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# Seasonal non-allergic rhinitis (SNAR) – A new disease entity? A clinical and immunological comparison between SNAR, seasonal allergic rhinitis and persistent non-allergic rhinitis*

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SUMMARY

*We have earlier described a group of patients suffering from rhino-conjunctivitis during the early pollen season, but with negative allergological investigation. The present study aimed to evaluate this syndrome called Seasonal Non-Allergic Rhinitis (SNAR). Seventeen patients with SNAR were compared with 20 patients with seasonal allergic rhinitis (SAR) and 13 patients with persistent non-allergic rhinitis (PNAR). They were analyzed with skin prick tests (SPT) and nasal provocation tests (NPT) with pollen extracts, and for IgE antibodies in serum and inflammation mediators in nasal lavage. Daily symptoms and medicine consumption were recorded. Late reactions after SPT occurred in two SNAR, eight SAR and two PNAR patients. Weak immediate and late reactions after NPT were induced in 3/15 and 7/15 SNAR patients, respectively, and in 1/13 and 5/13 PNAR patients. All SAR patients had immediate and 9/18 had late reactions. The total IgE levels were lower in SNAR compared to SAR. In the SNAR group 1/15 was positive in Phadiatop®. Increased tryptase levels after NPT were only observed in SAR. The SNAR patients had high daily symptom scores already before birch pollen season. Sneezing was more common in SNAR and SAR than in PNAR; eye-symptoms more prominent in SAR than in SNAR or PNAR. SNAR seems to be different from SAR and PNAR regarding immunological mechanism and symptom period. We conclude that the cause of SNAR is unknown.*

*Key words: allergic rhinitis, IgE, nasal provocations, non-allergic rhinitis, skin prick test*

## INTRODUCTION

Non-infectious rhinitis can be allergic or non-allergic. Allergic forms of rhinitis can be seasonal or perennial [1]. Seasonal allergic rhinitis (SAR), often called hay fever, is in Sweden caused by allergy towards pollen from birch and other deciduous trees, with a symptom period in April - May, from grasses, with symptoms mainly in June - July and from mugwort, with symptoms mainly in the month of July - August.

Non-allergic rhinitis, which is sometimes referred to as hyperreflectory rhinopathy or vasomotor rhinitis, is usually regarded as a disease with perennial (persistent) nasal symptoms, i.e. persistent non-allergic rhinitis (PNAR) [1]. In routine work at the Lung and Allergy Clinic in Halmstad, however, a number of patients have been observed, having seasonal rhino-conjunctivitis symptoms, who at clinical allergy investigation showed no signs of pollen allergy, in spite of the fact that they reported a symptom period mainly coinciding with the early pollen season. In an earlier study, 86 patients with similar case history were compared with birch pollen allergic patients and patients with PNAR. The term Seasonal Non-Allergic Rhinitis (SNAR) was used to describe this new disease entity [2]. It was concluded from that study that SNAR had more characteristics in common with PNAR than with SAR. The causes of the strictly seasonal symptoms of this syndrome are, however, not evident.

Pollen-borne allergic rhinitis is a typical example of an IgE-mediated allergy. The symptoms start when allergens bind to specific IgE-antibodies on the surface of mast cells leading to

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the release of tryptase, cytokines, leukotrienes and prostaglandins. This follows by an inflammation cascade with infiltration of T helper cells and eosinophils into the airways, a hallmark of the allergic late phase reaction [3]. Activated eosinophils produce toxic proteins such as eosinophil cationic protein (ECP) that cause tissue destruction [4]. The role of neutrophils in allergic inflammation is unclear. The neutrophil-derived myeloperoxidase (MPO) is primarily elevated in nasal lavage during exposure to non-specific irritants or during airway infections [5, 6].

The aim of the present study was to further evaluate the disease entity SNAR by examining and comparing three groups of patients with diagnosis of SNAR, SAR and PNAR. The groups were compared regarding symptoms and drug consumption during the birch and grass pollen seasons. Skin prick test (SPT) was performed with several pollen allergens, and nasal provocation test (NPT) with extracts of birch or timothy pollen. Furthermore, serum concentrations of total IgE and specific IgE antibodies to various pollen allergens were measured, as well as tryptase, ECP and MPO in nasal lavage before and after NPT.

