Clinical characteristics of recurrent acute rhinosinusitis in children

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Summary

Objective: **Recurrent acute rhinosinusitis (RARS) is defined as multiple episodes of acute rhinosinusitis in which the symptoms and signs of infection resolve completely between episodes. Limited data are available on the characteristics and preventive therapy of RARS. This study evaluated the clinical characteristics and predisposing factors of RARS in children as well as the preventive therapy.**

Methods: **Medical records of children with RARS diagnosed between January 2010 and December 2012 were obtained. Demographic data, presenting symptoms, predisposing factors and preventive therapy were reviewed.**

Results: **Ninety-four children with RARS were recruited. The mean age was 7.7±2.6 years, with a mean age of onset of 4.0±1.4 years. Sixty-one patients (64.9%) were boys and 56 patients (59.6%) had family history of atopy. The most common presenting symptom of RARS was purulent nasal discharge (100.0%), followed by nasal congestion (68.1%) and postnasal drainage (31.9%). The most common predisposing factor for RARS was immunoglobulin G subclass deficiency (78.7%), followed by non-allergic rhinitis (64.9%) and allergic rhinitis (35.1%). Sixty-five children (69.1%) received preventive therapy for RARS. The responses to preventive measures were: 80.0% (32/40 patients) to oral antibiotic prophylaxis, 50.0% (11/22 patients) to adenotonsillectomy, 91.7% (11/12 patients) to specific allergen immunotherapy, 27.3% (3/11 patients) to gentamicin nasal irrigation, and 66.7% (4/6 patients) to intravenous immunoglobulin.**

Conclusion: **The most common presenting symptoms of RARS in children were purulent nasal discharge, nasal congestion and postnasal drainage. Children with RARS should be evaluated for the presence of underlying conditions such as immunodeficiency and allergic disease, which led to the appropriate management for these children.** ***(Asian Pac J Allergy Immunol 2015;33:276-80)***

Keywords: *Sinusitis, child, allergic rhinitis, immune deficiency disease, immunoglobulin, antibiotic prophylaxis*

Introduction

Rhinosinusitis is defined as inflammation of the nose and paranasal sinuses. It is a common complication of viral upper respiratory infection (URI) or allergic inflammation, particularly in children.[1,2] It causes significant physical symptoms, has a negative impact on the quality of life and can substantially impair daily function.[3-5] The prevalence of rhinosinusitis in the general population varies from 2–16% depending on the season and climatic variations.[6-8] Although the prevalence of rhinosinusitis in the pediatric population is less well established, 5–13% of children with viral URI will develop acute rhinosinusitis with a subset of these subsequently progressing to recurrent or chronic rhinosinusitis.[9,10]

Recurrent acute rhinosinusitis (RARS) is defined as multiple episodes of acute rhinosinusitis where symptoms and signs of infection resolve completely between episodes.[11,12] The microbiology of RARS is similar to that of isolated episodes of acute rhinosinusitis (*Streptococcus pneumonia, Haemophilus influenzae*, and *Moraxella catarrhalis*).[13] However, bacterial resistance to antimicrobial therapy develops in RARS and contributes to the persistence of pathogens in the sinuses.[13] RARS is uncommon in healthy children; thus, underlying conditions including allergic rhinitis (AR), non-allergic rhinitis

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Submitted date: 24/11/2014
Accepted date: 8/5/2015

(NAR), immunodeficiency, ciliary dysfunction, and anatomical abnormalities of the osteomeatal complex including septal deviation, nasal polyps and concha bullosa should be investigated.[2,14,15] Currently, there are limited data on the characteristics of RARS and no treatment options have been systematically evaluated for the prevention of RARS in children. In this study, we evaluated the clinical characteristics, predisposing factors and preventive therapy of RARS in children at the Paediatric Allergy Clinic, Siriraj Hospital, Mahidol University.

