ภาวะภูมิคุ้มกันบกพร่องปฐมภูมิกลุ่มที่มีความบกพร่องของเม็ดเลือดขาวชนิดบีชนิดที่มีการสร้างแอนติบอดีผิดปกติในผู้ป่วยเด็ก 12 ปีที่มีอาการไซนัสอักเสบเรื้อรัง: รายงานผู้ป่วย

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บทคัดย่อ

บริบท ผู้ป่วยเด็กที่เป็นโรคภูมิคุ้มกันบกพร่องปฐมภูมิ มักมีประวัติติดเชื้อทางเดินหายใจซ้ำโดยเฉพาะโรคไซนัสอักเสบเรื้อรัง

วัตถุประสงค์ ศึกษาอาการทางคลินิกของผู้ป่วยเด็กอายุ 12 ปี ที่มีภาวะไซนัสอักเสบเรื้อรังตั้งแต่อายุ 4 ปี ที่ได้รับการวินิจฉัยภาวะภูมิคุ้มกันบกพร่องปฐมภูมิกลุ่มที่มีความบกพร่องของเม็ดเลือดขาวชนิดบีชนิดที่มีการสร้างแอนติบอดีผิดปกติ

กรณีศึกษา ผู้ป่วยเด็กชายอายุ 12 ปี มีโรคประจำตัวเป็นโพรงจมูกอักเสบจากภูมิแพ้ มีภาวะไซนัสอักเสบเรื้อรัง ตั้งแต่อายุ 4 ปี ไม่ตอบสนองต่อรักษาด้วยยาสเตียรอยด์ชนิดพ่นจมูก และยาปฏิชีวนะหลายกลุ่ม ตรวจความสมบูรณ์ของเม็ดเลือดและระดับอิมมูโนโกลบูลินอยู่ในเกณฑ์ปกติ IgG 705 มก./ดล., IgA 108 มก./ดล., IgM 54 มก./ดล. การทดสอบภูมิแพ้ทางผิวหนัง ให้ผลบวกต่อหญ้า Bermuda, วัชพืชผักโขม,เชื้อรา Cladosporium และไรฝุ่นชนิด Dermatophagoides pteronyssinus (Dp) วัดความสามารถในการตอบสนองต่อแอนติเจนที่เป็นpolysaccharide โดยการฉีดวัคซีน 23-valent unconjugated polysaccharide ต่อเชื้อ Streptococcal pneumoniae โดยตรวจซีรัมก่อนได้รับวัคซีน และหลังได้รับวัคซีน 4 สัปดาห์ พบว่า ระดับแอนติบอดีน้อยกว่า 1.3 มก./มล. สัดส่วนน้อยกว่าร้อยละ 50 ของ serotype ทั้งหมด ผู้ป่วยได้รับการวินิจฉัยภาวะภูมิคุ้มกันบกพร่องปฐมภูมิกลุ่มที่มีความบกพร่องของเม็ดเลือดขาวชนิดบีชนิดที่มีการสร้างแอนติบอดีผิดปกติ รักษาโดยให้ยาปฏิชีวนะเพื่อป้องกันการติดเชื้อซ้ำและรับ pneumococcal polysaccharide conjugated vaccine (13-valent) ไม่พบการกลับเป็นซ้ำของภาวะไซนัสอักเสบเรื้อรังอีก

สรุป ภาวะภูมิคุ้มกันบกพร่องปฐมภูมิกลุ่มที่มีความบกพร่องของเม็ดเลือดขาวชนิดบี ชนิดที่มีการสร้างแอนติบอดีผิดปกติพบได้ในผู้ป่วยมีภาวะไซนัสอักเสบเรื้อรัง หากได้ทราบการวินิจฉัยที่ชัดเจนในเวลารวดเร็วจะช่วยให้ผู้ป่วยมีโอกาสได้รับการรักษาที่เฉพาะที่ทำให้หายขาดจากโรคได้

คำสำคัญ โรคภูมิคุ้มกันบกพร่องปฐมภูมิ ความบกพร่องของเม็ดเลือดขาวชนิดบีชนิดที่มีการสร้างแอนติบอดีผิดปกติ ไซนัสอักเสบเรื้อรัง

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Specific antibody deficiency (SAD) in a 12-year-old child presented with chronic rhinosinusitis: A case report

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Abstract

Introduction: A group of illnesses collectively known as primary immunodeficiency disorder (PID) are caused by immune system abnormalities, and increase the patient's vulnerability to infection – particularly chronic rhinosinusitis (CRS) – and is challenging to identify.