## MATERIALS AND METHODS

### *Patients*

SNAR group

From the patients register at the Lung and Allergy Clinic, 36 patients, who according to earlier examinations fulfilled the criteria of SNAR, were invited. The criteria were symptoms of rhinitis during the pollen season (April - August) at least one of the last two years and negative SPT with a standard allergen panel consisting of standardized extracts of pollen (birch, timothy and mugwort), dog, cat and horse epithelium, Dermatophagoides pteronyssinus and unstandardized extracts of Cladosporium and Chironomid (red mosquito larvae) [7]. Seventeen patients accepted to take part in the study (Table 1). One of the patients moved from Halmstad after having been included in the study and could not come for in vivo- or in vitro-testing.

SAR group

The SAR group was matched with the SNAR group according to age and sex. All had positive (>2+) SPT results with birch and/or timothy pollen extract, performed during one of the three latest years, and suffered from seasonal rhino-conjunctivitis during the pollen season at least one of the two latest years. Two patients, who earlier had been classified as SNAR, had later developed a pollen allergy with positive SPT to birch pollen and were therefore included in the SAR group. Of 36 patients selected, 20 individuals accepted to take part in the study (Table 1).

PNAR group

The PNAR group consisted of patients having perennial rhinitis symptoms and negative SPT results with the standard allergen panel. Two patients, who earlier had been regarded to have SNAR, were found to have only perennial symptoms according to the present history and were therefore included in the PNAR group. Of the 16 invited individuals, 13 accepted to take part in the study (Table 1).

*History*

The patients' case history was obtained via a questionnaire, in which we asked for type of symptoms, duration, season and eliciting factors (like birch twigs, strong smells, birch pollen related foods). The patients were asked to grade their symptoms according to the following scale: 0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = severe symptoms, regarding the following symptoms during spring and summer: blocking, running, sneezing, impaired sense of smell, itching of the eyes, breathlessness. Furthermore, their symptoms were recorded on a visual analogue scale (1 = no or very slight symptoms, 10 = very severe symptoms).

*Skin prick tests*

SPT was performed before the pollen season in accordance with the routines at the clinic [8] and in accordance with consensus documents [9]. The following Soluprick 10 HEP pollen allergens (ALK-Abello, Hørsholm, Denmark) were used: birch, alder, hazel, elm, oak and six different grasses (timothy, meadow foxtail, cocksfoot, oat grass, meadow fescue and rye) and mugwort. The wheals were measured after 10-15 minutes and recorded in accordance with Nordic guidelines [10]. Thus, a wheal reaction of the same size as that of a positive histamine reference (histamine HCl 10 g/l) was recorded as three

Table 1. Patients and inclusion criteria.

| | **SNAR** | **SAR** | **PNAR** |
|---|---|---|---|
| Number of patients | 17 | 20 | 13 |
| Males/Females | 2/15 | 5/15 | 5/8 |
| Age (mean and range) | 37 (18-71) | 37 (18-66) | 43 (19-74) |
| Skin prick tests (with standard allergen panel) | Negative | Positive* | Negative |
| Symptoms | Rhinitis or rhino-conjunctivitis | Rhinitis or rhino-conjunctivitis | Rhinitis or rhino-conjunctivitis |
| Season for symptoms | Spring or spring/summer | Spring or spring/summer | All year around |

* Positive (>2+) for birch and/or timothy pollen

plus (3+) and a wheal half the size of the positive control was recorded as 2+. Reactions ≥2+ were regarded as positive. No oral antihistamines were allowed five days before the testing. The patients were asked to report if late SPT reactions occurred after 4 h, 8 h or the following morning.

*Nasal provocations*

The provocations were performed as follows: with a Carlsberg pipette 25 μl control solution was delivered on the inferior turbinate in the nasal cavity on each side. If there were no local symptoms the provocation was proceeded with application of 25 μl allergen extract (Aquagen, birch or timothy pollen, ALK-Abello) on the inferior turbinate in each nasal cavity. With 10 minutes intervals, allergen extracts of stepwise increasing concentration (100, 1000, 10.000 and 100.000 SQ-units/ml) was administered bilateral in the nasal cavity. During the challenge procedure symptoms of sneezing, running nose, nose block, itching and respiratory symptoms were continuously measured on a symptom chart using a 4-point scale (0 = no, 1 = mild, 2 = moderate, 3 = severe symptoms). If the calculated sum of the scores for each symptom exceeded 3 the provocation was considered positive and further provocation was omitted. If the test subject was free from symptoms after provocation with the allergen extract of the highest concentration, a further provocation was made with pure pollen grains from birch or grass. Late symptoms were registered at home during the next 24 hours by the test subjects using the same symptom score and chart as above.