Methods

Study design

A retrospective medical chart review was performed including all paediatric patients (1–15 years of age) who were diagnosed as having rhinosinusitis in the Paediatric Allergy Clinic at Siriraj Hospital, Mahidol University between January 2010 and December 2012 using the ICD-10 code. The ICD-10 codes used to search for medical records were as follows: J01.0, acute maxillary sinusitis; J01.1, acute frontal sinusitis; J01.2, acute ethmoidal sinusitis; J01.3, acute sphenoidal sinusitis; J01.4, acute pansinusitis; J01.8, other acute sinusitis; J01.9, acute sinusitis; J32.0, chronic maxillary sinusitis; J32.1, chronic frontal sinusitis; J32.2, chronic ethmoidal sinusitis; J32.3, chronic sphenoidal sinusitis; J32.4, chronic pansinusitis; J32.8, other chronic sinusitis; and J32.9, chronic sinusitis. Patients who fulfilled the diagnostic criteria of RARS by the American Academy of Pediatrics (AAP) were recruited. Acute rhinosinusitis was defined as persistent symptoms of an URI lasting more than 10 days but less than 30 days or worsening symptoms of an URI after initial improvement or severe symptoms at onset (purulent nasal discharge for 3–4 days with high fever).[1,11,12] RARS was defined as the presence of 3 episodes of acute rhinosinusitis in 6 months or 4 episodes in 12 months, each lasting less than 30 days and separated by intervals of at least 10 days during which the patient is asymptomatic.[11,12] On the other hand, patients who had symptoms of rhinosinusitis (purulent nasal discharge, postnasal drainage, nasal congestion, facial pain, cough) lasting more than 90 days and were asymptomatic for less than 10 days between episodes of rhinosinusitis were diagnosed as having chronic rhinosinusitis[2,8,11] and were excluded from this study. The study was approved by the Siriraj Institutional Review Board (094/2556(EC4)).

Demographic data, presenting symptoms, predisposing factors and preventive therapy, were determined. The responses to preventive therapy were determined by the reduction of acute rhinosinusitis episodes in the 12 months after receiving preventive therapy. The patients who had a 50 percent reduction in episode numbers of acute rhinosinusitis in the 12 months after receiving preventive therapy were classified as the responder group. All patients were evaluated for the presence of allergic sensitization and immune function (serum immunoglobulin (Ig) levels, serum IgG subclass levels and antibody responses to pneumococcal vaccination). Skin-prick test (SPT) was performed with a panel of the most prevalent local aeroallergens, including house dust mites *(Dermatophagoides pteronyssinus (Dp), Dermatophagoides farina (Df))*, American and German cockroaches, cat and dog dander, grass pollens (Bermuda, Johnson), Acacia, Careless weeds and moulds (*Alternaria* spp., *Cladosporium* spp., *Penicillium* spp., *Aspergillus* spp. and *Fusarium* spp.). Commercial allergens from ALK-Abello (Port Washington, NY, USA) were used. Histamine (10 mg/ml) and saline were used as positive and negative controls, respectively. A positive SPT was defined as a wheal diameter of 3 mm or larger, to at least 1 of these aeroallergens.

Serum IgG, IgA, IgM and IgG subclass levels were measured by nephelometry, using reagents and an automated system (Siemens). IgG subclass deficiency was defined using low level criteria (lower than 2 standard deviations [SD] of normal levels for age) or low percentage criteria (<60, 20, 5 and 1% of IgG_1, IgG_2, IgG_3 and IgG_4, respectively).[16] Antibody titres to pneumococcal capsular polysaccharide (4, 6B, 7F, 9N, 9V, 14, 18C and 23F) were measured in serum samples obtained before and 4–6 weeks after vaccination, using an enzyme-linked immunosorbent assay (ELISA). Specific antibody deficiency was defined as antibody titres <1.3 μg/ml after vaccination or a <4-fold increase after vaccination.[17,18]

Statistical analysis

Demographic data, presenting symptoms, pattern of symptoms, predisposing factors and preventive therapy were analysed using descriptive statistics (frequency, mean, median, standard deviation and range).

Table 1. Demographic and clinical data of patients with recurrent acute rhinosinusitis.

