REVIEW ARTICLE

Rhinitis in children: Common clinical presentations and differential diagnoses

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Abstract

Rhinitis is a common presentation in childhood. Acute virally induced rhinitis is generally self-limiting and usually does not require medical attention. Whilst allergic rhinitis is the focus of the paediatric allergist, the presentation of other diseases or comorbidities that can complicate or mimic allergic rhinitis needs to be considered. Effects on the child's quality of life also need to be addressed. Rhinitis can be associated with asthma and other significant comorbidities: importantly, non-allergic rhinitis can sometimes be a consequence of systemic immune impairment. The diagnosis of rhinitis is based on clinical findings with directed investigations. Nasal nitric oxide measurement is an emerging diagnostic tool and helpful particularly in relation to evaluating the differential diagnosis in more difficult rhinitis. Successfully identifying the cause of rhinitis in childhood and associated comorbidities can ensure that the patient is successfully treated as described in the recently published EAACI Pediatric Rhinitis Position Paper.

Rhinitis is very common in childhood, and it can affect up to 45% of children in some regions of the world (1). It is an umbrella term for a group of conditions with the common symptoms of nasal congestion, rhinorrhoea, sneezing and itching. The presence of two or more of these symptoms, for more than 1 h on two or more days, is the only requirement for diagnosis (2). When acute, rhinitis is self-limiting and generally does not require medical attention. However, when chronic it can impact significantly on the child's quality of life and can disrupt family dynamics (3–4). A correct diagnosis is essential to deliver appropriate treatment and ensure optimal treatment outcomes.

The differential diagnosis of rhinitis is wide; however, rhinitis in children is usually caused by infection or allergy. Infectious and allergic rhinitis can coexist thus confounding the clinical presentation and impacting on disease severity in a synergistic manner, as evidenced in asthma (5). Furthermore, because of the strategic anatomical and functional connection of the nose with the eye, middle ear, adenoid–tonsillar (Waldeyer's ring) tissue and the lower airway, the clinical presentation of rhinitis in childhood can include features of conjunctivitis, otitis media, adenoidal hypertrophy and bronchial asthma. Children with an underlying immune deficiency may have other infections or failure to thrive. A detailed clinical history and comprehensive examination are therefore required. The response to previous therapy can provide additional clinical insight. Basic allergy tests are valuable in the assessment of a child presenting with rhinitis, and other investigations are sometimes required to confirm or exclude other potential underlying causes such as immunodeficiency or cystic fibrosis.

When referring to allergic rhinitis, it is important to remember that nasal disease is only one aspect of the atopic spectrum. Allergic rhinitis can be associated not only with conjunctivitis and asthma but also with eczema and food allergy. A peculiar form of comorbid food allergy, highly prevalent in patients with pollen-induced allergic rhinitis, is the so called 'pollen food syndrome' (PFS) otherwise termed 'oral allergy syndrome' (OAS). Here, children will experience local oral symptoms of pruritus and swelling with fruits (e.g. pear, peach) that cross-react with pollens.

Anatomical factors that can give rise to nasal symptoms also need to be considered. Persistent unilateral symptoms of rhinitis can be a warning sign of significant nasal septal deviation, foreign body retention, antrochoanal nasal polyp

and congenital malformations such as unilateral choanal atresia. Isolated persistent rhinorrhoea can represent a cerebro-spinal fluid (CSF) leak.

We present four patients who illustrate some of the diagnostic processes and frequently associated comorbidities of rhinitis. This article expands on the approach recently described in the recent EAACI Pediatric Rhinitis Position Paper (6).

Case 1: A case of classic severe allergic rhinitis with associated 'fruit aversion'

A 13-yr-old boy presented to the paediatric rhinology clinic with a long-standing history of allergic rhinoconjunctivitis. His symptoms started in March each year with a peak of severity in June. During this period, he experienced bilateral nasal obstruction with associated clear nasal secretion, sneezing attacks, nasal and ocular itch and occasionally a wheezy chest. He was a keen athlete involved in cross -country running but, unfortunately, at the peak of the hay-fever season he could not practise any outdoor sport because of severe ocular symptoms and wheezing. On a few occasions, he had experienced itchy mouth and throat, not associated with other symptoms, whilst eating peanut and hazelnut, although he was not avoiding nuts. His mother described him as a 'fussy eater' and she was worried about his diet as he did not like 'healthy food' such as fresh fruits and vegetables. When specifically asked about the symptoms experienced after eating fruit he reported mouth itching and discomfort when eating apple and several other fruits. He was, however, able to consume fruit juice and cooked vegetables or fruits in dessert. He had a past history of eczema. His GP had prescribed standard anti-allergy therapy (antihistamines, intranasal corticosteroids and cromoglycate eye drops), but this treatment was of minimal benefit. He was very concerned because these symptoms were impacting on his school performance and self-esteem.

