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Eosinophilia in nasal secretions compared to skin prick test and nasal challenge test in the diagnosis of nasal allergy

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SUMMARY

This study was aimed to assess the usefulness of eosinophilia measurements in nasal smears (ENS) in the diagnosis of nasal allergy. Nasal smears were taken from 84 patients with histories suggestive of allergic rhinitis. The smears were stained by the Giemsa method and examined by light microscopy. Positive results were demonstrated in 69.2% of the samples. All the 84 patients also had a skin prick test (SPT); the percentage of correct correlation between ENS and SPT was 71.4%. Forty-two patients underwent nasal challenge test (NCT) and the percentage of correct correlation between ENS and NCT was 69%. Nine patients had negative SPT, but positive ENS. All were nasally challenged with 4 proving positive. This leaves 5 individuals (5.9% of the 84 studied) in the non-allergic rhinitis with eosinophilia category. Based on these findings, it is suggested that the assessment of eosinophils in nasal smears should be given more relevance and be more commonly used in the diagnosis of nasal allergy.

INTRODUCTION

Nasal allergy is a very common condition affecting 10–15% of the population (Fleming and Crombie 1987; Franklin 1989) and is increasing in incidence (Davies 1989). Although not life-threatening, it can be a very disturbing problem for the affected individuals and can cause a broad spectrum of consequences from occasional absences from work to variable degrees of social isolation. That is why we consider that any test which contributes to an accurate diagnosis, followed by the corresponding treatment, is important.

Obviously, a careful clinical history and physical examination are basic in the diagnosis of nasal allergy. However, there are several complementary tests which have proved useful. The most widely used are skin tests (various methods), *in vitro* tests (mainly RAST) and nasal challenge. None of these is completely

reliable and often the diagnosis is based exclusively on clinical findings. Thus, considering the relative unreliability of these tests, and also that some of the methods are expensive and not widely available, we have been interested in a review of the presence of eosinophils in nasal secretions (ENS) as a complementary diagnostic tool of nasal allergy. Since the procedure of collecting, processing and examining nasal smears is relatively simple, quick and cheap, it could become a significant aid in the diagnosis and management of allergic rhinitis, particularly in those centres with less economic and technical resources.

The presence of eosinophils in nasal secretions of allergic patients was initially described by Ehrlich in 1879 (Bickmore, 1981). Since then, knowledge about the role of these cells in allergic phenomena has been increasing, but, however, a complete understanding of their functions has not yet been reached (Mygind, 1982). The general view of these cells is as effector cells in the immune response, combating parasites in helminthic infections and damaging tissues and cells in hypersensitivity diseases (Gleich, 1989). According to Masuyama et al. (1988), eosinophils migrate from the nasal submucosa through the intercellular space projecting pseudopodia into the apical region of the space and splitting the junctions between epithelial cells, in order to reach finally the lumen of the nose, where they can be easily identified within nasal secretions as part of the nasal cytogram. However, a "normal nasal cytogram" has not yet been described. Most authors agree that eosinophils are not usually, or only occasionally, present in the smears of non-allergic patients. Nevertheless, there are several reports describing the significant increase of eosinophils in nasal secretions of allergic patients who have recently been exposed (one hour to 3 days) to allergic triggering factors (Mygind, 1982; Malmberg et al., 1985). On the basis of such findings the assessment of the presence of eosinophils in nasal secretions has become another diagnostic tool of nasal allergy. However, perhaps unfairly, it has not been given importance within the diagnostic spectrum of allergic rhinitis.

Through this work we have tried to evaluate the validity of the detection of ENS in those patients with symptoms of nasal allergy by comparing it with two different methods, skin prick test (Mangi, 1985) and nasal challenge test (Eccles, 1989).

