, there was an improvement or regression of seasonal rhinitis after the age of 10 in 40% of students suffering the onset of hay fever in early childhood and in 29% of those who had their first symptoms in adolescence. In the adolescent-onset group, a quarter reported that their symptoms had increased since the onset, but this seldom occurred in the early onset group. However, hay fever ceased in only 7% and perennial rhinitis in 4% of students with these symptoms [6]. Another study that followed 903 college freshmen for 7 years after entering college found hay fever as a new disease in 12.6%, perennial rhinitis in 4.8%, and asthma in 2.5%, the annual incidences being 1.8, 0.7 and 0.35%, respectively [7].

An entire community, Tecumseh, USA, was studied in two surveys 4 years apart. The diagnostic criterion of probable allergic rhinitis was a report of hay fever, sinus trouble, or persistent nasal symptoms together with two of the following: (1) itching of eyes, nose, or throat, or burning or watering of eyes; (2) association of symptoms with exposure to allergen(s); or (3) diagnosis of hay fever or allergic rhinitis by physician. The incidence in Tecumseh residents during this period was 2% and the prevalence 8.7%. Remission, that is, non-occurrence of allergic rhinitis for two or more years, was found in 5% of female subjects and 10% of male subjects [8].

Patients with asthma or hay fever followed for 10–40 years were reported to present a decrease in severe asthmatic symptoms and a progressive loss in serum antibodies to *Dermatophagoides pteronyssinus*, and there was no apparent tendency for skin test reactivity to decline with time [9].

A Finnish study of rhinitis patients without asthma reported that hypersensitive rhinitis showed complete remission in 2% of cases, became less severe in 54%, was equally severe in 26%, and was more severe in 18% of subjects at follow-up after 7 years. The prognosis of

allergic rhinitis in patients with at least two positive skin tests was better than the prognosis of non-allergic rhinitis. The symptoms disappeared or become less severe in 62% of allergic patients, but only in 46% of patients with non-allergic eosinophilic rhinitis and 42% of those with non-allergic non-eosinophilic rhinitis [10].

A comprehensive questionnaire study of 9,946 households with a total of 22,285 persons was recently published. In this study, the frequency of self-diagnosed rhinitis (“seasonal allergy” or “allergy all the time”) was 14.2% (seasonal 8.8% and perennial 5.4%), with the highest figure (18%) between the ages of 18 and 49, decreasing gradually after the age of 50–8% in subjects over 65 [11].

Finally, there is a report that after a 20-year follow-up, including individuals over 60 years of age, rhinitis symptoms tended to become milder and allergic skin reactivity usually decreased in the long term; however, it is possible that these changes occurred independently of each other. In this study, the change in rhinitis symptom severity appears to be unrelated to the decrease in skin test reactivity [12].

To our knowledge, no detailed reports exist on the association between skin test and serum total (tIgE) and specific IgE (sIgE) results, nasal eosinophils, and aging in light of the duration of the disease and changes in symptom severity. In this follow-up study, we compared the results of an in vivo test (SPT) and an in vitro test (serum total and specific IgE, and nasal eosinophil counts) in the same series of allergic rhinitis patients tested on two occasions more than 10 years apart.

Methods

Patient population

We analyzed monosensitized adult patients consecutively referred to the Outpatient Allergy Units of the Dipartimento di Medicina Interna e Specialistica (DIMIS), ex Dipartimento di Medicina Clinica e delle Patologie Emergenti, of the University of Palermo, Italy, between January 1990 and December 1995 for evaluation of their allergic rhinitis without asthma symptoms. None of the patients underwent specific immunotherapy as part of the therapy for allergic rhinitis, and they presented no other allergic diseases, such as atopic dermatitis, eczema, or nasal polyps. The age range ranged between 44 and 56 years.

A total of 313 subjects (177 female subjects and 136 male subjects), with ages ranging between 44 and 56 years (mean age, 48.2 ± 2.9 years), were selected.

All patients presented with a clinical diagnosis of allergic rhinitis without asthma based on patient-reported symptoms, physical examination, and a normal baseline lung function test (baseline FEV₁ $\geq 80\%$ of predictive

value). All patients had positive SPT responses for 1 out of 17 common airborne allergens (see below), as determined by using the SPT method.