On examination, he had the typical transverse nasal crease (a horizontal line near the lower end of the nose), nasal blockage with a pale oedematous nasal mucosa and hyperaemic conjunctivae. His chest was clear on auscultation. The skin prick test (SPT) to a standard panel of environmental allergens was positive for grass pollen (20 mm) and birch pollen (10 mm) only. In addition, he had a positive test to hazelnut (5 mm).

The clinical history reported is typical of severe allergic rhino-conjunctivitis secondary to pollen allergy. The age, the presence of symptoms of itching and sneezing, suggestive of histamine release and neurogenic inflammation, and the presence of conjunctivitis are all factors pointing to a diagnosis of pollen allergy.

The prevalence of allergic rhinitis (AR) steadily increases with the child age, from early childhood to adolescence, particularly when both parents are atopic (7, 8). Moreover, amongst children with the ARIA 'severe persistent'(11) form of the disease between 50% and 70% have severe symptoms significantly impacting on their daily life as shown by the analysis of the German 'Multicenter Allergy Study' (MAS) birth cohort performed by Keil and co-workers (Fig. 1).

Allergic conjunctivitis is the commonest comorbidity of allergic rhinitis (9), particularly when the triggering allergen is pollen. The other relevant comorbidities in our case were seasonal asthma and PFS, the diagnosis of which could have been missed. Grass pollen sublingual immunotherapy was undertaken and when added to the rest of his treatment, led to excellent clinical benefit for his rhinoconjunctivits. There was no impact on his PFS, and he needed to continue avoiding 'difficult' fresh foods. This case allows us to review the association of allergic rhinitis with two important comorbidities, asthma and PFS.

Association between rhinitis and asthma in children

Bronchial asthma and allergic rhinitis often coexist, and rhinitis is a major risk factor for the development of asthma. In recent years, the link between these two pathologies, as manifestation of the same inflammatory process in the 'united airways' hypothesis, has been extensively studied and supported by the findings of several adult and paediatric studies.

In a questionnaire-based survey involving 404 children with asthma aged 3–18 yr, allergic rhinitis was associated with asthma in 58.7% of the cases (10). In the German 'Multicentre Allergy Study' (MAS), birth cohort allergic rhinitis up to the age of 5 was found to be a predictor for the development of wheezing between the ages of 5 and 13 yr (adjusted relative risk 3.82, $p < 0.001$). In this group of children, 41.5% of all new cases of wheezing occurred amongst children with preceding allergic rhinitis. This suggests that allergic rhinitis in preschool children is a significant predictive factor for subsequent

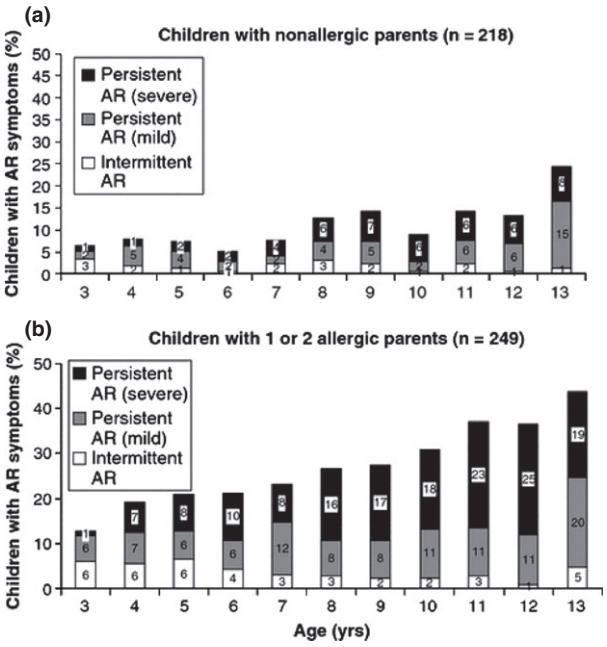

Figure 1 (a) Children with non-allergic parents (n = 218). (b) Children with one or two allergic parents (n = 249). Reproduced from Keil et al. (7).

wheezing (11). A subsequent analysis of the same birth cohort using the ARIA classification of allergic rhinitis showed a higher prevalence of wheezing episodes per annum amongst the children with 'severe persistent' AR (7).

