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Original Article

Epidemiological and clinical features of patients with primary antibody deficiency disorders in the East of Turkey

Mehmet Yavuz Ozbey[1], Mehmet Aslan[1], Erdem Topal[2]

[1]Inonu University, Faculty of Medicine Department of Pediatrics, Malatya, Turkey
[2]Inonu University, Faculty of Medicine Department of Pediatric Allergy and Immunology, Malatya, Turkey

Abstract

Aim: To describe the demographic and clinical features of patients diagnosed with primary antibody deficiency
Material and Methods: The medical records of pediatric patients who were diagnosed with primary antibody deficiency were reviewed. Patients were diagnosed with primary antibody deficiency based on the European Society for Immunodeficiencies diagnostic criteria.
Result: A total of 60 patients with primary antibody deficiency were identified; 39 patients (65%) were male and median age was 5 (1-18) years of age, while median diagnosis age was 3 (6 mo-14 yr) years. Twenty-one patients (35%) were diagnosed with transient hypogammaglobulinemia of infancy, thirteen (21.7%) with selective Ig A deficiency, five (8.3%) with congenital agammaglobulinemia, five (8.3%) with selective Ig M deficiency, five (8.3%) with unclassified hypogammaglobulinemia, four (6.7%) with Ig G subclass deficiency, two (3.3%) with severe combined immune deficiency, two (3.3%) with common variable immunodeficiency, two (3.3%) with hyper Ig M syndrome, and one patient was diagnosed with pneumococcal vaccine responsiveness, respectively. Eleven patients (18.3%) had consanguinity and six patients (10%) had family history. The most common complaint was frequent respiratory tract infections. Four patients had dermatitis in addition to infection. Three patients had hematopoietic stem cell transplantation and 23 patients (38.3%) received intravenous immunoglobulin treatment. Two patients died during the follow up.
Conclusion: Our results indicated that diagnosis is delayed and the patients who are diagnosed with primary antibody deficiency frequently have respiratory tract infections.

Keywords: Epidemiology; Intravenous Immunoglobulin; Primary Antibody Deficiency.

INTRODUCTION

Primary antibody deficiencies are a heterogeneous disease group which occur due to deficiencies in the functioning of immune system as a result of inherited gene defects (1). Primary antibody deficiencies are the most common immune deficiencies and they are characterized by a broad disease spectrum in which specific antibody production against antigens is damaged as a result of the defect in any of the steps critical for B cell development (2-4). According to The International Union of Immunological Societies (IUIS) classification, primary antibody deficiency is classified as congenital agammaglobulinemia, variable immunodeficiency syndrome, diseases associated with the lowness of at least two immunoglobulin isotype with the presence of low or normal B cell, hyper Ig M syndrome, selective Ig M deficiency, Ig G subclass deficiency, selective antibody deficiency and Transient Hypogammaglobulinemia of Infancy (THGI) (5). Although immune deficiencies occur with a heterogeneous clinic, common characteristics of all are chronic and/or recurrent infections. Especially pyogenic infections are the most common infections (6). Most commonly influenced system is the respiratory tract and this is followed with gastrointestinal system involvement (7). In infections which have a severe course and which do not respond well to treatment especially after the first 4-6 months of life, immune antibody deficiency should be suspected (6,8). In primary antibody deficiencies, the basis for treatment consists of timely IVIG replacement therapy and antimicrobial therapy (6). Delays in diagnosis and treatment have a negative effect on the patient's prognosis. For this reason, early detection of the disease is important in terms of early diagnosis and prevention of complications.

The aim of our study is to increase awareness in physicians on the issue by presenting demographic and clinical features of patients with primary antibody deficiency in our clinic.

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Corresponding Author: Erdem Topal, Inonu University, Faculty of Medicine Department of Pediatric Allergy and Immunology, Malatya, Turkey, **E-mail:** erdemtopal44@gmail.com

MATERIAL and METHODS

A total of 60 patients who were diagnosed with primary antibody deficiency at Inonu University Faculty of Medicine Turgut Özal Medical Centre Pediatric Allergy and Immunology Clinic between the years 2013 and 2016 were included in the study. "European Society for Immunodeficiencies (ESID)" diagnostic criteria were used for the diagnosis of primary antibody deficiency (9). The patients' files were reviewed retrospectively. The patients' demographic data such as age and gender and their complaints for referral, diagnosis age, clinical features, family history and laboratory findings were analyzed. Within this context, blood relative parents, immunodeficiency history in the family, history of child loss due to similar disease, clinical features at the moment of admission, physical examination findings, and treatments received and complications which developed in the follow-up were recorded.

Statistical Analysis

SPSS (SPSS for Windows, Version 17.0, SPSS Inc, U.S.A) program was used for statistical analysis. Variables of qualitative data were given as number and percentage, while data of quantitative variables were given as mean (min-max). Approval was taken from Inonu University Faculty of Medicine local ethical board with the data and number 2017/10-5. All participants provided written informed consent.

RESULTS

Demographic features

Sixty patients with primary antibody deficiency were included in the study. 21 (35%) of the patients were females, while 39 (65%) were males. Patients' mean age was 5 years (1-18) of age, while their mean diagnosis age was 3 (6 months – 14 year) years of age. 11 (18.3%) of the patients had a history of relative marriage. 6 (10%) of the patients had history of primary antibody deficiency in the family. When the etiology of primary immunodeficiency coursing with primary antibody deficiency was examined, 21(35%) were found to have transient hypogammaglobulinemia of infancy, 13 (21.7%) had selective Ig A deficiency, 5 (8.3%) had congenital agammaglobulinemia, 5 (8.3%) had selective Ig M deficiency, 5 (8.3%) had unclassified hypogammaglobulinemia, 4 (6.7%) had Ig G subclass deficiency, 2 (3.3%) had severe combined immune deficiency, 2 (3.3%) had common variable immunodeficiency, 2 (3.3%) had hyper Ig M syndrome and 1 (1.7%) patient had pneumococcal vaccine responsiveness (Table 1).