During the challenge procedure acoustic rhinometry was used to evaluate the reaction of the nasal mucosa [11, 12]. Mean value of the area in the valve plane ($cm^2$) and mean value of the volume in the anterior nasal segment ($cm^3$) was measured before testing and after each provocation.

*Recording of symptoms and medicine during the pollen season*

All the patients recorded symptoms (eye symptoms, blocking, itching and running nose, sneezing, and coughing) according to a 4-grade scale (0 = no symptoms, 1 = slight symptoms, 2 = moderate symptoms, 3 = severe symptoms) as well as the consumption of antihistamine tablets, local antihistamines for eyes or nose and nasal steroids. The number of tablets, doses of inhalations or number of eyedroppers were recorded: 1 tablet, 1 dose etc = 1 score, 2 tablets, 2 doses etc = 2 score etc. The mean score per week was calculated.

If the patient had an infection or did not stay in the hometown it was recorded in the protocol. The patient protocols were mailed to us every second week. The recordings were performed from March 6 to July 30, 1995.

*Measurement of serum IgE antibodies*

The presence of IgE antibodies in patients′ sera to common inhalant allergens was investigated using Phadiatop® (Pharmacia Diagnostics AB, Uppsala, Sweden). The concentrations of total and specific IgE antibodies were analyzed using Pharmacia CAP System™ (Pharmacia Diagnostics AB). Specific IgE antibodies were measured against grass pollen (timothy) and various tree pollen (gray alder, common silver birch, hazel and mountain juniper). The cut-off value of the specific IgE assay was 0.35 $kU_A/l$.

*Analyses of inflammation mediators in nasal lavage*

The concentrations of tryptase, ECP and MPO were determined in nasal lavage collected before and after NPT. The immunoassays used were UniCAP® Tryptase, UniCAP® ECP and Pharmacia MPO RIA (all from Pharmacia Diagnostics AB). The nasal lavage samples were diluted 1:2 in sample diluent prior to analyses according to the recommendation of the manufacturer (personal communication). The cut-off values of the immunoassays were 1 ng/ml (tryptase), 2 ng/ml (ECP) and 8 ng/ml (MPO).

*Recording of pollen*

The number of pollen in the air was recorded in Halmstad using a Burkard's Volumetric Spore Trap placed on the roof of a building at Halmstad hospital. The pollen tapes were sent five days a week to the Botanical Institution at University of Gothenburg for analyses [13].

*Statistical methods*

For comparisons of clinical data between the groups $\chi 2$ test was used. To identify significant differences in concentrations of serum IgE antibodies, and tryptase, ECP and MPO in nasal lavage samples, the Wilcoxon-signed ranks test and Mann-Whitney U-test (two tailed p-value) were used for within group and between group comparisons, respectively. All p values $<0.05$ were regarded as significant.

*Ethics*

The study was approved by the Ethic Committee of University of Lund.

## RESULTS

*Case histories*

The majority of the patients in the SNAR group (12/16) had rhinitis or rhino-conjunctivitis only during spring or spring and summer whereas all the patients in the PNAR group had perennial symptoms ($p<0.001$). Of the patients in the SNAR group, 3/16 had symptoms in spring and autumn and 1/16 in summer and autumn. In the SAR group 9/19 had symptoms only at springtime, 6/19 in springtime and summertime and 2/19 in summertime. Two patients had symptoms also out of the pollen season. There was no significant difference between the SAR and SNAR group regarding symptoms season according to the questionnaire. The SAR group had more severe eye symptoms than the SNAR and PNAR groups ($p<0.01$), but there was no significant difference between the groups regarding other symptoms. Patients in the SNAR group complained of symptoms induced by flowers ($p<0.05$) and birch twigs ($p<0.01$) more often than the PNAR group (Table 2). There

Table 2. Factors eliciting symptom according to patients´ answers to a questionnaire.

| Eliciting factor | SNAR | SAR | PNAR | Significance of differences |
|---|---|---|---|---|
| Scent of flowers | 14/16 | 12/17 | 4/9 | SNAR>PNAR P<0.05 |
| Birch twigs | 10/14 | 15/17 | 1/9 | SNAR>PNAR P<0.01; SAR>PNAR P<0.001 |
| Nuts | 5/15 | 12/18 | 2/10 | SAR>PNAR P<0.05 |
| Fresh fruit | 6/14 | 13/18 | 1/10 | SAR>PNAR P<0.001 |