In the Isle of Wight unselected birth Cohort rhinitis at the age of 10 was one of the risk factors for adolescent-onset asthma (OR 2.35; p = 0.027) (12).

In a study involving 227 children with rhinitis between the ages of 6 and 15 yr, bronchial hyper-responsiveness (BHR) was two times more frequent in children with allergic rhinitis than in those with non-allergic rhinitis (55.7% vs. 25.5%, respectively) (13). Similar prevalence of asthma in children with allergic rhinitis and non-allergic rhinitis was observed in children of the Copenhagen prospective study on asthma in childhood birth cohort, suggesting a link between upper and lower airways beyond simple allergy. The prevalence of asthma in children with allergic rhinitis was 21% vs. 5% (p = 0.002) when compared to asymptomatic controls and similarly it was 20% vs. 5% (p = 0.001) in the group of children with non-allergic rhinitis. However, although the prevalence of BHR (23% vs. 9%, p = 0.008) and fractional exhaled nitric oxide (FeNO) [15.9 parts per billion (ppb) vs. 6.6 ppb; p < 0.001) were significantly higher in the allergic rhinitis group, they were not raised in children with non-allergic rhinitis, suggesting that there is a different endotypes of asthma in children with non-allergic rhinitis (14).

Allergic rhinitis combined with asthma severity is a major risk factor for emergency care admission in children (5–18 yr of age) with established bronchial asthma (15). Allergic rhinitis has a major impact on asthma control as suggested by a cross-sectional study involving 203 children with asthma aged 5–18 yr. In this study, the asthma control questionnaire (ACQ) scores were significantly worse in children with allergic rhinitis than in those without (p = 0.012). An ACQ score ≥1.0 (incomplete asthma control) was significantly more likely in children with allergic rhinitis than in those without (OR 2.74, p = 0.008). Interestingly after adjustment for nasal corticosteroid therapy, allergic rhinitis was no longer associated with incomplete asthma control (OR 0.72, p = 0.150), suggesting that recognition and treatment of allergic rhinitis with nasal corticosteroids may improve asthma control (16).

Pollen Food Syndrome: role of cross-reactivity at molecular level

PFS is a clinical syndrome characterized by symptoms manifesting after ingestion of raw fruits, nuts, vegetables and spices (17). It has been recently reported in 31% of Swedish 8-yr-old children with rhinitis who were sensitized to birch pollen (10), and in 29% of northern Italian 8-yr-old children allergic to grass pollen, of whom the majority (2/3) were polysensitized (18). The commonest symptoms are oral pruritus, lip, tongue and throat oedema, pharyngitis and laryngitis; more severe reactions have been reported but only in a minority of cases. The suggested mechanism is IgE cross-reactivity between the implicated plant-derived food and the primary sensitizing pollen(s). The prevalence and pattern of triggering food can vary widely in relation to the specific regional pattern of sensitization. Birch, grass and mugwort pollen-related food are the most frequently offending agents in central and northern Europe. Grass, ragweed, pellitory and olive tree pollen-related food are implicated in the Mediterranean area (Table 1) (19–21). The allergens responsible for this peculiar form of food allergy are ubiquitous plant antigens belonging mainly to two large protein families: the Bet v1 family (birch pollen major allergens are highly cross-reactive with several plant food allergens) and the profilin family (which includes the Bet v2 minor birch pollen allergen also highly cross-reactive with other pollen and plant-derived food) (22).

