Case Report

Chronic Rhinosinusitis and Recurrent Nasal Polyps in Two Children with IgG Subclass Deficiency and Review of the Literature

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Chronic rhinosinusitis (CRS) is a chronic inflammatory disorder of mucosa of the nose and the paranasal sinuses. Two major forms of CRS can be differentiated; CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). The pathophysiology and etiology of nasal polyps (NPs) are partly understood. IgG subclass deficiency was shown to be associated with an increased susceptibility to infections. However, the association between NPs and IgG subclass deficiency has never been reported.

Objectives: *To report two cases of recalcitrant CRS and recurrent NPs with IgG subclass deficiency.*

Case report: *Two children (6 and 8 year-old boys) were referred to the Pediatric Allergy/Immunology Clinic, Siriraj Hospital due to a prolonged history of CRS and recurrent NPs. Both of them were treated with aggressive medical (topical and systemic corticosteroids, antibiotics, leukotriene antagonist, nasal irrigation) as well as surgical therapy, without significant improvement. Immunologic investigation in both patients showed that IgG, IgA, and IgM level were normal. IgG subclasses level in patient No. 1 were IgG1 1,235 (280-1120) mg/dl (79%), IgG2 235 (30-630) mg/dl (23.5%), IgG3 27.3 (40-250) mg/dl (1.74%), and IgG4 92.4 (11-620) mg/dl (5.9%). IgG subclasses level in patient No. 2 were IgG1 1,139 (280-1120) mg/dl (82.5%), IgG2 170 (30-630) mg/dl (12.3%), IgG3 5.6 (40-250) mg/dl (0.4%), IgG4 65.7 (11-620) mg/dl (4.8%). The diagnosis of CRS and recurrent NPs with IgG3 subclass deficiency in the first patient and IgG2/IgG3 subclass deficiency in the second patient were made. Patient No. 1 was given monthly IVIG therapy for the total of 7 courses and medications were gradually tapered. Currently, the patient is doing well after the cessation of IVIG therapy for 3 months. Patient No. 2 denied the IVIG treatment and was lost to follow up.*

Conclusion: *We reported two cases of recalcitrant CRS and recurrent NPs in children. Immunologic work up revealed IgG subclass deficiency. The treatment with monthly IVIG improved CRS and NPs in treated patient which brought up the possibility of association between NPs and IgG subclass deficiency. Further study on the direct role of IVIG in NPs will be needed in the future.*

Keywords: *Chronic rhinosinusitis, Immune deficiency, Immunoglobulin subclass, IVIG, Nasal polyps*

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Rhinosinusitis is a group of disorders characterized by inflammation of mucosa of the nose and the paranasal sinuses (PNS). Acute rhinosinusitis (ARS) has sudden onset and lasts up to 8 weeks. Chronic rhinosinusitis (CRS) lasts 8 weeks in adult and 12 weeks in children [1]. ARS is usually infectious in nature, whereas CRS might results from a wide range of processes. Although CRS covers a spectrum of diseases, 2 major forms can be differentiated; CRS with

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nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) [1-3].

Nasal polyps (NPs) are edematous semi-translucent masses in the nasal and paranasal cavities, mostly originate from the mucosal lining of the sinuses and prolapsing into the nasal cavities. The pathophysiology and etiology of NPs are partly understood and there is no valid classification of polyp subgroups to allow prediction of outcome after medical or surgical therapy. Moreover, recurrences are frequent regardless of treatment and repeated surgical interventions may lead to unsatisfactory healing and complications due to scar formation. Mucosal wound healing may also be impaired as a result of poorly defined factors in the inflamed mucosa. Topical or oral corticosteroids and sinus surgery are currently the main therapeutic tools [1].

Human IgG can be subdivided into 4 subclasses: IgG1, IgG2, IgG3, and IgG4. IgG subclass deficiency was shown to be associated with an increased susceptibility to infections. It is diagnosed when patients have low levels (below 2 standard deviations) of age-adjusted geometric mean of one or more IgG subclass [4]. Most frequently reported infections associated with this condition are recurrent upper respiratory tract infections, including sinusitis and otitis media. Although patients with IgG subclass deficiency may present with CRS, the association between NPs and IgG subclass deficiency has never been reported in the medical literature. Here, we described 2 patients who presented with CRS and NPs refractory to aggressive medical and surgical treatment. Immunologic work up showed IgG subclass deficiency and intravenous immunoglobulin (IVIG) therapy resulted in decreasing episodes of infection and shrinkage of NPs.