Objective: This study reviewed the adaptive immunity of a 12-year-old boy to Streptococcus pneumonia, in the context of the patient's first clinical presentation of CRS at 4 years old.

Case presentation: A 12-year-old boy was first diagnosed with allergic rhinitis at 2 years old. However, at 4 years old he was diagnosed with chronic rhinosinusitis. He was treated with intranasal corticosteroids and multiple antibiotics, which provided mild clinical recovery between episodes. Blood cell counts, IgG subclass assay and immunoglobulin level assay were normal. IgG 705 mg/dL, IgA 108 mg/dL, IgM 54 mg/dL. Percutaneous prick skin tests were positive for Bermuda grass, Carelessweed, Cladosporium and Dermatophagoides pteronyssinus (Dp). Despite treatment his continued recurrent infections led to an evaluation of a specific antibody response to polysaccharide pneumococcal antigens. He responded to less than 50% of the 8 pneumococcal serotypes after 23-valent unconjugated pneumococcal vaccine, resulting in a diagnosis of SAD, with a treatment of a prophylactic antibiotic and pneumococcal polysaccharide conjugated vaccine (13-valent). He showed clinical improvement, with mild infections, and controlled rhinitis.

Conclusion: There are several PIDs related to allergic diseases. A SAD against pneumococcal serotypes is a primary antibody deficiency, that should be immediately considered in children, who've developed CRS that does not improve (in spite of aggressive treatment). Further investigations are needed to exclude them.

Keywords: Primary immunodeficiency disorder, Specific antibody deficiencies, Chronic rhinosinusitis

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Introduction

Chronic rhinosinusitis (CRS) is a disease characterized by chronic inflammation of the sinonasal tissue. The diagnosis requires 12 weeks or longer of compatible symptoms. CRS is a prevalent disease with a high annual cost of treatment. Patients usually undergo evaluation, nasal endoscopy, sinus computed tomography (CT) scans and/or immune deficiency if the refractory disease is still present.[1] Two of the most common bacterial agents that cause sinusitis are Streptococcus pneumoniae (S. pneumoniae) and Hemophilus Influenza.

Recent publications have begun analyzing the burden of specific antibody deficiencies (SAD) against pneumococcal serotypes and their impact on healthcare.[2] SAD is a humoral immunodeficiency characterized by normal levels of IgG, IgA, IgM and IgG subclasses, but fails with polysaccharide antigens, and is most often discussed in its relation to S. pneumoniae.[3] To establish the SAD diagnosis, an inadequate IgG antibody response to more than 50% of pneumococcal serotypes after unconjugated pneumococcal immunization are needed. An adequate response is defined as a post-immunization titer of ≥1.3 μg/mL or ≥4 times the pre-immunization value.[4,12] The incidence of SAD in the general population is unclear. SAD was found to occur in 6–14% of individuals.[5,6] The incidence of SAD in Thai children is found at 16.4%.[7]

According to certain studies, there may be a connection between SAD and CRS. If CRS is linked to severe or recurrent infections, a complete medical evaluation should be performed to identify the underlying cause. This may involve looking into the possibility of a specific antibody deficiency. This study reviewed a difficult-to-treat CRS, that was not controlled despite appropriate medical management. Being aware of clinical characteristics of SAD can help diagnose and treat patients earlier.

Objective

To describe the case of a 12-year-old boy who was presented with chronic rhinosinusitis since he was 4 years old. His SAD diagnosis was problematic. Knowing the clinical features of SAD raises the awareness of this condition to physicians, leading to prompt diagnosis and appropriate management. A delayed diagnosis may impair the quality of life.

Methods

The record of this single patient was reviewed along with the collected relevant clinical data. A review of the literature on SAD was made. The data for this retrospective descriptive study was gathered from the medical records of the outpatient clinic at Burapha University Hospital between 2016 and 2022. The Research Ethics Committee of Burapha University, Chonburi, Thailand, approved this study (HS105/2566).