Table 3. Results of skin prick tests (SPT).

| Extract for SPT | Skin reaction | SNAR n=17 | SAR n=20 | PNAR n=13 |
|---|---|---|---|---|
| Birch pollen | Immediate reaction only | 0 | 10 | 0 |
| | Both immediate and late reaction | 0 | 8 | 0 |
| | Late reaction only | 0 | 0 | 2 |
| Other tree pollen | Immediate reaction only | 0 | 10 | 0 |
| | Both immediate and late reaction | 0 | 7 | 0 |
| | Late reaction only | 1 | 0 | 1 |
| Grass pollen | Immediate reaction only | 0 | 10 | 0 |
| | Both immediate and late reaction | 0 | 6 | 0 |
| | Late reaction only | 2 | 1 | 1 |
| Mugwort pollen | Immediate reaction only | 0 | 2 | 0 |
| | Both immediate and late reaction | 0 | 1 | 0 |
| | Late reaction only | 2 | 1 | 1 |

Immediate reactions were recorded after 10-15 minutes. Late reactions were recorded by the patients after 4h, 8h or the following morning.

was no significant difference between SNAR and SAR regarding symptoms from flowers and birch twigs. Nuts and fresh fruits more often induced allergic symptoms in SAR than SNAR and more often in SNAR than in PNAR group. However, it was statistically significant only between the SAR and PNAR groups (Table 2). There was no significant difference between the groups regarding symptoms induced by tobacco smoke, perfumes, car exhaust, printing ink, weather and foods other than nuts and fresh fruits.

Hypersensitivity against acetyl salicylic acid (ASA) was reported by 3/15 of the SNAR patients, 2/19 of the SAR and 1/13 of the PNAR patients.

*Skin prick tests*

All the SAR patients had positive immediate type reaction at SPT with birch pollen or timothy pollen whereas the SNAR and the PNAR group had negative immediate skin tests with all the allergens used (Table 3). It should be noticed that two patients, who according to earlier test results were regarded as SNAR, later on had developed positive SPT with pollen and now were included in the SAR group. Late SPT reactions occurred in two SNAR patients and two PNAR patients (Table 3).

*Nasal provocations*

NPT with pollen allergens was performed on 15 SNAR patients, 19 SAR patients and 13 PNAR patients. All individuals in the SAR group had positive NPT (Table 4). Three of 15 patients in the SNAR group and 1/13 in the PNAR group had a positive immediate type NPT with birch pollen in spite of a negative SPT. Only in one of these cases allergen in solution (100.000 SQ units/ml) induced symptoms whereas the other cases only got symptoms on provocation with pollen grain. Of the patients in the SNAR group 7/15 reported a late reaction after the provocation. Among these were the three individuals who had a positive immediate reaction. Of the patients in the PNAR group 5/13 reported late reaction. Included in this group was the patient who had a positive immediate reaction and the two persons who earlier had been regarded as SNAR patients but in this study were included in the PNAR group due to their present case history (Table 4).

The curves from the rhinometry recordings did not show any changes with increasing allergen concentration in the SNAR and PNAR groups, whereas the SAR group showed signs of increasing mucosal oedema with increasing allergen concentration (Figure 1).

*Recording of symptoms and medicine during the pollen season*

The patients in the SNAR and PNAR groups had symptoms already at the start of the recordings (March 6, 1995) and their symptoms gradually decreased during the period. The SAR group had only slight symptoms at the start of the recordings and very much increased symptom scores during the pollen season. The consumption of medicine was high at the start in the SNAR group and was gradually decreasing during the pollen

Table 4. Results of nasal provocation tests with birch and/or timothy pollen.

| Nasal reaction | SNAR n=15 | SAR N=19 | PNAR n=13 |
|---|---|---|---|
| Immediate reaction only | 0 | 10* | 0 |
| Both immediate and late reaction | 3 | 9 | 1 |
| Late reaction only | 4 | 0 | 4 |

* Missing data regarding late reactions for one patient.