Case Report

Patient No. 1 is a 6-year-old Thai boy referred to the Siriraj Pediatric Allergy/Immunology Clinic, due to a one-year history of CRS and NPs. Past medical history revealed no history of cardiopulmonary disease. He was seen at a private hospital and was treated with antibiotics (azithromycin, amoxicillin/clavulanate on 2 occasions), decongestant and nasal saline irrigation, without any improvement. He was referred to the Department of Otorhinolaryngology, Siriraj Hospital and subsequently discovered to have NPs. Physical examination showed polypoid masses, pink to red middle turbinates, purulent nasal discharge (Figure 1) and adenoid hypertrophy. He was treated with prednisolone 10 mg/day (0.30 mg/kg/day), amoxicillin/clavulanate, montelukast, mometasone nasal spray, nasal saline irrigation and loratadine for 3 weeks. The dose of prednisolone was then decreased to 5 mg/day (0.15 mg/kg/day) along with the above medications which resulted in decreased polyps size but persistent purulent nasal discharge. The treatment was continued for 3 months

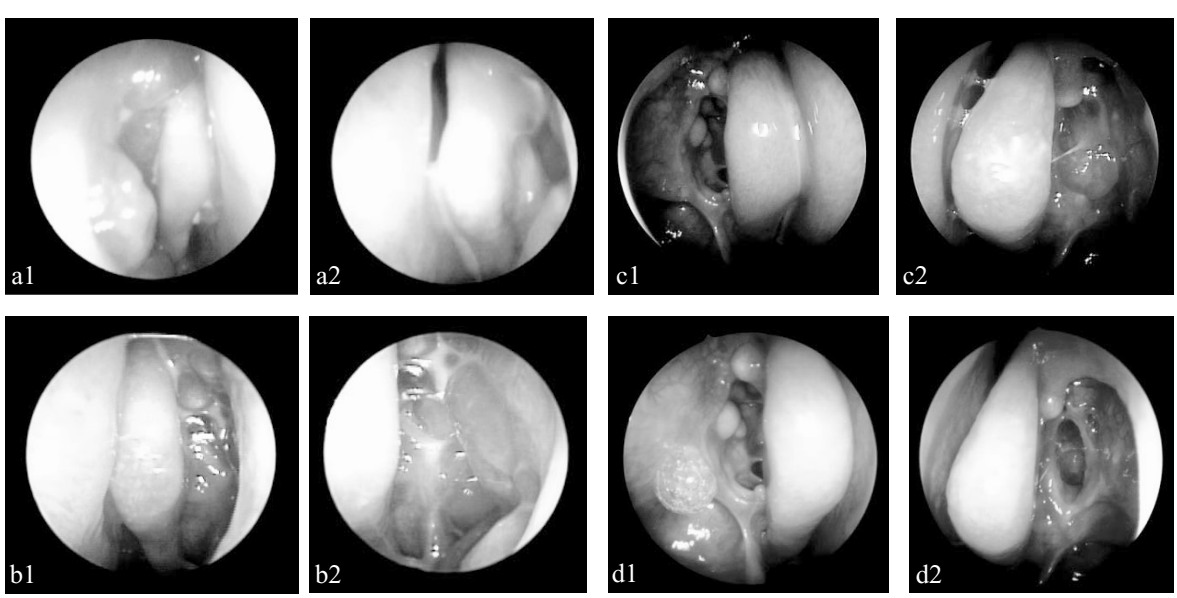

Fig. 1 Endoscopic findings of right (1) and left (2) nasal cavities of patient No. 1. Figures al and a2 were obtained prior to IVIG therapy which showed semitranslucent masses (polyps) on the right nassal cavities (a1) and mucopurulent discharge on the left nasal cavities (a2). Figures b, c, and d were obtained 1, 3, 6 months post IVIG therapy. The shrinkage of polyps on both sides were observed