At the time of diagnosis, blood was collected for analysis of serum tIgE levels and sIgE levels, using the same allergens used to perform the SPT.

The family history of atopy, as also the history of smoking and the onset of respiratory symptoms, was obtained from each patient. Clinical evaluations included also rhinoscopy and spirometry, symptom scoring on the visual analogue scale (VAS), and medication use, referring to the previous year.

The study was approved by the Institutional Review Board of the Dipartimento di Medicina Clinica e delle Patologie Emergenti of the University of Palermo, Italy, and it was conducted according to the Declaration of Helsinki. Authorization of the study was not required according to our institutional policy and the ethical committee of our institution, as procedures done were part of routine diagnostic testing. However, written informed consent for the study was obtained from each patient in compliance with our institutional policy.

Assessment of symptoms

The variation of the nasal symptoms was evaluated on the basis of the compilation of the VAS performed at moment of the diagnosis and at the evaluation of 2009 [13]. Each VAS was represented by a 100-mm horizontal line with 0 and 100 on the left and right ends, respectively. Subjects were instructed that 0 indicated “nasal symptoms not at all bothersome” and that 100 indicated nasal symptoms extremely bothersome. The distance between 0 and the marks the subjects made on the scale was measured with a Digimatic caliper (Mitutoyo, Kawasaki, Japan). We considered a change of nasal symptoms to be significant if the VAS score showed a 30% decrease compared with the first VAS score.

Using the formula, described below in the paragraph “Statistical analysis”, rhinitis was regarded as increased when $\Delta\%$ was >30 (more severe); unchanged when $\Delta\%$ was between $+29$ and -29% (equal); decreased when $\Delta\%$ was between -30 and -99% (less severe); and finally resolved when $\Delta\%$ was -100% (complete remission) [13, 14].

Skin prick test

Patients underwent the SPT on the volar aspect of the forearm, using a standard panel of aeroallergens present in our geographic area (Alk Abellò, Milan, Italy). The panel consisted of the following extracts: grass (*Phleum pratense*, *Dactyla glomerata*, *Festuca elatior*, *Lolium perenne*, and *Poa pratensis*); weeds [mugwort (*Artemisia vulgaris*)], wall pellitory of the wall or sticky weed (*Parietaria*

judaica and *Salsola kali*); trees birch (*Betula verrucosa*), Olive tree (*Olea europea*) and Cypress (*Cupressus arizonica*); house dust mite (*Dermatophagoides pteronyssinus* and *D. farinae*); moulds (*Alternaria alternata*, *Cladosporium herbatum*, and *Aspergillus fumigatus*); animal dander (cat and dog); negative control (glycerinated saline) and positive control (histamine, 10 mg/mL). All allergens used for SPT are produced from the same manufacturer using the same “use in-house methods” to standardize their products in 1990 and 2008, the Histamine equivalent Prick (HEP). Positive responses were defined as any wheal with a diameter 3 mm greater than negative control, 15 min after application. The diameter was assessed by measuring the minimum + maximum diameter/². Wheal diameters were reported for each patient [15].

Serum total and specific IgE

A blood sample was processed at the time of diagnosis and at follow-up. On both occasions, serum total IgE and specific IgE were determined using Unicap 100[®], with the fluoroimmunoassay technique (Phadia, Uppsala, Sweden), according to the manufacturer’s instructions. Results for both serum tIgE and sIgE were expressed in kilounits per liter (kU/L and k_AU/L, respectively) and equilibrated against the World Health Organization standard for IgE, that is, 1 kU for tIgE and 1 k_AU for sIgE, equal to 2.4 ng/mL, respectively. Serum total IgE was determined with a detection limit of 2 kU/L and an upper limit of 5,000 kU/L. Serum specific IgE was determined with a detection limit of 0.35 k_AU/L and an upper limit of 100 k_AU/L at the time of diagnosis and with a detection limit of 0.1 k_AU/L and an upper limit of 100 k_AU/L at the time of follow-up [16]. Specific IgE was measured in all patients for the same allergens used in the SPT (17 allergens). All the patients were monosensitized (i.e., they had a positive SPT for only one allergen and presented specific IgE in the serum for the same allergen) at the time of diagnosis.