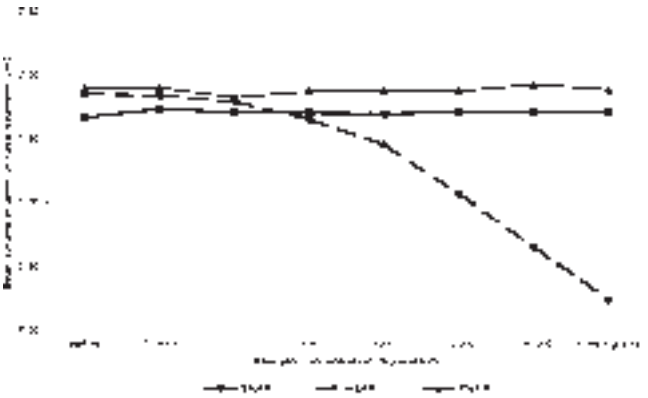

Figure 1. Rhinometry after provocation with birch or grass pollen in the three patient groups. The mean values of the volume ($cm^3$) in the anterior nasal segment are shown.

season. In the PNAR group medicine consumption was low initially and slowly increased during the observation period. The SAR group showed an obvious increase in medicine consumption week number 19, after the peak of the birch pollen season.

The pollen recordings showed that the maximum count for birch pollen occurred week number 17 and for grass pollen week number 26. Figure 2 shows the mean weekly symptom and medication score in the three patients groups as well as the pollen counts.

The most common symptoms recorded during the pollen season were in the SNAR group sneezing. In the SAR group the main symptoms were sneezing and less often eye symptoms, blocking nose and running nose. In the PNAR group blocking nose was most common, followed by sneezing and running nose.

*Serum IgE levels*

Analyses of total and specific serum IgE antibodies were performed in 14 patients in the SNAR group, 16 patients in the SAR group and 11 patients in the PNAR group. The total IgE levels were significantly lower in the SNAR group (13.5 [2.4 - 459] kU/l, median with range) compared to the SAR group (33.2 [9.1 - 200.3] kU/l, $p<0.05$). No significant differences in total IgE between the PNAR group (41.1 [2.0 - 187.5] kU/l) and the SNAR or SAR groups were noted.

In the SNAR group 1/14 patients was positive in Phadiatop, an indication of circulating IgE antibodies against inhalant allergens. All 16 patients tested in the SAR group were positive in Phadiatop, while all 11 patients analyzed in the PNAR group were negative. Specific IgE antibody measurements revealed that all patients in the SNAR group, including the Phadiatop-positive patient, were lacking serum IgE antibodies against all tree and grass pollen allergens tested. All patients in the SAR group had circulating IgE antibodies against one or more of the pollen allergens tested (frequencies of IgE reactivity: timothy, 50%; grey alder, 75%; common silver birch, 81%; hazel, 69%; mountain juniper, 0%). None of the patients in the PNAR group had IgE antibodies to the pollen allergens tested.

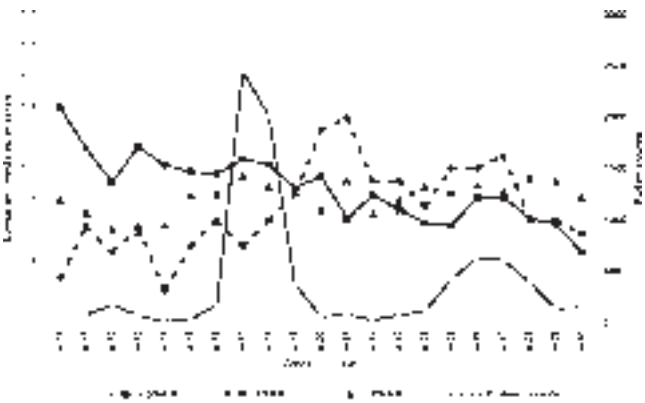

Figure 2. Pollen counts and symptom and medication score before and during the birch and grass pollen season. Weakly means, calculated from patients' daily recordings.

*Inflammation mediators in nasal lavage*

The concentrations of tryptase, ECP and MPO were determined in nasal lavage samples collected from 15 patients in the SNAR group, 19 patients in the SAR group and 11 patients in the PNAR group. The concentrations were below the cut-off values of the immunoassays for most of the patients. No significant differences between the study groups were observed. Neither were any significant differences observed within the SNAR and PNAR groups between nasal lavage samples collected before and after NPT. It was, however, significant increased tryptase levels in the SAR group after NPT (11.0 ± 33.8 ng/ml, mean ± SD) compared to before NPT (1.4 ± 1.6 ng/ml, $p<0.05$). Six of 19 patients in the SAR group and none in the SNAR and PNAR groups showed increased tryptase levels in nasal lavage after NPT (Figure 3A). Furthermore, there was a trend towards increased ECP levels in nasal lavage after NPT in the SAR group (Figure 3B). No significant changes or trends were observed for MPO in nasal lavage (data not shown).