The ability to measure specific IgE against the different molecular components of pollens and pollen-related food could be a useful tool in the differential diagnosis and risk assessment of patients with rhinitis reporting symptoms on exposure to plant-derived food (23). In the specific case of our patient, for example, the clinical implications of the sensitization to hazelnut could have been better understood by measuring specific IgE to the hazelnut molecular components (component resolved diagnostic or CRD). Moreover CRD could help in multisensitized patients, as in our case, to discriminate the truly multisensitized from the cross-reactive ones; positive specific IgE to Phl p1 and Phl p5 are for example markers of genuine sensitization to grass pollen (24), positive specific IgE to Bet v1 indicate primary sensitization to birch or homologous tree pollen; whilst positive specific IgE to Phl p7, Phl12 and Bet v2 are markers of cross-reactivity as they are highly cross-reactive allergens.

In the absence of such tests, the story of inability to eat raw food whilst tolerating it once cooked suggests that a heat – labile profilin allergen is responsible – and that the occurrence of severe symptoms is unlikely meaning there is no need for an adrenaline auto-injector.

The ability to characterize children sensitization profile at a molecular level could also potentially become a useful tool for monitoring progression towards the development of clinically evident AR in at risk subjects. In the MAS birth cohort study, the investigators were able to detect Phl p1-specific IgE, several

Table 1 Common cross-reactivity between pollens and plant-derived foods

Pollen	Cross-reacting foods
Birch	Apple, pear, cherry, peach, nectarine, apricot, tomato, kiwi, carrots, potato, parsnip, green pepper, fresh spices, celery, peanuts, hazelnut, walnut, almond, lentil, beans, peas and soya bean
Grass	Melon, water melon, oranges, tomato, potato, kiwi, peanut and carrot
Mugwort	Celery, carrot, spices (parsley, caraway seeds, fennel seed, coriander seeds, aniseed, paprika, garlic and onion) pepper, mango, leek, mustard, broccoli, cabbage, cauliflower, chamomile and kiwi
Ragweed	Melon, zucchini, cucumber and banana
Pellitory	Pistachio and Swiss chard
Olive Pollen	Peach, pear, melon and kiwi

years in advance, in more than 75% of children that went on in developing classic AR in pre/early adolescence (25). Moreover in this specific population, the serum level of Phl p1-specific IgE steadily rose over the years in parallel with the number of sensitizations towards a wide array of other grass pollen molecular components which, however, increased with a slower trend when compared to Phl p1 (Figs 2 and 3). These findings are of significant relevance as one could speculate that earlier intervention with molecular targeted specific immunotherapy can lead to a much better response to allergen specific immunotherapy modifying the disease progression and its burden.

Case 2: A common case of allergic rhinitis that was missed

A 6-yr-old girl with snoring, cough, constant mouth breathing and frequent episodes of upper respiratory tract infections was referred by her general practitioner to an Ear, Nose and Throat clinic to evaluate whether she required an adenoidectomy. Instead of the requested surgical review, she had an appointment allocated in the paediatric rhinology and allergy clinic.

The history reported by her parents was of 2 yr of constant nasal blockage associated with frequent 'colds' which had worsened over time. As a result, the girl was snoring most nights but did not have daytime somnolence or history of sleep apnoea.

She had often complained of a sensation of ear blockage but had no history of recurrent otitis and neither her parents nor her school teacher had concerns about her hearing. Her parents' additional worry was a chronic dry cough occasionally associated with wheeze. When specifically asked, they reported that their daughter was occasionally troubled by bouts of sneezing attacks that could manifest at any time of year but were more frequent in spring. She had suffered with very mild facial eczema in infancy, but this had not required pharmacotherapy.

There was significant family history of atopy: her dad had asthma and mum had hay fever. She lived in a carpeted flat with her parents and two siblings with whom she shared the bedroom and bunk beds.

On examination, she was a chronic mouth breather with pronounced allergic shiners (darkened skin area beneath the eye lids), a very blocked nose with large inferior turbinates, grade II tonsils [tonsils occupying 26–50% of the oropharyngeal width (26)] and few expiratory wheezes on auscultation. Flexible nasendoscopy showed an enlarged adenoidal pad in the nasopharynx, but this was not obstructing the post-nasal space.