Parameters	Patients with RARS (n = 94)
Age (yrs, mean±SD)	7.7±2.6
Age of onset (yrs, mean±SD)	4.0±1.4
Sex, n (%)	
Male	61 (64.9)
Female	33 (35.1)
Family history of atopy, n (%)	56 (59.6)
Presenting symptoms, n (%)	
Purulent nasal discharge	94 (100.0)
Nasal congestion	64 (68.1)
Postnasal drainage	30 (31.9)
Fever	20 (21.3)
Epistaxis	9 (9.6)
Facial pain	4 (4.3)

RARS, recurrent acute rhinosinusitis; SD, standard deviation.

Table 2. Predisposing factors for recurrent acute rhinosinusitis.

Predisposing factors	Number of patients (%) (n = 94)
IgG subclass deficiency	74 (78.7)
Isolated IgG_3 subclass deficiency	30 (31.9)
$IgG_{2,3}$ subclass deficiency	24 (25.5)
$IgG_{1,3}$ subclass deficiency	10 (10.6)
Isolated IgG_2 subclass deficiency	6 (6.4)
Isolated IgG_1 subclass deficiency	4 (4.3)
Non-allergic rhinitis	61 (64.9)
Allergic rhinitis	33 (35.1)
Adenotonsillar hypertrophy	32 (34.0)
Asthma	24 (25.5)
Specific antibody deficiency	5 (5.3)
Nasal polyps	0 (0)

Ig, immunoglobulin.

Results

Demographic data and clinical characteristics

Ninety-four children (2.3–14.1 years of age) diagnosed with RARS were recruited. Demographic data and clinical characteristics are shown in Table 1. The mean age was 7.7±2.6 years and the mean age of onset was 4.0±1.4 years. Sixty-one patients (64.9%) were boys. Fifty-six patients (59.6%) had a family history of atopy. The most common presenting symptom of RARS was purulent nasal discharge (100.0%), followed by nasal congestion (68.1%) and postnasal drainage (31.9%). In contrast, facial pain was the least common presenting symptom in children with RARS (4.3%).

Predisposing factors

The most common predisposing factor for RARS was IgG subclass deficiency (78.7%), then NAR (64.9%) and AR (35.1%; Table 2). No patients had nasal polyps. All patients with IgG subclass deficiency had low IgG subclass percentages, although IgG subclass levels were within normal ranges for their age. The most common IgG subclass deficiency was isolated IgG_3 (31.9%), then IgG_2/IgG_3 (25.5%) and IgG_1/IgG_3 (10.6%).

Aeroallergen sensitization was detected in 35.1% of the patients. The most common aeroallergen sensitization was *Dp* (84.8%), then *Df* (78.8%), American cockroach (48.5%), German cockroach (27.3%), Bermuda grass (27.3%), cat dander (27.3%), Johnson grass (24.2%), dog dander (15.2%), Acacia (9.1%) and *Alternaria* spp. (6.1%).

Preventive therapy

All patients received antibiotics, adjunctive medications (intranasal corticosteroids, non-sedating antihistamines, decongestants and normal saline irrigation) and treatment for co-morbidities, according to standard treatments. Patients still had multiple episodes of acute rhinosinusitis after receiving these treatments. Sixty-five patients received preventive therapy for RARS (Table 3). Methods of preventive therapy included oral antibiotics (amoxicillin, azithromycin) prophylaxis (61.5%), adenotonsillectomy (33.8%), specific allergen immunotherapy (18.5%), gentamicin nasal irrigation (16.9%) and intravenous immunoglobulin (IVIG) 400–600 mg/kg every four weeks (9.2%). Forty patients with RARS received oral antibiotic prophylaxis and 32/40 patients (80.0%) responded well. Twelve patients with moderate-to-severe persistent AR received specific allergen immunotherapy and 11/12 patients (91.7%) responded. Six patients with IgG subclass deficiency who did not response to other preventive therapy received IVIG and 4/6 patients (66.7%) responded. In the 2-to-4 year follow-up, 29 patients did not receive preventive therapy for RARS and only 13 patients (13.8%) with RARS developed spontaneous remission without preventive therapy.

Table 3. Preventive therapy for recurrent acute rhinosinusitis.