## DISCUSSION

In the present study a group of patients with seasonal rhinoconjunctivitis and negative SPT (SNAR group) were compared with a group of hay fever patients (SAR) and a group of patients with persistent non-allergic rhinitis (PNAR). SPT with 12 different pollen allergens, recorded after 10-15 minutes, as in routine diagnostic work, was negative in the SNAR group. Late reactions were, however, reported by two patients. NPT with birch pollen was positive in three patients of the SNAR group. Furthermore, seven patients reported a late nasal reaction. The

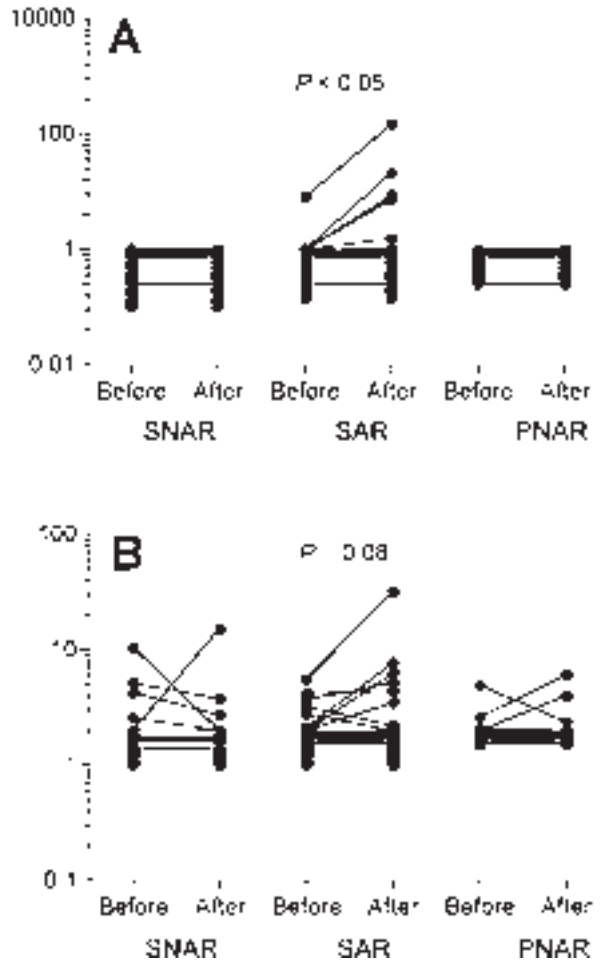


Figure 3. Concentrations of tryptase (A) and ECP (B) in nasal lavage samples from patients in the SNAR, SAR and PNAR groups before and after nasal provocation with birch or timothy pollen allergens.

symptom and medication score during pollen season did not increase in the SNAR group; they rather had high scores before the pollen season and their score gradually decreased.

Patients in the SNAR group had significantly lower total IgE levels than the patients in the SAR group. It does not exclude an IgE-mediated mechanism, however, since total IgE is a rather unspecific marker for allergic symptoms [14]. Allergen-specific IgE antibodies are more sensitive and specific markers for seasonal pollen allergy [14]. By using the Phadiatop test, circulating serum IgE antibodies specific for common inhalant allergens can be detected [7]. In our study, one of the patients with the diagnosis of SNAR was positive in Phadiatop but we could not find any IgE antibodies to the pollen allergens tested. This may indicate an allergy to perennial allergens rather than to seasonal pollen allergens.

The syndrome SNAR has earlier been described in a study where patient data were retrospectively analyzed [2]. That study indicated that SNAR patients compared to birch pollen allergics had symptoms earlier in springtime than pollen allergics and more often got symptoms from flowers and strong smells. The age of the SNAR patients was higher than the age of the birch pollen allergic patients and there were more women in the SNAR group than in the group of pollen allergics. It was concluded that SNAR seemed to have more in common with PNAR than with seasonal allergic rhinitis.

Our SNAR patients have, according to their histories, seasonal symptoms. It is probable that in the present study the registration of symptoms started too late to catch the start of their symptom season.