Eosinophil counts in nasal fluid

Nasal lavage was performed using a disposable metered-dose nasal inhaler (Markos, Monza, Italy) filled with normal sterile saline solution at room temperature. This device consists of a plastic cup with two compartments. The central compartment was filled with sterile saline solution, while the external compartment collected the liquid after washing. The total input of saline solution was approximately 8 mL (4 mL per nostril for 5 min). To collect the nasal washings, the subjects were instructed to take active breath during a Valsalva maneuver in order to harvest nasal fluid in the cup. The samples obtained were stored on ice and centrifuged at 400g for 10 min at 4°C. The individual

variation in the recovered versus introduced volume was $86 \pm 8\%$. Nasal eosinophil counts were performed on the nasal lavage. One cytospin slide for each sample (1×10^{-4} cells in 170 μL per slide) was centrifuged at 10g for 10 min in a Shandon cytocentrifuge (Shandon Southern Ltd., Runcorn, UK). The slides were immediately fixed in 95% ethyl alcohol, dipped in Wright-Giemsa stain, and examined under oil immersion by light microscopy at a magnification of $\times 400$. Eosinophils were expressed as a percentage of 300 cells counted [17, 18]. All the specimens were examined by the same blinded microscopist (V.D.), who did not know the clinical histories, the results of the SPT and the specific serum IgE, or the severity of the rhinitis symptoms [15].

Statistical analysis

The differences between the data at time of diagnosis and these of 2008 were analyzed with Wilcoxon test because the normal distribution was rejected [Kolmogorov–Smirnov reject Normality ($P < 0.0001$)].

The normal distribution of the variables (VAS, SPT levels of serum total IgE and serum-specific IgE, nasal eosinophil count, and ratio serum sIgE/tIgE) was rejected, using Kolmogorov–Smirnov test. Therefore, the results are presented as median and 25th and 75th percentiles (P25th and P75th), and the differences between the data at time of diagnosis and at the second evaluation were analyzed with Wilcoxon test. For statistical analyses, a value of $P = 0.05$ was considered statistically significant.

For the calculation of the ratio serum-specific IgE/total IgE, we used the following formula:

$$\text{Ratio serum sIgE/tIgE} = \frac{\text{serum specific IgE}}{\text{serum total IgE}} \times 100.$$

For each variable, we calculated the variation between the value at the time of diagnosis and at the time of follow-up ($\Delta\%$), using the following formula [16]:

$$\Delta\% \text{ variation of variable} = \frac{(-\text{variable at diagnosis} + \text{variable at follow-up})}{\text{variable at diagnosis}} \times 100.$$

Finally, the correlation between the variables was evaluated with Spearman's rank correlation.

Analyses were performed using the statistical package and the R statistical software package (version 2.10.0).

Results

One hundred and eight patients tested between 1990 and 1995 were re-tested in 2009. From 2008 to 2009, 108 of

these patients (69 women and 49 men; mean age, 62.1 years; range 59–69 years) participated in the present study for assessment of long-term changes in the rhinitis and allergy status after an average follow-up of 16.3 years (range 14.0–19.0 years). Information on the duration of rhinitis symptoms, changes in rhinitis symptom severity, present and past history of nasal disorders, therapy received for rhinitis, smoking habits, and onset of asthma was gathered with the help of a questionnaire completed by all patients. At follow-up, no patients had developed a new positive skin reaction, while 31 patients had changed from positive to negative SPT. Only one of the patients who had changed from positive to negative SPT was positive to *Dermatophagoides*, whereas 30 patients were positive to pollens (15 to grass, 11 to mugwort, 3 to *Cupressus arizonica*, and 1 to *Olea europea*).