with 5 mg/day of prednisolone, montelukast, mometasone nasal spray, loratadine and alternating antibiotics according to the clinical of CRS. The otorhinolaryngologist decided to do adenoidectomy with bilateral uncinectomy, polypectomy, and left anterior, right anterior and posterior ethmoidectomy. The operative findings were bilateral polyps from middle meatus, uncinate processes and maxillary sinuses. The pathologic findings showed mild chronic rhinitis of right inferior turbinate, acute and chronic sinusitis with congestion and edema of left maxillary sinus, mild inflammatory nasal polyps and reactive lymphoid hyperplasia of adenoid tissue. Two months after surgery, recurrent bilateral NPs were discovered and patient still had persistent purulent nasal discharge. The allergists/immunologists were consulted for further investigation and management. The work up showed Hct 36.8 %, WBC 16,900 cells/mm^3 (PMN 40%, L 49%, Eo 3.3%, M 7%), Plt 432,000 /mm^3. His urine analysis was normal. Serum BUN, creatinine, electrolytes were normal. The ESR was 8 mm/hr. His c-ANCA, anti-MPO, anti-PR3, and anti HIV were negative. ANA was weakly positive at 1:160. Immunologic work up included IgG 1,562 (633-1280) mg/dl, IgA 132.8 (33-202) mg/dl, IgM 152.9 (48-207) mg/dl, IgE 131.2 IU/ml, IgG1 1,235 (280-1120) mg/dl (79%), IgG2 235 (30-630) mg/dl (23.5%), IgG3 27.3 (40-250) mg/dl (1.74%), and IgG4 92.4 (11-620) mg/dl (5.9%). Post vaccination pneumococcal antibody increased a 15.9 fold in titer compared to baseline. The skin prick tests

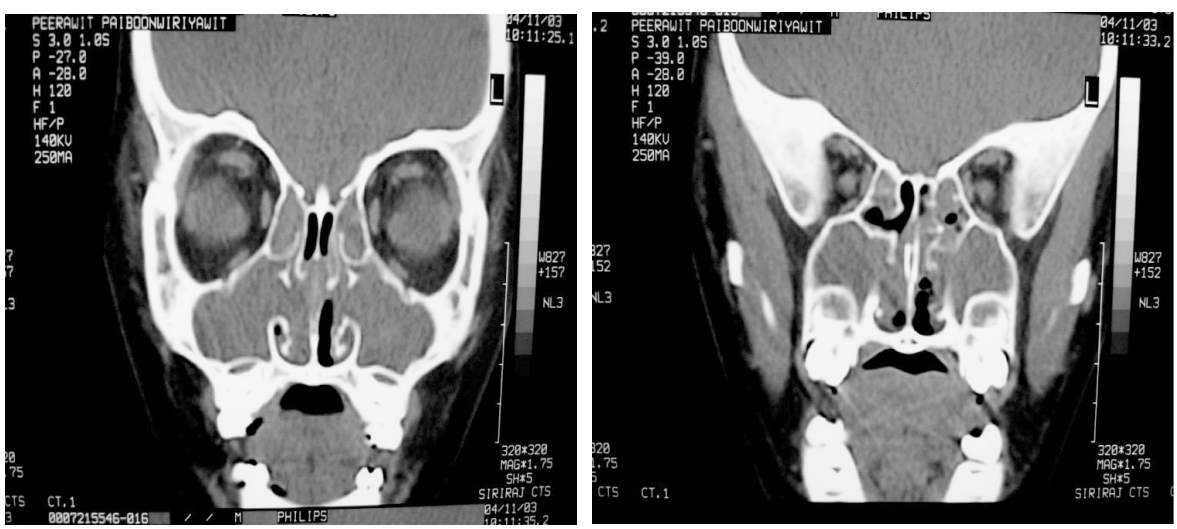

Fig. 2 The computerized tomography (CT) scan of paranasal sinus (PNS) of patient No. 1 showed soft tissue mass, occupying nasal cavity, ethmoid, sphenoid, frontal and maxillary sinuses. There was destruction of nasal turbinate and osteomeatal complex (OMC)