MATERIAL AND METHODS

Between January and June 1990, 84 adult patients (41 males and 43 females) attending the Rhinitis Clinic at the Royal National Throat, Nose and Ear Hospital with histories suggestive of nasal allergy, were tested. Patients with nasal polyps were not included. Nasal smears were taken in the knowledge that they had probably been exposed to the suspected allergen(s) during the last 48 hours. In many of these patients samples were taken more than once. A total of 276 smears were collected, 246 of them corresponding to 123 pairs (right and left nostrils of

the same individual). In all these patients skin prick tests were performed and 42 of them also had nasal challenge. Nasal secretions were taken under direct view by wiping the mucosa with a cotton swab according to the method suggested by Bickmore (1981). The swabs were then rolled onto a glass slide, fixed with a water-soluble aerosol fixative (Cytospray, Solmedia, Colchester) and stained by the Giemsa technique (Cook, 1974) using a standard Giemsa staining solution (Gurr, BDH, Poole, Dorset). Slides were rinsed in distilled water, differentiated in weak uretic acid (1:10,000 v/v) until the section was predominantly pink, then rinsed in distilled water, dehydrated, cleared, and mounted in Canada balsem. Next, they were examined under light microscopy using a conventional Leitz microscope. First, the slides were screened overall at ×25 and ×100, and then they were carefully examined using magnification powers of ×250, ×400 and ×630. As the density of the cell population on the smears was variable, it was impossible to have an objective measurement of the number of eosinophils in each sample, so we adopted a semi-quantitative assessment to evaluate the different numbers of eosinophils found. Therefore, we used the following simple scheme for this purpose, slightly modified from Mygind (1982):

(−): Eosinophils absent or very few present,

(+): Approximately 10–50% eosinophils of the total amount of leukocytes,

(++): More than 50% of eosinophils of the total amount of leukocytes.

For the purpose of this study, both (+) and (++) have been considered as a positive finding.

Skin prick tests (SPT) were performed using a set of 10 common allergens identified as aetiologic factors in allergic rhinitis (grass pollen, house dust, house dust mite, *Cladosporium, Aspergillus,* feathers, cat dander, egg, milk, tree pollen) supplied by BioDiagnostics Ltd (Allergo Pharma). Normal saline solution and histamine were used as negative and positive controls, respectively. The response was read 10–15 min later and was considered positive if a wheal at least 2 mm larger than the negative control appeared. Many patients had positive responses to several antigens, however; for the purpose of this study one positive response was considered as a positive SPT.

Nasal challenge test (NCT) was performed on those patients with a more difficult diagnosis. It was based on the evaluation of four cardinal symptoms, i.e. obstruction, itching, sneezing and watery discharge. These symptoms were scored before and 10 min after challenge using a visual analogue scale from 0 to 10, on which the patients scored the severity of symptoms. Nasal obstruction was measured by anterior rhinomanometry using a NR6D Mercury rhinomanometer. The allergens used in the provocation test were some of the above-mentioned inhalant allergens (obtained as intranasal preparations from Allergo Pharma), according to history and clinical findings of each patient. A single allergen was tested on each occasion, initially at 1 : 100, then 1 : 10, then neat. They were sprayed into the

nostril(s) – taking precaution to avoid bronchial challenge – and the response was evaluated 10–15 min later as described above. It was considered a positive NCT when an increase of at least 100% in the symptomatology or rhinomanometry compared to the previous assessment was obtained.

Nasal smears were numbered and examined blindly, without knowing the patient's name or the results of their SPT and NCT.

RESULTS

A total of 276 samples of nasal smears belonging to suspected nasal allergic sufferers were examined. Of these, 191 samples (69.2%) showed positive ENS, while the other 85 (30.8%) were negative. The positive group consisted of two sub-groups: The strongly positive (++) with 35 samples (12.7% of the total), and the less strongly positive (+) with 156 samples (56.5% of the total).