Skin prick tests were positive for house dust mite (8 mm) and birch pollen (4 mm). Her FEV_1 was 62% of her predicted value and the fractional exhaled nitric oxide (FeNO) was 25 parts per billion (normal range in our laboratory <20 ppb). A diagnosis of allergic rhinitis with associated asthma was made, and she was treated with a very short course of oral corticosteroids with standard anti-allergy therapy inclusive of advice on HDM reduction measures, antihistamine, a non-systemically bio-available nasal corticosteroid, antileukotriene receptor antagonist and a low-dose inhaled corticosteroid. The latter was withdrawn 2 months later; her lower respiratory symptoms did not reappear, and further tests for asthma (lung function test and FeNO) were normal.

Adenoidal hypertrophy in children with nasal allergy – is surgery always indicated?

In this case, the parental concern and main feature on presentation was nasal blockage. Furthermore, nasal allergy was not considered as a possible differential diagnosis by the child's general practitioner, whose main concern was to rule out adenoidal hypertrophy.

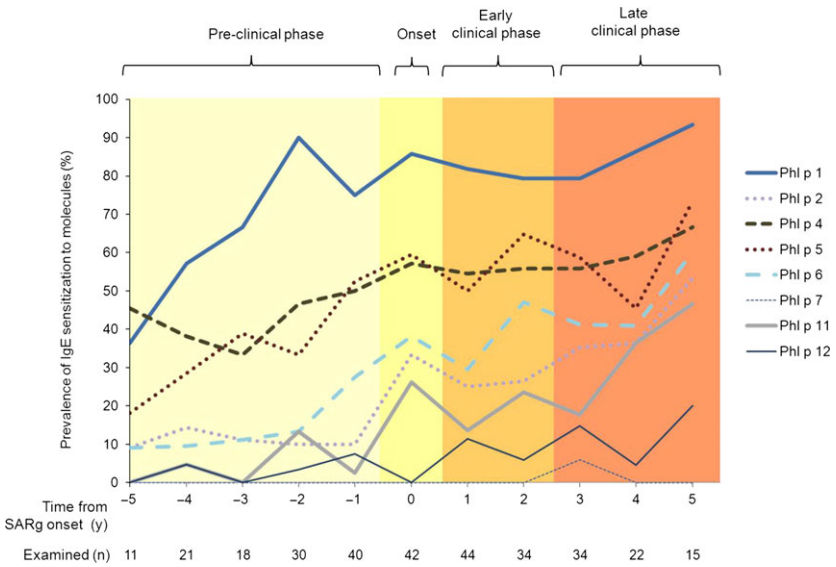

Figure 2 IgE to P pratense allergenic molecules from the onset of grass-related seasonal allergic rhinitis. Lines show the prevalence of IgE sensitization (ISAC class ≥1) to the 8 *P. pratense* allergenic molecules in children whose sera were available at each time point. The number of children examined at each time point is indicated under the *x*-axis. Clinical stages of seasonal allergic rhinitis are also indicated. Reproduced from Hatzler et al (25).

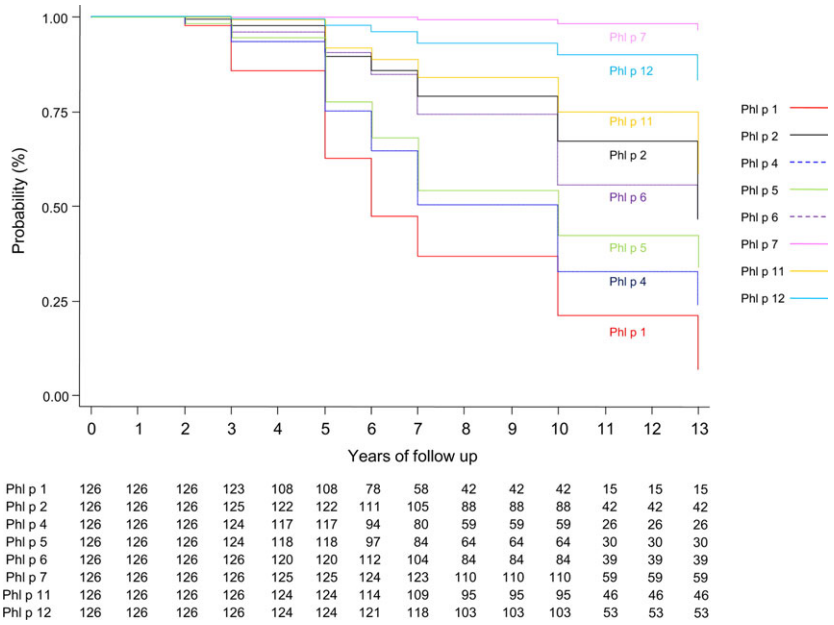

Figure 3 Probability of remaining free of sensitization to individual allergenic molecules of *P. pratense*. Kaplan–Meier plots of the probability of remaining free of IgE sensitization to each of eight allergenic molecules of *P. pratense* are shown. The number of the subjects at risk is shown below the *x*-axis. Reproduced from Hatzler et al (25).