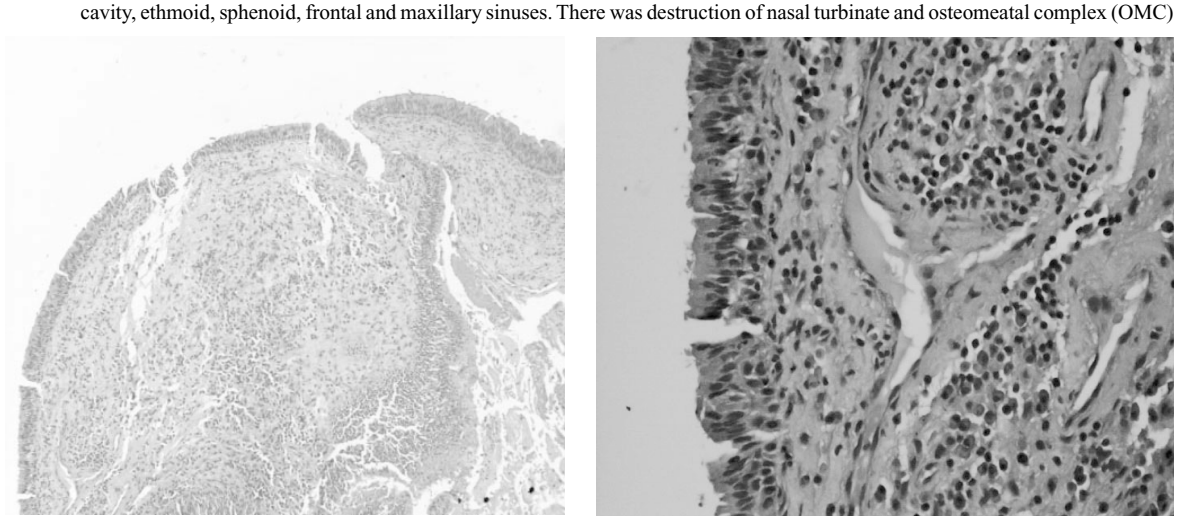

Fig. 3 Pathology of the nasal muscosa and ethmoid sinus of patient No. 1 showed chronic inflammation with mucous containing numerous eosinophils

(SPT) to foods and aeroallergens were negative. Specific IgE for mixed molds and intradermal skin test for *Aspergillus* antigen (1:1,000) was negative. The saccharine test was within normal limit. The aspirin oral challenge test was negative. The chest X-ray (CXR) was normal. The computerized tomography (CT) scan of the PNS showed soft tissue masses occupying nasal cavity, ethmoid, sphenoid, frontal and maxillary sinuses. There was a destruction of nasal turbinates and osteomeatal complex (OMC) (Figure 2). The biopsy of nasal mucosa and ethmoid sinus showed chronic inflammation with mucous containing numerous eosinophils (Figure 3). The bacterial culture from nasal cavities was negative. The fungal culture from nasal cavities revealed *Candida non albicans* and *Aspergillus spp.*. The diagnosis of CRS and recurrent NPs with IgG3 subclass deficiency was made. The patient was put on oral clindamycin and itraconazole plus gentamicin nasal irrigation in addition to montelukast, mometasone nasal spray, and loratadine. The azithromycin prophylaxis was started once the infection improved. However, patient still had relapses of sinusitis shortly after the cessation of antibiotics despite a prolonged course of antibiotic treatment and prophylactic antibiotic. The authors decided to start monthly IVIG (400 mg/kg) administration. After the 2nd dose of IVIG, CRS was significantly improved and the NPs were decreased in size. The IVIG was continued for the total of 7 courses and medications were gradually tapered. At the time the IVIG was stopped, the patient was on mometasone nasal spray, nasal saline irrigation and azithromycin prophylaxis. Currently, the patient is doing well after the cessation of IVIG therapy for 3 months.