Comparison VAS, SPT, serum sIgE, tIgE and ratio sIgE/tIgE and nasal eosinophil (nEOS)

The changes in VAS, SPT, serum sIgE and tIgE, ratio sIgE/tIgE, and nEOS are shown in Table 1. VAS, serum sIgE, ratio sIgE/tIgE, and nEOS were significantly decreased, while the SPT wheals and serum tIgE were unchanged. Using Spearman's rank correlation to analyze whether the changes were related to age, we found that the changes in VAS (Rho 0.27 (95% CI 0.10–0.43), $P = 0.002$) and nEOS (Rho 0.22 (95% CI 0.04–0.38), $P = 0.01$) were significantly age correlated. Also, $\Delta\%$ VAS and $\Delta\%$ nEOS were significantly correlated (Rho 0.49 (95% CI 0.33–0.61), $P < 0.0001$). We analyzed SPT test, serum-specific IgE and total IgE, and nasal eosinophil counts related to VAS, as reported in the “Methods” section. With regard to the changes in $\Delta\%$ of VAS, the nasal symptoms were completely resolved in 27 patients (22.9%), they were less

Table 1 Changes of the VAS, diameters of the wheals (mm), serum-specific IgE (kU_A/L) and total IgE (kU/L), ratio sIgE/tIgE, and nasal eosinophil counts

	At the time of diagnosis	At follow-up	<i>P</i>
VAS	68.0 (63.0–76.0)	53.5 (29.0–70)	<0.0001
SPT	5 (4–5)	4 (2–6)	0.08
Serum sIgE	6.2 (2.1–24.6)	5.3 (0.3–26.9)	0.01
Serum tIgE	162.5 (104.0–187.0)	162.5 (100.0–189.0)	0.7
Ratio sIgE/tIgE	3.6 (1.2–20.0)	2.6 (0.2–19.3)	0.008
nEOS	4.0 (2.0–7.0)	2.0 (1.0–7.0)	0.005

severe in 28 patients (23.7%), equally severe in 51 patients (42.2%), and more severe in 12 (10.2%). There was no difference between the four groups as regards patient age ($P = 0.08$).

$\Delta\%$ of SPT, serum sIgE, serum tIgE, ratio sIgE/tIgE, and nEOS in patients with complete nasal symptom remission

As shown in Table 2, patients reporting a complete nasal symptom remission presented significant differences ($P < 0.0001$) between current data and the data at the time of diagnosis of SPT [$\Delta\%$ -33.0 (-50.0 to -20.0)], serum sIgE [$\Delta\%$ -73.6 (-88.0 to -51.3)], ratio serum sIgE/tIgE [$\Delta\%$ -73.3 (-86.8 to -48.4)], and nEOS [$\Delta\%$ -50.0 (-100.0 to 0.0)], while we did not find any difference compared with serum tIgE ($P = 0.8$) [$\Delta\%$ 1.3 (-8.1 to 5.9)].

$\Delta\%$ of SPT, serum sIgE, serum tIgE, ratio sIgE/tIgE, and nEOS in patients with less severe nasal symptoms

Patients reporting less severe nasal symptoms presented significant differences ($P < 0.0001$) in nEOS [$\Delta\%$ -50.0 (-71.4 to -33.3)], but no differences were found when comparing SPT ($P = 0.6$) [$\Delta\%$ -0.0 (-33.3 to 8.3)], serum sIgE ($P = 0.1$) [$\Delta\%$ -38.5 (-80.7 to 8.4)], serum tIgE [$\Delta\%$ 2.3 (-1.8 to 5.4)], ($P = 0.9$), and ratio serum sIgE/tIgE ($P = 0.1$) [$\Delta\%$ -35.6 (-81.1 to 5.0)].

$\Delta\%$ of SPT, serum sIgE, serum tIgE, ratio sIgE/tIgE, and nEOS in patients without change in nasal symptoms

Patients reporting equally severe nasal symptoms presented no differences when comparing SPT ($P = 0.6$) [$\Delta\%$ -0.0 (-33.3 to 20.0)], serum sIgE ($P = 0.4$) [$\Delta\%$ -9.2 (-62.5 to 8.1)], serum tIgE ($P = 0.8$) [$\Delta\%$ 3.9 (-5.7 to 7.7)], ratio sIgE/tIgE ($P = 0.1$) [$\Delta\%$ -9.2 (-62.8 to 5.8)], and nEOS ($P = 0.5$) [$\Delta\%$ 0.0 (-33.3 to 16.6)].