Treatment	Outcome, n (%)	
	Responders	Non-responders
Oral antibiotic prophylaxis (n = 40)	32 (80.0)	8 (20.0)
Adenotonsillectomy (n = 22)	11 (50.0)	11 (50.0)
Allergen immunotherapy (n = 12)	11 (91.7)	1 (8.3)
Gentamicin nasal irrigation (n = 11)	3 (27.3)	8 (72.7)
Intravenous immunoglobulin (n = 6)	4 (66.7)	2 (33.3)

Discussion

Rhinosinusitis is a common disease in children. Most clinical research and practice guidelines have focused on acute rhinosinusitis, but not RARS or chronic rhinosinusitis. RARS is difficult to diagnose and might overlap with chronic rhinosinusitis. In this study, RARS was defined as the presence of 3 episodes of acute rhinosinusitis in 6 months or 4 episodes in 12 months, each lasting less than 30 days and separated by intervals of at least 10 days during which the patient is asymptomatic.[11,12] The most common presenting symptoms of RARS in children were purulent nasal discharge, nasal congestion and postnasal drainage. These presenting symptoms are similar to previous studies of acute and chronic rhinosinusitis in children, which reported that common presenting symptoms of acute rhinosinusitis were purulent rhinorrhea, cough, nasal congestion and postnasal drainage.[19,20] In addition, Poachanukoon et al. compared the clinical characteristics of acute rhinosinusitis and chronic rhinosinusitis in children, and found acute rhinosinusitis had common presenting symptoms similar to chronic rhinosinusitis.[21]

IgG subclass deficiency was the most common predisposing factor for RARS in our study, mainly isolated IgG_3 subclass deficiency. This finding is consistent with results from previous studies,[16,22,23] indicating that IgG_3 subclass deficiency was the most common IgG subclass deficiency in children and was associated with recurrent respiratory infections, especially recurrent rhinosinusitis. In contrast, some studies reported that IgG_2 subclass deficiency was the most prevalent IgG subclass deficiency in paediatric patients and associated with recurrent sinopulmonary infections caused by encapsulated organisms.[24,25] The clinical relevance of isolated IgG_3 subclass deficiency remains controversial. IgG_3 plays an important role in host defence against *Moraxella catarrhalis* and the M component of *Streptococcus pyogenes*, which are pathogens responsible for upper and lower respiratory infections.[26] Thus, isolated IgG_3 subclass deficiency patients would be more predisposed to recurrent respiratory infections. In addition, NAR, AR, adenotonsillar hypertrophy and asthma were common predisposing factors for RARS in our study. These findings are consistent with previous studies by Choi et al.[14] and Vichyanond et al.,[27] which reported that AR, atopy and asthma were predisposing factors for chronic and recurrent rhinosinusitis. In contrast to our study, immunodeficiency was not reported and only 2.4% of cases underwent immunological evaluation in the study by Choi et al.[14]

Forty patients with RARS in our study received oral antibiotics (amoxicillin, azithromycin) as prophylaxis to prevent RARS and 80% of patients responded to this preventive therapy. However, antibiotic prophylaxis to prevent RARS has not been systematically evaluated.[11,28] Therefore, a prospective randomized controlled trial to determine the efficacy of preventive therapy is required. Specific allergen immunotherapy was effective in preventing RARS in children with moderate-to-severe persistent AR. Although adenoidectomy to remove the adenoid pad, a bacterial reservoir for the sinuses, has been proposed as first-line surgical management and studies support the efficacy of adenoidectomy in children with chronic/recurrent rhinosinusitis,[29,30] only 50% of patients with adenotonsillectomy in our study responded to this preventive therapy.

In conclusion, the most common presenting symptoms of RARS in children were purulent nasal discharge, nasal congestion and postnasal drainage. Children with RARS should be evaluated for the presence of underlying conditions such as immunodeficiency and allergic disease, to determine the appropriate disease management. However, a prospective randomized controlled trial is needed to determine the efficacy of preventive therapies for RARS.

Acknowledgements

This study was supported by a Siriraj Grant for Research Development from the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

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