Patient No. 2 is an 8-year-old Thai boy who was referred to the Siriraj Pediatric Allergy/Immunology Clinic due to recurrent NPs and CRS for 2 years. Past medical history revealed no history of cardiopulmonary disease. He was first seen at a private hospital and polypectomy was done. Six months later, he developed recurrent NPs and CRS and was referred to the Department of Otorhinolaryngology, Siriraj Hospital. He was treated with prednisolone 15 mg/ day (0.5mg/ kg/day), cetirizine, amoxicillin/clavulanate, and mometasone nasal spray. His clinical signs and symptoms of CRS did not improve after 2 months of therapy, so the oto-rhino-laryngologist decided to perform endoscopic sinus surgery. The operative finding revealed right polyp grade 2 at sphenoethmoidal recess, mucoid cysts in bilateral anterior and posterior ethmoid sinuses. The montelukast was added to the above therapy. Three months post operation, his clinical signs and symptoms of CRS did not improve and the allergists/immunologists were consulted for further investigation and management. At this point, anterior rhinoscopic examination revealed polypoid mass in both nostrils with purulent nasal discharge. The laboratory work up showed Hct 38.5%, WBC 13,600 cells/mm^3 (PMN 43.96 %, L 48.5%, E 1.0%, M 6.3%), Plt 388,000 /mm^3. The serum BUN, creatinine, electrolytes and urine analysis were normal. Immunologic work up revealed IgG 1,296 (633-1280) mg/dl, IgA 143.6 (33-202) mg/dl, IgM 100.6 (48-207) mg/dl, IgE 68.3 IU/ml, IgG1 1,139 (280-1120) mg/dl (82.5%), IgG2 170 (30-630) mg/dl (12.3%), IgG3 5.6 (40-250) mg/dl (0.4%), IgG4 65.7 (11-620) mg/dl (4.8%). Post-vaccinated anti-pneumococcal antibody showed 6.3 folds increase in titer compared to baseline. The SPT to aeroallergen and foods were weakly positive to house dust mites. The specific IgE for mixed molds and intradermal skin test for *Aspergillus* antigen (1:1,000) were negative. The saccharine test was normal. The aspirin oral challenge test was negative. The bacteria and fungal culture from nasal cavities were negative. The CXR was normal. The axial CT scans of PNS revealed total opacification of all paranasal sinuses. There was suggested of a few polyps within the maxillary sinuses, more conspicuous on the left, located at the roof of the antrum. The diagnosis of CRS and recurrent NPs with IgG2/IgG3 subclass deficiency was made. Since the CRS and NPs of this patient were not improved with systemic or topical corticosteroids, leukotriene antagonist, aggressive antibiotics and endoscopic sinus surgery, the authors decided to initiate IVIG therapy. The family denied the IVIG treatment and was lost to follow up.

Discussion

CRS is one of the most common chronic conditions. Factors contributing to CRS include anatomical defect, allergy, immune deficiency, cystic fibrosis, ciliary dyskinesia, autoimmune disease, aspirin associated respiratory disease and microbial factors [1,2]. Recent studies indicated that the host response to colonization of the sinonasal mucosa with microorganisms such as superantigens-producing *S aureus* and colonizing fungi, plays an alternative role in the development of CRS [2]. Patients who have positive evidence of allergy to the colonizing fungus are considered to have allergic fungal rhinosinusitis (AFRS). This condition typically demonstrates 5 characteristics: gross production of eosinophilic mucin containing noninvasive fungal hyphae, nasal polyposis, specific

radiographic findings, immunocompetence, and allergy to cultured fungi [5]. Histologically, CRSsNP is characterized by a predominantly neutrophilic inflammation with a lesser contribution of eosinophils, whereas CRSwNP is characterized by eosinophilic inflammation [5]. The mechanism of eosinophilic inflammation in NPs is unclear since total IgE concentrations, eosinophilic cationic protein (ECP), IL-4, or IL-5 concentrations in NPs are not different in atopic versus nonatopic subjects. These indicate that the phenotype of systemic allergy defined as SPT positivity does not correlate with the local features of allergic inflammation in NPs [1]. Therefore, the direct role of allergic factors in CRS has long been controversial even though slightly less than half of the patients with CRSwNP have associated allergies [6]. However, as mentioned above, a role has been proposed for IgE specific for staphylococcal-derived superantigens in the pathogenesis of CRSwNP [7].

Approximately 20% of patients with CRS have NPs [8]. The presence of NPs is a factor contributing to poor response to medical therapy of rhinosinusitis and it often needs a combination of surgical and long-term medical interventions [9]. The polypoid disease is generally recurrent, despite the medical treatment. In contrast, the nonpolypoid sinusitis generally responds more favorably to medical therapy and in some cases have total resolution of symptoms [9]. NPs can be classified as; 1) antrochoanal polyps which is a large, isolated, unilateral non-eosinophilic formation, 2) idiopathic unilateral or bilateral, eosinophilic polyps without involvement of lower airways, 3) bilateral eosinophilic polyposis with concomitant asthma and/or aspirin sensitivity, 4) polyposis with underlying systemic disease (e.g., cystic fibrosis, primary ciliary dyskinesia, Wegener's granulomatosis, Kartagener's syndrome, etc.) [1].