Our present study cannot explain the cause of the symptoms of SNAR. One possible explanation could be unspecifically acting substances in pollen grains eliciting symptoms. Another explanation could be a pollen allergy, not discovered in routine SPT. The finding of one Phadiatop-positive patient in the SNAR group indicates that an underlying respiratory allergy could be the reason for the symptoms for that particular patient diagnosed only by case history and SPT. For diagnosis of a clinically relevant allergy, a combination of the information obtained from history, skin tests and specific IgE tests is the most sensitive indirect method [16]. For a definite diagnosis, a placebo-controlled challenge in the relevant organ should be performed. Even nasal provocations, however, have limitations, and the methods we used for recording immediate as well as late reactions cannot definitely differ between true IgE-responses and unspecific reactions. Local measurement of specific IgE in nasal reactions were not performed in this study, but should be used in future studies on SNAR.

A localized nasal allergy, called 'entopy', has been suggested as a possible explanation behind PNAR (idiopathic rhinitis) [17] and increased number of IgE+ cells, mast cells and eosinophils have been observed in nasal mucosa of these patients [18].

The positive NPT with pollen in some of the SNAR patients, as well as some late reactions after NPT, could indicate a 'localized pollen allergy' in these patients. Also the fact that two patients who earlier had been regarded as SNAR patients were found to be SPT positive when tested at the start of the study (they also had specific IgE antibodies to pollen allergens), could indicate a connection between SNAR and birch or grass pollen allergy.

Another possibility could be chemical pollutions bounded to pollen grains inducing symptoms [19]. The symptom score curves, however, do not support a reaction related to tree or grass pollen, since the patients in the SNAR group had symptoms already before the pollen season and their symptoms gradually decreased during the registration period. Their symptoms did not increase during a period with high pollen counts. Furthermore, in only the SAR group did nasal provocation with pollen allergens induce mucosal oedema and a significant increase in the nasal lavage levels of tryptase, a sign of mast cell degranulation. We also observed a trend towards increased ECP levels in the nasal lavage samples of the SAR patients. The increase in ECP might have been more apparent if the nasal lavage fluid sampling after NPT had been performed later, i.e. during the late phase response as shown by others [20].

An allergy with sensitization against allergens not included in the present study is of course possible, although pollen recordings do not indicate that other pollens occur in early springtime [21], nor do allergenic moulds occur during this period in Sweden. Furthermore, clinically significant allergy against other tree pollen is very seldom found in Sweden [22]. An allergy not possible to demonstrate with present diagnostic methods is another possibility. In routine diagnostic work using SPT, late skin test reactions are usually not recorded. Two of our SNAR-patients reported positive late skin reaction. It is not clear whether such reactions have clinical significance [23].

We cannot either exclude that the symptoms of the SNAR patients are caused by unknown substances in the outdoor or indoor air in springtime. MPO is a marker for neutrophilic activity even if also monocytes can synthesize lower amounts of MPO. Increased MPO concentrations in nasal lavage have been shown to be associated with exposure to non-specific irritants [5] or upper respiratory tract infections [6]. We did not observe any elevated MPO levels in the SNAR group, nor in the SAR and PNAR groups. So involvement of neutrophils in the manifestation of SNAR could not be demonstrated.

To conclude, patients with seasonal rhinitis occur with negative results of allergy testings. The present study indicates that these patients have a disease different from seasonal allergic rhinitis (SAR) and persistent non-allergic rhinitis (PNAR) regarding immunological mechanism and symptom period. We call this syndrome Seasonal Non-Allergic Rhinitis (SNAR). Still, we cannot exclude that some of the SNAR patients might have a pollen allergy, not disclosed by standard skin prick tests. For most of the SNAR patients, however, the reason for their symptoms is unknown. It may be an unspecific hypersensitivity against substances occurring in outdoor or indoor air in springtime.