Among all 84 patients who had both evaluation of nasal smears and SPT, we found the following correlation between both methods. Fifty-four of the patients with positive SPT had also positive ENS (++ or +). Six of the patients with negative SPT also had negative ENS. Fifteen patients with positive SPT had negative ENS and 9 patients with negative SPT showed positive response (++ or +) for ENS. Therefore, we found that in 60 (54 + 6) out of 84 patients (71.4%) there was a correct correlation between the results of the SPT and ENS. Meanwhile, in 24 (15 + 9) out of the 84 patients (28.6%) this correlation was incorrect (Table 1).

Regarding the group of 42 patients who had both nasal eosinophilia evaluation and nasal challenge test, we found that 23 patients with positive NCT were also positive (++ or +) for nasal eosinophilia. Six patients with negative NCT had negative nasal eosinophilia; 5 patients had positive NCT with negative ENS and 8 patients with negative NCT showed positive findings (++ or +) for ENS. Thus, we have found a correct correlation between the results of ENS and NCT in 29 (23+6) out of 42 patients (69%) and incorrect correlation in 13 (5+8) out of 42 patients, that is 31% (Table 2). Twenty-nine (25 + 4) of these 42 patients showed correct correlation between NCT and SPT (69%), meanwhile 13 (10 + 3) out of 42 patients had incorrect correlation (31%). These results are summarized in Table 3 and Figures 1A and 1B.

The 9 patients with negative SPT and positive ENS were challenged nasally with their suspected allergen; 4 gave positive results, leaving 5 in the so-called non-allergic rhinitis with eosinophilia category which corresponds to 5.9% of the 84 patients studied.

Finally, it is interesting to point out that among those patients with positive ENS, 22% of them showed eosinophilia in only one nostril, despite both nostrils being freely exposed to the environmental allergens. This finding is in accordance with the reports of Malmberg et al. (1985). When patients were tested on more than one occasion there was concordance of results in 81% of cases. A single positive

result for eosinophilia on one occasion was counted as positive. Repeat sampling is advisable to avoid false-negative results.

Table 1. Correlation between eosinophilia in nasal smears and skin prick test.

	Number	Percentage
Correct	60 (54 + 6)	71.4%
Incorrect	24 (15 + 9)	26.6%
	84	100%

Table 2. Correlation between eosinophilia in nasal smears and nasal challenge tests.

	Number	Percentage
Correct	29 (23 + 6)	69%
Incorrect	13 (5 + 8)	31%
	42	100%

Table 3. Correlation between nasal challenge tests and skin prick tests.

	Number	Percentage
Correct	29 (25 + 4)	69%
Incorrect	13 (10 + 3)	31%
	42	100%

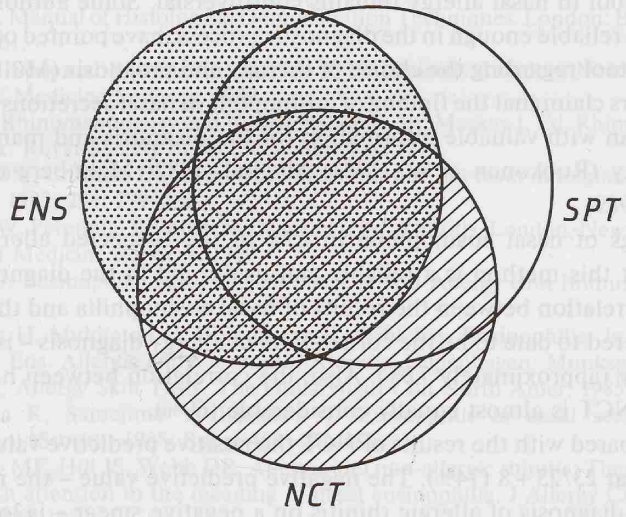

Figure 1A. The correlations between SPT, ENS and NCT in the 42 patients who underwent all three investigations are shown as a Venn diagram, where unshaded represents SPT, lined NCT and dotted ENS. The correlations were 69% between ENS and NCT as well as between NCT and SPT, and 71% between SPT and ENS.