Our 2 patients had CRSwNPs which did not respond well to aggressive medical and surgical therapy. Thus, a search for an underlying disease contributing to this condition was warranted. Patient No. 1 had normal saccharin test which made the diagnosis of ciliary dyskinesia unlikely. He had negative SPT to aeroallergens and foods which helped exclude allergic diathesis. The aspirin challenge test was negative which excluded aspirin sensitivity. Since the fungal culture from nasal cavities showed *Candida non albicans* and *Aspergillus spp.*, the SPT and intradermal test to *Aspergillus* was done and the result was negative. These evidences, together with the non-characteristic CT scan of PNS, helped to rule out AFRS. Since there was some destruction of nasal turbinate and OMC from CT scan of PNS, the c-ANCA and anti-PR3 were done with negative result. These findings, together with normal renal function, helped to exclude Wegener's granulomatosis. The patient did not respond to gentamicin nasal irrigation which was introduced to get rid of colonizing bacteria. The IgG level was slightly higher than the normal range probably was due to persistent infections. However, this patient had lower level of IgG3 subclass than normal subjects (27.3 vs 40-250 mg/dl) resulted in lower proportion of this subclass compared to the normal range (1.73 vs 5-10 %). The only specific antibody that we could measure in this patient was the antibody response to pneumococcal vaccine which showed more than four folds rising of antibody. Results of the work up of patient No. 2 were not different from those of patient No. 1 except the weakly positive SPT to house dust mites, lower than the normal proportion of IgG2 (12.3% vs normal 20-25%), and the low level of IgG3 (5.6 mg/dl vs normal 40-250 mg/dl). The role of allergy in this patient was not clear since none of the anti-allergic treatments were effective. Thus, NPs in both patients might be most compatible with type 4 of the classification of NPs and the possible associated systemic disease was IgG3 deficiency in patient No. 1 and IgG2/IgG3 deficiency in patient No. 2.

Isolated or combined deficiencies of IgG1, IgG2 and IgG3 have been associated with increased risk of infections. The most common infections in these group of patients are recurrent upper respiratory tract infections, including sinusitis, otitis, and rhinitis [4]. The proportion of IgG subclass is normally maintained within a relatively narrow range: IgG1, 60-65%; IgG2, 20-25%; IgG3, 5-10%; IgG4, 3-6% [10]. Each IgG subclass has an individual pattern of development [11]. IgG1 and IgG3 levels, increasing quickly with age in infant, are efficient activators of the classical complement pathway and are directed mainly against protein antigens [4]. IgG2 and IgG4 reach adult levels at puberty [4]. Deficiency of IgG1 results in low level of total IgG and is often associated with susceptibility to bacterial infections. IgG2 is primarily directed against polysaccharide antigens, resulting in a functional immaturity of children in their defense against infections with encapsulated bacteria such as *Streptococcus pneumoniae* and *Haemophilus influenzae*. The subclass-associated specificities can be replaced by antibodies belonging to a different subclass although these antibodies show a lower affinity and would thus be expected to function

inferiorly[11]. For example, in IgG2-deficient individual, antibody to polysaccharides is predominantly IgG1 [4]. IgG3 has the shortest half-life (7 days as compared to 21 days for all other IgG subclasses). Deficiency of IgG3 may lead to frequent upper respiratory tract infections, recurrent bronchitis and bronchopneumonia [12]. A susceptibility to viral infections or a protracted clinical course of viral infections has been suggested [11]. Infection-prone patients with IgG3 deficiency were reported to have lower level of IgG2 to a bacterial polysaccharide even though the total IgG2 level is normal [13]. Although IgG4 represents a minor portion of the total IgG, it may be of clinical importance, as IgG4-deficient individuals have been reported to suffer from recurrent infections. Furthermore, raised levels of IgG4 antibodies are often noted against selected protein antigens after chronic exposure [11].

The mechanisms of IgG subclass deficiency are not completely understood. Although deletions of single or multiple immunoglobulin heavy chain genes have been demonstrated in few cases, most deficiency are due to dysregulation of the expression of the γ genes [11]. The wide variablility in the clinical expression, types and degrees of deficiencies, lead to the notion that this condition is a syndrome caused by more than one mechanisms. Asymptomatic individuals with IgG subclass deficiencies has been found in both blood donors and among the relatives of patients with a variety of immune-deficiencies including family members of patient with IgG subclass deficiencies.[12, 14] Thus, one must be cautious to the clinical interpretation of IgG subclass deficiencies. Moreover, the normal value of each ethnic group is needed for clinical interpretation of the absolute value for deficiency , due to a wide range of normal value in general population. In Thailand, Vichyanond et al published the range of IgG, IgA, IgM and IgG subclasses in Thai children [15]. Although the sample size was small, this study demonstrated that the level of IgG2 subclass in Thai children was higher than those observed in children at the same age in the standard reference [4]. If the normal range of IgG2 level in Thai children (191-565 mg/dl) was used for patient No. 2, his IgG2 level would be absolutely low (170 mg/dl). In contrast, if the normal range in the standard reference (30-630 mg/dl) was used, his IgG2 level remained in the normal range and we could identify him as having lower proportion of IgG2 subclass only.