$\Delta\%$ of SPT, serum sIgE, serum tIgE, ratio sIgE/tIgE, and nEOS in patients with more severe in nasal symptoms

Patients with more severe nasal symptoms presented significant differences in nEOS ($P = 0.03$) [$\Delta\%$ 24.2 (20.1 to 35.6)], but no differences in SPT ($P = 0.7$) [$\Delta\%$ 0.0 (-20.0 to 18.3)], serum sIgE ($P = 0.9$) [$\Delta\%$ -5.4 (-7.9 to 8.6)], serum tIgE ($P = 0.6$) [$\Delta\%$ 5.5 (-5.6 to 9.6)], or the ratio sIgE/tIgE ($P = 0.1$) [$\Delta\%$ -5.4 (-30.9 to 9.2)] (Table 3).

Table 2 Comparison of SPT (wheal mm), serum-specific IgE (kU/L), serum total IgE (kU/L), and nasal eosinophil counts (%) at diagnosis (1st) and at follow-up (2nd)

	SPT			sIgE			tIgE			Ratio sIgE/tIgE			Nasal eosinophil counts		
	1st	2nd	P	1st	2nd	P	1st	2nd	P	1st	2nd	P	1st	2nd	P
Complete remission [N = 27, age 63.0 (± 2.7)]	4	2	<0.0001	2.4	0.3	<0.0001	186	180	0.8	1.2	0.2	<0.0001	1	1	<0.0001
	4-4	2-4		1.1-2.8	0.2-1.3		154-210	160-221		0.6-2.1	0.1-0.66		1-2	0-1	
Less severe [N = 28, age 63.2 (± 2.2)]	5	5	0.6	5.4	1.8	0.1	168	166	0.9	3.6	1.0	0.1	5	2	0.0001
	4-6	2-6		1.4-14.3	0.3-16.8		97-190.5	100-183.5		0.8-10.1	0.2-11.6		2-6	1-2	
Equal severe [N = 51, age 63.7 (± 2.1)]	5	5	0.6	14.2	14.6	0.4	164	156	0.8	12.4	14.6	0.5	5	4	0.5
	4-6	2-6		5.4-34.6	0.3-30.2		90-178	95-186		2.8-22.3	0.4-27.2		3-7	2-8	
More severe [N = 12, age 64.9 (± 1.2)]	5	4.5	0.7	53.6	50.7	0.9	106.5	117.5	0.6	43.2	29.9	0.7	15.0	19	0.03
	4-5.5	4-6.5		33.4-59.3	33.2-63.6		104-135.5	98.5-161		23.0-55.2	23.4-59.4		12.5-16.5	16-20.5	

Table 3 $\Delta\%$ of SPT (wheal mm), serum-specific IgE (kU_A/L), serum total IgE (kU/L), and nasal eosinophil counts (%) comparing the data at the time of the diagnosis and at the follow-up

	Complete remission ($\Delta\%$ -100)	Less severe ($\Delta\%$ -30 to -99)	Without changes ($\Delta\%$ -29 to 29)	More severe ($\Delta\%$ $\geq$ 30)
SPT	-33.3 (-50.0 to 20)	0.0 (-33.3 to 8.3)	0.0 (-33.3 to 20)	0.0 (-20 to 18.3)
Serum sIgE	-73.6 (-88.0 to -51.3)	-38.5 (-80.7 to 8.4)	-9.2 (62.5 to 8.1)	-5.4 (-7.9 to 8.6)
Serum tIgE	1.3 (-8.1 to 5.9)	2.3 (-1.8 to 5.4)	3.9 (-5.7 to 7.7)	5.5 (-5.6 to 9.6)
Ratio sIgE/tIgE	-73.3 (-86.8 to -48.4)	-35.6 (81.1 to 5.0)	-9.2 (62.8 to 5.8)	-5.4 (-30.9 to 9.2)
nEOS	-50 (-100 to 0.0)	-50.0 (-71.4 to 33.3)	0.0 (-33.3 to 16.6)	24.2 (20.1 to 35.6)

$\Delta\%$ of nasal symptoms at the time of the diagnosis and at the follow-up, evaluated with VAS (see text)

