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ORIGINAL ARTICLE

Bronchial hyperreactivity in children with antibody deficiencies

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Abstract
Background: Antibody deficiency comprises a heterogeneous group of disorders characterised by the body's inability to mount an effective antibody response to pathogens. Although it has been reported that asthma and allergic disease are frequent in antibody deficiencies, there are no data that evaluate and compare bronchial hyperreactivity (BHR) in all groups of antibody deficiencies. In this study, we aimed to evaluate and compare the frequency of BHR in patients with different antibody deficiencies.
Methods: The study was carried out on 113 patients between ages 5 and 18 diagnosed with antibody deficiencies. The patients and their families were questioned on their history of asthma and allergic diseases. Allergic skin prick tests and non-specific bronchial provocation test with methacholine was done for all patients. Complete blood count and serum total IgE levels were measured.
Results: The mean age of the patients was 10.8 ± 3.8 years and 66.4% were male. Within the study group 41.6% of the patients had selective IgA deficiency, 24.8% had IgG subclass deficiency, 14.2% had partial IgA deficiency, 10.6% had common variable immunodeficiency, 6.2% had transient hypogammaglobulinaemia and 2.7% X-linked agammaglobulinaemia. In total group, 42.5% had bronchial hyperreactivity with methacholine challenge test. BHR was more significant in both patients with selective IgA deficiency and partial IgA deficiency compared to those with IgG subclass deficiency ($P = 0.041$ and $P = 0.038$, respectively).
Conclusion: BHR was high in antibody deficiencies, especially selective IgA deficiency compared to IgG subclass deficiency.

Introduction

Antibody deficiency comprises a heterogeneous group of disorders characterised by the body's inability to mount an effective antibody response to pathogens. Antibody deficiency disorders may be congenital or they may develop

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later in life in response to environmental triggers or iatrogenic factors.[1,2] It has been reported that asthma and allergic disease are frequent in antibody deficiencies.[3–6]

Asthma is an immunological disease that includes multiple inflammatory and clinical phenotypes, characterised by airway inflammation and bronchial hyperreactivity (BHR), and recurrent wheezing, cough, and shortness of breath.[7] Airway hyperreactivity to various stimulant agents is a characteristic feature of bronchial asthma. Determination of airway hyperresponsiveness with methacholine challenge is a safe, simple, standardised, and reproducible diagnostic tool used in clinical practice to establish the presence of asthma.[8]

With regard to BHR in antibody deficiencies, two studies have been done; one being on selective IgA deficiency and the other on common variable immune deficiency.[9,10] To our knowledge, there is no study that evaluates BHR in all groups of antibody deficiencies in the literature. In this study, we aimed to evaluate and compare the frequency of BHR in patients with different antibody deficiencies.

Materials and methods

Study design and population

This study was undertaken in Ankara Children's Health and Diseases Hematology-Oncology Hospital between June 2011 and January 2012, with the approval of the local ethics committee. The study was done on 113 patients between ages 5 and 18 diagnosed with antibody deficiencies. The patients and their families were questioned on their history of asthma and allergic diseases. Allergic skin prick tests and non-specific bronchial provocation test with methacholine was done for all patients. Since it can affect the methacholine challenge test, patients who developed bronchiectasis were excluded from the study. Complete blood count and serum total IgE levels were measured for all patients. A documented informed consent was taken from the patients and their parents.

Antibody deficiencies

Patients were diagnosed and classified according to the clinical and laboratory criteria of PID reported by the IUIS Primary Immunodeficiency Diseases Classification Committee.[11] Two types of IgA deficiency may be distinguished: selective IgA deficiency, with IgA level less than 6 mg/dl, and partial IgA deficiency, with a level greater than 6 mg/dl but less than 2 standard deviations below the age-adjusted mean level.

Allergy skin prick tests

Allergy skin prick testing was performed for all of the patients for Dermatophagoides pteronyssinus, Dermatophagoides farinae, Cat and Dog dander, Alternaria, Cockroach, Aspergillus, Clodosporium, Betulaceae, Grass mix, Tree mix, Artemisia, Oleaceae, Saliceae, Parieteria, egg, wheat, peanut, hazelnut, milk, sesame, soya, fish, histamine, and negative controls (Stallergens, Antony, France). These tests were performed on the volar surface of both forearms, with results recorded after 15 min. Results were considered positive when the mean wheal diameter was at least 3 mm larger than that produced by the control.

Bronchial provocation tests

Methacholine challenge was performed according to a protocol described by Cockcroft et al.[12] as detailed previously.[13] Briefly, after saline inhalation, doubling concentrations of methacholine were inhaled during a 2-min tidal breathing period every 5 min, starting with 0.06 mg/mL up to 8 mg/mL or until a decrease in FEV1 of at least 20% (PC20) was obtained. The concentration of agents producing a PC20 was calculated by linear interpolation on the log dose–response curve. A PC20 of 8 mg/mL or less was considered to represent a positive test result. Duplicate spirometry was performed at 0.5 and 1.5 min after each inhalation. As suggested,[14] methacholine was diluted in saline. The test was performed during the children's asymptomatic periods or at least four weeks after respiratory tract infection. On the challenge day, patients were queried about prior use of drugs, and none had used short- or long-acting agonists, antihistamines, or inhaled oral corticosteroids/leukotriene receptor antagonists for at least 24 h, 1 week, and 3 months before the study, respectively.

Statistical analysis

Statistical analysis was performed using the SPSS packet program. Values were either provided as numbers and percentages, or as mean ± standard deviation, where applicable. Comparisons of the frequency of allergic diseases and other variables between patients with antibody deficiencies were made using the Chi-square test, Fisher's exact test and student's *t*-test. A *P*-value of $\leq$0.05 was considered indicative of statistical significance.

Results

The mean age of the patients was 10.8 ± 3.8 years, and 66.4% were male. Within the study group 41.6% of the patients had selective IgA deficiency, 24.8% had IgG subclass deficiency, 14.2% had partial IgA deficiency, 10.6% had common variable immunodeficiency, 6.2% had transient hypogammaglobulinaemia and 2.7% X-linked agammaglobulinaemia.

Allergic evaluation revealed that 62.8% of the patients had ever wheezing, 36.3% had current wheezing, 33% had physician-diagnosed asthma, 51.3% had a history of allergic rhinitis, 22.1% had a history of atopic dermatitis, 18.6% had a positive skin prick test and 42.5% had bronchial hyperreactivity with methacholine challenge test (Table 1).

When patients with selective IgA deficiency and IgG subclass deficiency were compared, those with IgA deficiency had a higher rate of ever wheezing ($P = 0.005$), whereas the rate of current wheezing was similar ($P = 0.301$). Patients with partial IgA deficiency and IgG subclass deficiency were similar in those with IgA deficiency with a history of ever wheezing and current wheezing ($P = 0.138$ and $P = 0.541$, respectively). Besides, individual or familial history of other