Unlike pollen-induced allergic rhinitis, where seasonal symptoms secondary to histamine release (itching and sneezing) in association with conjunctivitis are easily recognized, mite-induced allergic rhinitis typically manifests predominantly with nasal blockage (27). Allergic rhinitis in children can be associated with adenoidal hypertrophy and IgE-mediated inflammation of the nasal mucosa is likely to play a role in both conditions. Medical treatment in such cases can be effective (28), unless concern about severe obstructive sleep apnoea syndrome (OSAS) is present, when surgery is required. Further studies are needed to better understand the link between allergic rhinitis and adenoidal hypertrophy.

Allergic rhinitis and asthma – does rhinitis treatment improve asthma outcome?

Asthma and rhinitis comorbidity has been already summarized in the comment to case 1. This case gives an opportunity to review the concept of minimal persistent inflammation (MPI) and its potential role in comorbid asthma. Continuous allergen exposure can lead to chronic inflammation which is also present in the absence of classic and clinically evident allergic rhinitis (29). This has been detected in patients with pollinosis but can be more relevant in patients with sensitization to perennial allergy (e.g. HDM and animal dander) because of the continuous allergen exposure. This status of chronic allergic inflammation can result in airway hyper-responsiveness with increased sensitivity to allergens, cell mediators and non-specific irritants which persist beyond the resolution of the acute allergic response. MPI is characterized by the presence of inflammatory cells (e.g. eosinophils and neutrophils) in the nasal mucosa and an increased expression of intercellular adhesion molecule 1 (ICAM-1) which is the major receptor for rhinoviruses, important triggers of asthma exacerbation in children (38). Although the specific underlying mechanisms have yet to be fully understood, it has been observed that asthma exacerbations in sensitized atopic children occur when a viral infection take place together with relevant allergen exposure suggesting a synergistic augmentation of the inflammatory pathways (5).

Good allergic rhinitis control by appropriate allergen avoidance and regular pharmacotherapy may reduce not only current symptoms of allergic rhinitis but also MPI and improve asthma control. A recently published meta-analysis of randomized controlled trials (RCTs) evaluating the efficacy of intranasal corticosteroids (INCS) in adult and children with allergic rhinitis suggests that treatment of rhinitis can improve some lower airway outcome measures. It is, however, yet unclear if intranasal corticosteroid therapy are sufficient as monotherapy for asthma, more studies are needed to address this question (31).

The possible diagnosis of rhinitis should always be considered when evaluating children with wheezing episodes and the treatment of asthma should always be reviewed in children with rhinitis, as sometimes effective upper airway therapy can reduce the need for inhaled corticosteroids.

Case 3: Does this child have allergic rhinitis?

A 3-yr-old Caucasian boy presented to our paediatric rhinology clinic with a 3-yr history of purulent nasal discharge often associated with nasal blockage. These symptoms were present throughout the year with slight improvement in the summer, when the family was regularly spending holiday time by the sea in the Mediterranean. The child was also troubled by occasional chesty cough for which he had received a few courses of antibiotic and salbutamol from his general practitioner. He had no history of red, itchy or watery eyes and no eczema. His general practitioner had requested some allergy blood tests which revealed a borderline positivity to house dust

mite (0.70 kU/l, normal range <0.35 kU/l). The child was given an antihistamine but this did not lead to any improvement. They were therefore referred to our clinic.

The child was born at term and had a birth weight on the 91st centile. He was breastfed for 2 wk then bottle fed. He fed well but had abdominal colic and recurrent vomiting, generally initiated by coughing almost from birth. The vomiting settled within the first year of life. He had suffered several episodes of acute otitis media treated with antibiotics and underwent adenoidectomy and grommet insertion at the age of 15 months. The ventilation tubes were reinserted once more a year later, but chronic ear discharge remained a problem. He had a positive family history of atopy.