Case presentation

The patient was a 12-year-old male with a family history of atopic disease. He has had symptoms of nasal itching, nasal congestion, sneezing and rhinorrhea since he was 2 years old. At 2 years old, the patient was diagnosed with Allergic rhinitis (AR). Oral antihistamines and intranasal corticosteroids were used in his treatment. The results of a skin prick test were positive for Dermatophagoides pteronyssinus (Dp), Bermuda grass, Carelessweed and Cladosporium. His aeroallergen sensitization was similar to cases researched that looked at a 5-year trend of allergen sensitization among children with AR, who visited the Burapha University Hospital's Pediatric Allergy Clinic between 2016 and 2020.[8]

At the age of four, he developed chronic rhinosinusitis after initially developing acute rhinosinusitis. For more than 12 weeks, the patient had nasal blockage, recurrent purulent rhinorrhea and facial pain. He was treated with multiple antibiotics and intranasal corticosteroids, though with mild clinical recovery. Despite treatment, his recurrent infections continued. A nasal endoscopy was performed to examine the nasal passages and evaluate the nasal mucosal. The nasal endoscopy revealed no deviation of the nasal septum, nasal polyposis, or other anatomical defect.

He was diagnosed with chronic rhinosinusitis and allergic rhinitis. He presented no recurrent episodes of otitis media or pneumonia. No prior pneumococcal vaccination history was present.

On examination, his height and weight were appropriate for his age. No fever, no dyspnea, no tachypnea and no desaturation. Cardiovascular examination was normal, lungs were clear to auscultation, and abdominal examination was unremarkable with no hepatosplenomegaly. No peripheral edema or rash was observed, and the neurological examination was also ordinary.

The patient's initial laboratory results, at age five, were normal. Normal blood cell counts are shown in Table 1 below. Moderated S. pneumoniae was found in the sinus discharge culture.

Table 1 Initial complete blood count panel at 5-years-old

Serum	Patient value	Reference range and units[9]
WBC	11,410	6,000-14,000/mm^3
Neutrophil	78	%
Lymphocyte	16	%
Hemoglobin	11.4 g	10.5-14.0/dL
Hematocrit	36	32-42%
Platelet count	336×10^3	$150\text{-}400\times10^3$ cells/mL

Table 2 shows that the results of the IgG subclass assay and immunoglobulin level assay were normal.

Table 2 Immunoglobulins level and IgG subclass level

Immunoglobulins level	Patient value (mg/dL)	Reference range and units (mg/dL)[10,11]
IgG	705	929±228
IgA	108	93±27
IgM	54	56±18
IgG1	373	360-810
IgG2	137	60-310
IgG3	44.1	9-160
IgG4	19.9	9-160

Antibody titers against the capsular polysaccharides of 8 pneumococcal serotypes were measured. The specific antibody response to polysaccharide pneumococcal antigens was evaluated – he responded to less than 50% of 8 pneumococcal serotypes after 23-valent unconjugated pneumococcal vaccine, as shown in Table 3. An adequate response is defined as a post-immunization titer of ≥1.3 µg/mL or ≥4 times the pre-immunization value.[4,12]

Table 3 Pneumococcal antibodies before and after 23-valent unconjugated pneumococcal vaccine

Pneumococcal serotype	Pre-vaccination (ug/ml)	Post-vaccination (ug/ml)
4	0.02	3.96
6B	0.07	0.09
7F	0.03	0.49
9N	0.05	3.25
9V	0.31	0.94
14	0.30	0.40
18C	0.14	7.60
23F	0.28	0.48

The patient, at 5-years-old, was diagnosed with SAD, and treated with a prophylactic antibiotic for 1-year (low dose and long-term macrolide therapy), and a pneumococcal polysaccharide conjugated vaccine (13-valent). His clinical condition improved; he had a few minor infections but no longer had sinusitis and his rhinitis was under control. After 3 years, at 8 years old, he had been off intranasal corticosteroids.

The patient's follow-up treatment of allergic rhinitis was with an allergist, and he was monitored for sinusitis until he twelve years old. He was no longer diagnosed with sinusitis, and the quality of his life had greatly improved.

Discussion

CRS is a highly prevalent illness with substantial annual treatment costs. Physician awareness of SAD is increasing with greater general knowledge of its clinical symptoms, resulting in the timely diagnoses and effective care of the disorder, especially when it presents with CRS. It is important to consider immunodeficiency disorders with the differential diagnosis of pediatric patients when presented with CRS, especially in cases where there is a lack of response to conventional therapies.

Conclusions

There are several PIDs related to allergic diseases. A SAD against pneumococcal serotypes is a primary antibody deficiency that should be immediately considered in children who have developed CRS that does not improve, in spite of aggressive treatment. Further investigations are needed to exclude them.

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