Discussion

The main result of our study demonstrated a decrease in VAS, serum sIgE, ratio sIgE/tIgE, and nEOS after the follow-up period, while the SPT wheals and serum tIgE were unchanged. Particularly, the nasal symptoms evaluated as $\Delta\%$ of VAS were completely resolved in 27 patients, in 28 patients were less severe, in 51 subjects were unchanged, and only in 12 subjects were more severe. However, when we examined the change in the nasal symptoms related to SPT, serum sIgE, ratio sIgE/tIgE, and nEOS, we found that: (1) the patients that reported a complete nasal symptom remission presented significant decreases of the SPT wheal, sIgE, ratio serum sIgE/tIgE, and nEOS; (2) the patients that reported less severe nasal symptom presented only a significant decreases of nEOS; (3) the patients that reported no change in nasal symptoms did not demonstrate no difference in SPT, serum sIgE, serum tIgE, ratio sIgE/tIgE, and nEOS; (4) patients that reported more severe nasal symptoms presented only a significant increase of nEOS. Several observations in the literature point to eosinophil inflammation as a cause of nasal symptoms in subjects with allergic rhinitis [1, 14, 17]. On the other hand, topical treatment with glucocorticosteroid reduces the nasal symptoms parallel with the reduction of inflammation of the nasal mucosa [19]. In our survey of elderly with rhinitis and positive SPT, we found no age-related decline in total serum IgE or in SPT wheal diameter. However, only in the 27 subjects that presented the complete of the nasal symptom remission at follow-up, we noted that on average, a considerably lower proportion of total IgE was directed against the allergen, with a low ratio serum sIgE/tIgE.

These differences may not result solely from aging. Previously, we used the ratio sIgE/tIgE as the criterion to decide for or against immunotherapy in monosensitized patients with allergic rhinitis [16]. The lower ratio serum-specific IgE and total serum IgE at the time of the diagnosis may indicate that the IgE response to allergen was responsible of a clinical allergy but only a sensitization to

the allergen. The lower ratio serum-specific IgE and total serum IgE at the time of the diagnosis may indicate that the IgE response to allergen was not specific. It has been reported that the percentage of allergen sIgE is approximately 25% of tIgE [16]. Allergic inflammation is initiated by allergen molecules cross-linking their corresponding receptor-bound sIgE on the mast cell and basophil surface [20, 21]. Although it is possible to quantify both serum tIgE and sIgE levels, serum tIgE levels are not measured because they are not useful in the specific clinical diagnosis of allergy to common aeroallergens [22]. Thus, a higher sIgE/tIgE ratio might reflect a higher level of allergen sIgE on the mast cell and basophil surface, whereas this probability is lower when the serum sIgE/tIgE ratio is low. The levels of total serum IgE were maintained for the duration of the follow-up, while the specific antibody response slightly decreased. Unfortunately, our data were insufficient to establish whether aging eventually loses its specific humoral response.

Our data demonstrate that the severity of allergic symptoms is related to certain factors, for example, nasal eosinophils other than the level of IgE. In a previous study, we demonstrated that nasal eosinophil count accurately distinguished patients with mild rhinitis from patients with severe rhinitis [23]. In allergic rhinitis, the tissue recruitment of eosinophils is a hallmark of the natural history of the disease and of untreated allergic inflammation with nasal steroids [17, 24, 25]. However, allergic rhinitis with eosinophilia has more severe symptoms, particularly nasal obstruction and rhinorrhoea [17, 23]. Eosinophilia may contribute to nasal mucosal dysfunction, through the granules released from eosinophil (i.e., the major basic protein and eosinophil cationic protein) that are capable of damaging the nasal epithelium and prolonging mucociliary clearance [17, 18, 23, 26]. The importance of nasal eosinophil count in the elderly has not been previously reported, and there is very little in the literature about eosinophil in the elderly.

In conclusion, the involution process of immune system in the elderly appears to affect only the specific immune

response. In this and a previous study, we did not find a significant change with regard to total IgE [27]. This study suggests that changes in rhinitis symptoms appear to be related to changes in the nasal eosinophils, independently of SPT and serum-specific IgE.

Acknowledgments This study was supported by grants from MIUR (Italian University and Research Ministry) (former 60% funds) to Gabriele Di Lorenzo.

Conflict of interest No support was received from the pharmaceutical and diagnostic industry. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject or material discussed in the manuscript a part those disclosed. No writing was utilized in the production of the manuscript.

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