On clinical examination, he had mucopurulent nasal discharge from both nostrils and in the post-nasal space, his eardrums were dull and no grommets were visualized. On auscultation, he had a few transmitted noises from the upper airway but there was no wheeze. There were no other abnormal findings on examination and he was growing on 75th centile both for weight and height.

Despite the mildly positive specific IgE to HDM (found in one-third of the population and not always clinically relevant), the clinical history is not typical of classical allergic rhinitis but it is suggestive of chronic infection. The presence of largely unremitting symptoms since the very first few weeks of life should raise the suspect of a potential primary immunodeficiency. Other investigations were therefore performed with full blood count, serum immunoglobulin levels, mannose binding lectin all within the normal range for his age. Nasal nitric oxide (nNO) measurements were around 50 parts per billion (ppb) (normal range 450–900 ppb) on three consecutive occasions, despite therapy with antibiotics and saline nasal douches.

Electron microscopy on a sample of cilia obtained with nasal brushing revealed the absence of both pairs of dynein arms consistent with a diagnosis of Primary Ciliary Dyskinesia (PCD).

Nitric oxide measurement relevance in differential diagnosis

Nitric oxide (NO) is a gas naturally released in the human respiratory tract where it acts as a local host defence mechanism. The measurement of FeNO from the lower airway is standardized, and in recent years, it has become a non-invasive tool in monitoring asthma control in view of its ability to increase with airway inflammation, particularly in eosinophilic asthma, and decrease with anti-inflammatory therapy (32). FeNO has, however, been found to be elevated in atopic individuals without subjective or objective evidence of airway hyper-reactivity (33).

Most NO comes from the nasal cavities and paranasal sinuses where it is inducible (iNO) in response to inflammatory cytokines, endotoxins or oxidant substances. An increased expression of iNOS (inducible Nitric Oxide Synthase) has been observed in the nasal epithelium of individuals with allergic rhinitis. Nasal NO (nNO) levels are related to inflammation in the upper airway where this gas has an important regulatory role in respiratory physiology and it forms one of the first lines of defence against micro-organisms with its ability to up-regulate ciliary motility (34). Measurement of nNO is usually low in patients with cystic fibrosis and conditions with obstruction of the ostiomeatal complex such as rhinosinusitis and nasal polyps; it is almost always very low (1/10 of normal values) in patients with PCD in whom it has a diagnostic value. nNO measurement has been suggested as a screening test to identify probable PCD cases (34).

Multiple factors contribute to variations in nNO levels and therefore obtaining reliable measurement can be sometimes challenging in young children. Scadding and Scadding have published guidance for the clinical interpretation of nasal and exhaled NO levels (Table 2) (34).

PCD is an autosomal recessive genetic disease and has a heterogeneous clinical presentation. It is caused by cilia ultrastructure defects which lead to ciliary dysfunction and decreased or total absence of ciliary motility. Due to the important role of mucociliary function in the upper airways host defence, patients with this condition are often troubled by chronic rhinosinusitis, otitis media with effusion and bronchiectasis. It can be associated with situs inversus (not present in our patient) and abnormal sperm motility with possible impact on fertility. Early diagnosis of PCD will allow the delivery of the appropriate therapy, especially physiotherapy to aid lower airway clearance, follow-up and family counselling.

Ventilation tubes are contra-indicated in PCD as chronic otorrhoea occurs. If hearing is significantly impaired in childhood hearing aids are the management of choice. Hearing problems usually resolve with growth, elevation and elongation of the eustachian tubes.

Treatment of rhinitis associated with PCD includes regular saline nasal douches plus antibiotic for acute exacerbations. Chest physiotherapy is necessary to prevent or treat bronchiectasis and the earlier this is started the better the prognosis.

Case 4: A child with chronic rhinosinusitis of unclear aetiology

A 14-yr-old boy was referred to the paediatric allergy clinic to investigate his chronic rhinitis. He had a history of persistent chronic nasal congestion associated with the production of large amount of mucus which was often mucopurulent. He had no history of nasal itch, sneezing or conjunctivitis. The symptom complex suggests rhinosinusitis (35) rather than rhinitis. He had never suffered with eczema, and there was no family history of allergies.