Although IgG subclass deficiency can lead to CRS, there is no report of the association between IgG subclass deficiency and NPs in medical literature. To our knowledge, this is the first report of patients who have CRS and NPs with IgG subclass deficiency. The mechanism of this association is unclear. We postulated that isolated IgG3 subclass deficiency in patient No. 1 and IgG2/IgG3 subclass deficiency in patient No. 2, caused chronic infection and inflammation of the PNS leading to the development of NPs, which made them difficult to clear infection of the PNS as an amplifying loop.

The management of NPs may involve medical approaches (topical or systemic corticosteroids), and surgical procedures (from the extraction of polyps in the nasal cavity to radical ethmoidectomy to eradicate all polyp tissue). Because nasal polyposis is a chronic disease with a high recurrent rate in about one third of patients, surgical over-treatment and its sequelae should be avoided. A combined treatment is recommended for long-term control of the disease. Topical corticosteroids may also reduce the incidence of recurrent polyp after surgery [16-18]. However, topical corticosteroids may be insufficient in severe bilateral polyps, and polyp growth may be observed despite treatment [19]. Systemic corticosteroids are extremely effective in reducing polyp size and symptoms [20]. However, polyps will recur rapidly in patients with severe disease, and little evidence thus far suggests that the natural course of the disease is influenced by long-term low-dose treatment regimes. Antibiotics are indicated in the case of superimposed bacterial infection. Functional endoscopic sinus surgery (FESS), is a standard treatment in patients resistant to medical treatment [21-23]. This procedure removes polyp tissues in the nose and sinuses with preservation of anatomic structures and healthy mucosa. An individualized management regimen for NPs may combine long-term topical steroids, short-term systemic steroids, and surgery. For IgG subclass deficiency, initial treatment with recurrent infections is appropriate use of antibiotics. Most investigators recommend that administration of IVIG be reserved for children with significant clinical symptoms and insufficient response to treatment with antibiotics [4]. Duration of IVIG administration is variable depending on the age and clinical course of individual patient [24]. The mechanisms of action of IVIG are complex. Antibodies in IVIG enhance opsonization and thus promote phagocytosis and antibody-mediated cellular cytotoxicity. The specific antibodies can neutralize pathogens and bacterial toxins. Anti-inflammatory action of IVIG involve the modulation of expression and function of Fc receptors, interference with comple-

ment activation and the cytokine network, provision of anti-idiotypic antibodies and modulation of T and B cell activation, differentiation and effector functions [25-26]. We postulated that the mechanisms which IVIG decreased NPs size and improved CRS in patient No. 1 were probably by the above functions but not the direct replacement of IgG3 subclass, since the half-life of IgG3 was 7 days but the IVIG therapy was given every month. If one wants to raise the IgG3 level, IVIG with high concentration of IgG3 subclass must be given every week.

In conclusion, we reported 2 cases of recalcitrant CRS and recurrent NPs in children. Immunologic work up revealed IgG3 subclass deficiency in the first patients and IgG2/IgG3 subclass deficiency in the second patient. The treatment with monthly IVIG improved CRS and NPs in treated patient which brought up the possibility of association between NPs and IgG subclass deficiency. Further study on the direct role of IVIG in NPs will be needed in the future.