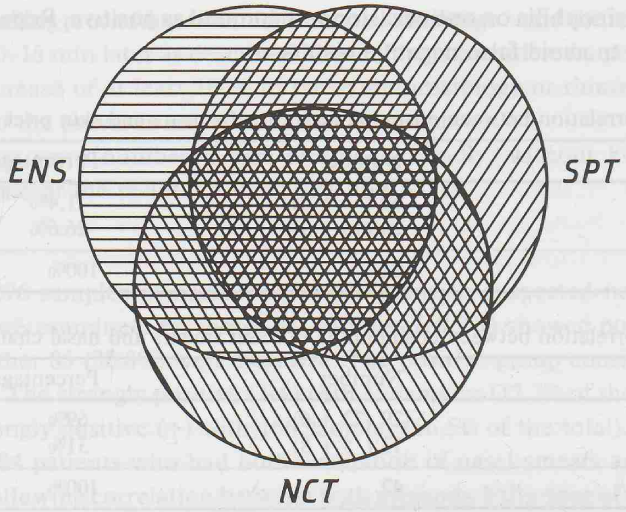

Figure 1B. The central, triple-lined portion represents patients who are positive by all three methods and could therefore be diagnosed by any one of them. The two-striped portion represents patients who could be diagnosed by one of two methods. The single-lined portions represent those patients who are positive on one diagnostic test only.

DISCUSSION

Although the assessment of eosinophils in nasal secretions in allergic patients is not a recent issue, it is not a widely used test. Moreover, its real usefulness as a diagnostic tool in nasal allergy remains controversial. Some authors who have not found it reliable enough in the diagnostic process, have pointed out that it can be a useful tool regarding the choice of therapy and prognosis (Mullarkey et al., 1980). Others claim that the finding of eosinophils in nasal secretions can provide the physician with valuable information for the diagnosis and management of nasal allergy (Ruokonen et al., 1981; Mygind, 1982; Malmberg et al., 1985; Franklin, 1989).

Our findings of nasal eosinophilia in 69% of the suspected allergic patients suggest that this method is a reliable and useful aid in the diagnosis of nasal allergy. Correlation between the results of nasal eosinophilia and the SPT – the test considered to date to be the cornerstone of allergy diagnosis – is reasonable in our study (approximately 72%). Also, the correlation between nasal eosinophilia and NCT is almost equally considerable (69%).

When compared with the results of NCT the positive predictive value of ENS is quite good at 23/23 + 8 (74%). The negative predictive value – the reliability to discard the diagnosis of allergic rhinitis on a negative smear – is low at 6/5 + 6 (54%). Thus, a negative result (especially if performed only once) cannot exclude nasal allergy, but a positive one lends support to the diagnosis.

The incidence of so-called non-allergic rhinitis with eosinophilia was very small

in this non-polyp population (5.9%) and may be still smaller since nasal challenge testing can give false-negative results, e.g. when performed with the incorrect allergen. It is likely that most patients in this category represent undiagnosed allergies with vasomotor rhinitis caused by underlying allergic inflammation. The symmetry of Figure 1 suggests that all three tests are looking at the same patient population. A nucleus of patients are positive on all three tests and could be diagnosed by any of them, others are positive on two, but there remains a subgroup (lined in Figure 1B) who are positive on one test only. Thus, unless a spectrum of tests is used in the assessment of nasal disease some patients with allergic rhinitis will be falsely considered to be non-allergic. This is an important consideration not only for those undertaking the treatment of patients but also in rhinological research where patients are frequently grouped into allergic and non-allergic on the basis of SPT alone. Therefore, taking into account that it appears to be reasonably accurate, relatively cheap and an easy diagnostic method, we believe that nasal eosinophilia should receive more attention from the physician. We suggest that the assessment of eosinophilia in nasal smears should be included as a relevant procedure in SPT-negative patients, along with the other available tests, and on more than one occasion if negative in order to improve the accuracy of diagnosis of the allergic disease of the nose.

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