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REFERENCES

1. Johansson SG, Hourihane JO, Bousquet J, et al. (2001) A revised nomenclature for allergy. An EAACI position statement from the EAACI nomenclature task force. Allergy 56: 813-824.
2. Eriksson NE (1991) Seasonal non-allergic rhinitis. A disease caused by pollution? Grana 30: 115-118.
3. Montefort S, Gratziou C, Goulding D, et al. (1994) Bronchial biopsy evidence for leukocyte infiltration and upregulation of leukocyte-endothelial cell adhesion molecules 6 hours after local allergen challenge of sensitized asthmatic airways. J Clin Invest 93: 1411-1421.
4. Venge P, Byström J, Carlson M, et al. (1999) Eosinophil cationic protein (ECP): molecular and biological properties and the use of ECP as a marker of eosinophil activation in disease. Clin Exp Allergy 29: 1172-1186.
5. Ahman M, Holmstrom M, Kolmodin-Hedman B, Thelin A (2001) Nasal symptoms and pathophysiology in farmers. Int Arch Occup Environ Health 74: 279-284.
6. Bachert C, van Kempen MJ, Hopken K, Holtappels G, Wagenmann M (2001) Elevated levels of myeloperoxidase, pro-inflammatory cytokines and chemokines in naturally acquired upper respiratory tract infections. Eur Arch Otorhinolaryngol 258: 406-412.
7. Eriksson NE, Ryden B, Jonsson P (1989) Hypersensitivity to larvae of chironomids (non-biting midges). Cross-sensitization with crustaceans. Allergy 44: 305-313.
8. Eriksson NE, Holmen A (1996) Skin prick tests with standardized extracts of inhalant allergens in 7099 adult patients with asthma or rhinitis: cross-sensitizations and relationships to age, sex, month of birth and year of testing. J Investig Allergol Clin Immunol 6: 36-46.
9. Dreborg S (1989) The skin prick test in the diagnosis of atopic allergy. J Am Acad Dermatol 21: 820-821.
10. Aas K, Belin L (1973) Standardization of diagnostic work in allergy. Int Arch Allergy Appl Immunol 45: 57-60.
11. Lenders H, Pirsig W (1990) Diagnostic value of acoustic rhinometry: patients with allergic and vasomotor rhinitis compared with normal controls. Rhinology 28: 5-16.
12. Scadding GK, Darby YC, Austin CE (1994) Acoustic rhinometry compared with anterior rhinomanometry in the assessment of the response to nasal allergen challenge. Clin Otolaryngol 19: 451-454.
13. Käpylä M, Penttinen A (1981) An evaluation of the microscopical counting method of the tapes in Hirst-Burkard pollen and spore trap. Grana 20: 131-141.
14. Droste JH, Kerhof M, de Monchy JG, Schouten JP, Rijcken B (1996) Association of skin test reactivity, specific IgE, total IgE, and eosinophils with nasal symptoms in a community-based population study. The Dutch ECRHS Group. J Allergy Clin Immunol 97: 922-932.
15. Eriksson NE (1990) Allergy screening with Phadiatop and CAP Phadiatop in combination with a questionnaire in adults with asthma and rhinitis. Allergy 45: 285-292
16. Eriksson NE (1977) Diagnosis of reaginic allergy with house dust, animal dander and pollen allergens in adult patients. IV. An evaluation of the clinical value of skin test, radioallergosorbent test, case history and combinations of these methods. Int Arch Allergy Appl Immunol 53: 450-458.
17. Powe DG, Jagger C, Kleinjan A, Carney AS, Jenkins D, Jones NS (2003) 'Entopy': localized mucosal allergic disease in the absence of systemic responses for atopy. Clin Exp Allergy 33: 1374-1379.
18. Powe DG, Huskisson RS, Carney AS, Jenkins D, Jones NS (2001) Evidence for an inflammatory pathophysiology in idiopathic rhinitis. Clin Exp Allergy 31: 864-872.
19. Traidl-Hoffmann C, Kasche A, Menzel A, et al. (2003) Impact of pollen on human health: more than allergen carriers? Int Arch Allergy Immunol 131: 1-13.
20. van Toorenenbergen A, van Wijk R, Vermeulen A, Zijlstra F (1992) Increase of albumin, eosinophil cationic protein, histamine, leukotrienes and mast cell tryptase in nasal lavage fluid after challange with inhalant allergen extract. Agents Actions (Special Conference Issue): C421-C424.
21. Strandhede SO, Wihl JA, Eriksson NE (1984) Tree pollen allergy. I. Features of plant geography and pollen counts. Allergy 39: 602-609.
22. Eriksson NE, Wihl JA, Arrendal H, Strandhede SO (1984) Tree pollen allergy. II. Sensitization to various tree pollen allergens in Sweden. A multi-centre study. Allergy 39: 610-617.
23. Lierl MB (2000) Isolated late cutaneous reactions to allergen skin testing in children. Ann Allergy Asthma Immunol 84: 294-298.

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