As a young child, he had several episodes of upper respiratory tract infections, otitis media and tonsillitis but no

Table 2 Guide to clinical interpretation of nasal NO in children. Modified from Scadding and Scadding (34)

Nasal NO level	Clinical relevance
<100 ppb (very low)	Consider PCD or CF
<450 ppb (low)	May reflect obstruction at sinus ostium
450–900 ppb (normal)	Does not exclude nasal disease
>900 ppb (raised)	Consistent with inflammation

history of chest infections. He had a complex past medical history, he was born prematurely at 28 wk and required chronic respiratory support for bronchopulmonary dysplasia but eventually he had made a good recovery. He reported no gastrointestinal problems. On examination, he had a congested nasal mucosa with abundant mucopurulent nasal secretions filling the nasal cavity, these were also very evident in the post-nasal space.

The child underwent routine skin prick testing to the most common environmental allergens which was negative. As a result of the clinical history and the abnormal findings on examination, an immunological work up was performed. He was found to have low IgA of 0.2 g/l (normal range for age 0.61–3.48), normal IgM of 0.3 g/l (0.23–2.59) and low IgG of 3.2 g/l (5.5–15.8). The IgG subclasses were also below the expected level and the specific IgG for tetanus toxoid antigen, *Haemophiluls influenzae* and Pneumococcal capsular antigen were below the optimum protective level. He had normal full blood count and lymphocytic B- and T subpopulations. These findings were consistent with hypogammaglobulinaemia.

He was referred to the local paediatric Immunology unit where he was further investigated and a diagnosis of common variable immunodeficiency (CVID) was made. He was commenced on regular antibiotic prophylaxis, in addition to non-systemically bio-available intranasal corticosteroids and regular saline nasal douches. With this treatment, his symptoms have significantly improved; however, immunoglobulin replacement therapy may be required in the future.

Rhinosinusitis is common in children; however, potential predisposing causes such as allergic and non-allergic rhinitis, ciliary dyskinesia, cystic fibrosis, gastroesophageal reflux, immunodeficiency (in particular antibody deficiency) and anatomic abnormalities should be considered when the symptoms become chronic and refractory to treatment. Recurrent upper respiratory tract infections including rhinosinusitis and recurrent middle ear infections have been reported as frequent initial manifestations of antibody defects (36). The most common antibody defects of early childhood are transient hypogammaglobulinemia of infancy (THI), IgG subclass deficiency, impaired polysaccharide immunity (otherwise termed selective or partial antibody deficiency) and selective IgA deficiency (37). CVID can affect the paediatric population and has been detected in a proportion of children (38–39). It is a complex and heterogeneous syndrome with various clinical phenotypes but is most commonly associated with recurrent respiratory tract infections resulting from insufficient production of antibodies. Autoimmunity (autoimmune cytopenias and organ-specific autoimmune diseases and an increased risk of malignancy, in particular lymphomas) is also features of CVID. CVID patients have abnormal differentiation of B-Lymphocytes into memory B-cells and then into plasma cells, with consequent defects in antibody production (40). High incidence of recurrent minor infections in immunocompetent children and the clinical overlap with atopic diseases often leads to diagnostic delay between the onset of symptoms, diagnosis and the initiation of specific therapy (antibiotic prophylaxis and/or intraveneous immunoglobulin) (38). Recurrent, unusual, severe or chronic infections should prompt the physician to consider measurements of serum immunoglobulin levels to prevent long-term morbidity and improve quality of life. In addition, as some primary immunodeficiencies can have genetic causes, a thorough family history including consanguinity has to be taken and screening of other family members may be indicated.

Conclusion and future perspective

In this article, we have described four patients that illustrate the diagnostic processes in paediatric rhinitis. Establishing the correct diagnosis can sometimes be challenging, but it is essential to deliver appropriate treatment and to establish the best long-term management for the individual. Rhinitis is common, and yet so often ignored, misdiagnosed, untreated or mistreated. A detailed clinical history is the most important tool. Comorbidities should not be ignored. Appropriate and targeted therapy can lead to excellent clinical outcomes and improvement in quality of life. An approach to managing rhinitis in childhood is presented in the recently published EAACI Pediatric Rhinitis Position Paper (6).

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