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โรคไซนัสอักเสบเรื้อรังและโรคริดสีดวงจมูกที่กลับเป็นซ้ำในผู้ป่วยเด็กที่มีภาวะภูมิคุ้มกันบกพร่องชนิด IgG subclass และทบทวนบทความทางวิชาการ

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ภาวะไซนัสอักเสบเรื้อรัง (CRS) เป็นการอักเสบของเยื่อบุจมูกและโพรงไซนัส สามารถแบ่งเป็นสองชนิดใหญ่ๆ ได้แก่ ภาวะไซนัสอักเสบเรื้อรังที่ไม่พบ (CRSsNP) และพบ(CRSwNP) ร่วมกับโรคริดสีดวงจมูก พยาธิกำเนิดและสาเหตุของโรคโรคริดสีดวงจมูกยังไม่เป็นที่ทราบอย่างแน่ชัด ภาวะภูมิคุ้มกันบกพร่องชนิด IgG subclass มีความสัมพันธ์กับการเพิ่มโอกาสการติดเชื้อ ยังไม่มีรายงานถึงความสัมพันธ์ระหว่างโรคริดสีดวงจมูก กับภาวะภูมิคุ้มกันบกพร่องชนิด IgG subclass มาก่อน

วัตถุประสงค์: *เพื่อรายงานผู้ป่วย 2 ราย ที่มีโรคไซนัสอักเสบเรื้อรังและโรคริดสีดวงจมูกที่กลับเป็นซ้ำร่วมกับภาวะภูมิคุ้มกันบกพร่องชนิด IgG subclass deficiency*

รายงานผู้ป่วย: *ผู้ป่วยเด็กชาย 2 ราย (อายุ 6 และ 8 ปี) ได้ถูกส่งต่อมารับการรักษาที่โรงพยาบาลศิริราช ด้วยเรื่องโรคไซนัสอักเสบเรื้อรังและโรคริดสีดวงจมูกที่กลับเป็นซ้ำ ผู้ป่วยทั้ง 2 รายได้รับการรักษาด้วยยา (รวมถึงยา steroid ชนิดพ่นจมูกและชนิดรับประทาน ยาฆ่าเชื้อ ยาต้าน leukotriene และการล้างจมูก) ร่วมกับการผ่าตัดอย่างเต็มที่ โดยไม่ได้ผลดีเท่าที่ควร การตรวจระดับภูมิคุ้มกันพบว่าทั้ง 2 ราย มี ระดับอิมมูโนโกลบูลิน IgG, IgA และ IgM ปกติ แต่ผู้ป่วยรายที่ 1 มีระดับของ IgG1 1,235 (280-1120) mg/dl (79%), IgG2 235 (30-630) mg/dl (23.5%), IgG3 27.3 (40-250) mg/dl (1.74%), and IgG4 92.4 (11-620) mg/dl (5.9%). ส่วนผู้ป่วยรายที่ 2 มีระดับของ IgG1 1,139 (280-1120) mg/dl (82.5%), IgG2 170 (30-630) mg/dl (12.3%), IgG3 5.6 (40-250) mg/dl (0.4%), IgG4 65.7 (11-620) mg/dl (4.8%). การวินิจฉัยเบื้องต้นคือ โรคไซนัสอักเสบเรื้อรังและโรคริดสีดวงจมูกที่กลับเป็นซ้ำ ร่วมกับภาวะภูมิคุ้มกันบกพร่องชนิด IgG3 subclass ในผู้ป่วยรายแรกและภาวะภูมิคุ้มกันบกพร่องชนิด IgG2/IgG3 subclass ในผู้ป่วยรายที่ 2 เนื่องจากผู้ป่วยทั้งสองรายไม่ตอบสนองต่อการรักษาด้วยยาและการผ่าตัดอย่างเต็มที่ แพทย์ได้ตัดสินใจให้การรักษาด้วยอิมมูโนโกลบูลิน (IVIG) ผู้ป่วยรายแรกตอบสนองดีต่อการรักษาด้วยอิมมูโนโกลบูลิน ส่วนผู้ป่วยรายที่ 2 ปฏิเสธการรักษาด้วยอิมมูโนโกลบูลินและขาดการรักษาต่อเนื่อง*

สรุป: *ได้นำเสนอผู้ป่วยที่เป็นโรคไซนัสอักเสบเรื้อรังและโรคริดสีดวงจมูกที่กลับเป็นซ้ำ การตรวจระดับภูมิคุ้มกันพบว่าทั้ง 2 รายมีภาวะภูมิคุ้มกันบกพร่องชนิด IgG subclass การรักษาที่ได้ผลดีด้วยด้วยอิมมูโนโกลบูลินบ่งบอกถึงความสัมพันธ์ระหว่างโรคริดสีดวงจมูกกับภาวะภูมิคุ้มกันบกพร่องชนิด IgG subclass*