Clinical features and follow-up

The most frequent complaint of referral was recurrent infections. The most frequently affected system was respiratory tract. Together with infections, dermatitis findings accompanied 4 (6.7%) patients. In patients with primary antibody deficiency, all had respiratory tract infection, especially pneumonia, irrespective of their immunodeficiency type. In addition, one of our patients with congenital agammaglobulinemia and another patient with a diagnosis of Hyper Ig M had been followed up with a diagnosis of arthritis initially, later they were diagnosed with immunodeficiency. A significant decrease was found in the frequency of patients who were given IVIG" replacement. The patient with XLA had sequela following meningoencephalitis. Two patients were found to die in the follow-up.

Table 1. Epidemiological and Clinical Features of Patients with Primary Antibody Deficiency

Variables	n (%)
Sex, male	39 (65)
Age, median (min-max), year	5 (1-18)
Age of diagnosis, median (min-max),year	3 (0.5-14)
Complaint of application	
Recurrent upper respiratory tract infections	49 (81.7)
Recurrent lower respiratory tract infection	22 (36.7)
Recurrent wheezing	25 (41.7)
Dermatitis	4 (6.7)
Skin infections	4 (6.7)
Oral candidiasis	1(1.7)
Arthritis	1 (1.7)
Recurrent diarrhea	1 (1.7)
Consanguinity	11 (18.3)
Family history	6 (10)
Etiology	
Congenital agammaglobulinemia	5 (8.3)
Severe combined immune deficiency	2 (3.3)
Common variable immunodeficiency	2 (3.3)
Hyper Ig M syndrome	2 (3.3)
Unclassified hypogammaglobulinemia	5 (8.3)
Transient hypogammaglobulinemia	21 (35)
Ig G subclass deficiency	4 (6.7)
Pneumococcal vaccine responsiveness	1 (1.7)
Selective Ig A deficiency	13 (21.7)
Selective Ig M deficiency	5 (8.3)

DISCUSSION

Our aim in this study was to present patients with primary antibody deficiency monitored in our clinic and to increase awareness of physicians in terms of the clinical features of these rarely seen diseases. We found that in our patients with primary antibody deficiency, the diagnosis was delayed, and the most frequent referral complaint was recurrent respiratory tract infections, especially lower respiratory tract infection.

Although both genetic and molecular diagnostic tests have been developed recently, diagnosis of immunodeficiency diseases are delayed. One of the most important reasons for this is the fact that physicians are not sufficiently aware of immunodeficiency diseases and clinical

presentations. As a result of this, patients' diagnosis age has been on the increase. Studies conducted have shown that there are 2.3 years of delay on average between the onset of complaints and diagnosis age in patients with immunodeficiency (10,11). In our study, although complaints generally started after the first 6 months of life, mean diagnosis age was 3 years of age. These results show that physicians do not recognize clinical results of immunodeficiency diseases.

Immunodeficiency is among the most commonly seen infections in patients. In immunodeficiency, infection type and affected system differ according to the defected cell. Immunodeficiencies with cell defect occur mainly with antibody deficiency. Recurrent lower and upper respiratory tract infection are seen in patients (10,11). In more than 90% of the immunodeficiencies coursing with primary antibody deficiency, sinopulmonary infections are seen (10,11). Patients in our study also had recurrent lower respiratory tract infections.

As in other immunodeficiencies, most of the antibody deficiencies are autosomal recessive. For this reason, we expect the frequency of immunodeficiencies to be higher when compared with western countries in which relative marriage is frequent. However, it won't right to give an exact number for frequency in our country since the existing data and incomplete and some of the patients died before diagnosis.

Our study had a few limitations. First of all, the study was a retrospective file scanning. Secondly, although diagnostic criteria were conducted according to ESID diagnostic criteria, genetic or molecular studies were not conducted on some patients.

CONCLUSION

As a conclusion, diagnosis is delayed in primary antibody deficiency. Patients who have frequent respiratory tract infection and those whose parents had blood relation, primary antibody deficiency should be suspected.

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Mehmet Yavuz Ozbey ORCID: 0000-0002-9895-4851
Mehmet Aslan ORCID: 0000-0003-0190-4274
Erdem Topal ORCID: 0000-0002-4439-2689

REFERENCES

1. Primary immunodeficiency diseases. Report of an IUIS Scientific Committee. International Union of Immunological Societies. Clin Exp Immunol 1999;118:1-28.
2. Gathmann B, Binder N, Ehl S, et al. The European internetbased patient and research database for primary immunodeficiencies: update 2011. Clin Exp Immunol 2012;167:479-91.
3. Driessen G, van der Burg M. Educational paper: primary antibody deficiencies. Eur J Pediatr 2011;170:693-702.
4. Javier FC 3rd, Moore CM, Sorensen RU. Distribution of primary immunodeficiency diseases diagnosed in a pediatric tertiary hospital. Ann Allergy Asthma Immunol 2000;84:25-30.
5. Bousfiha A, Jeddane L, Picard C, et al. The 2017 IUIS Phenotypic Classification for Primary Immunodeficiencies. J Clin Immunol 2018;38:129-43.
6. Fried AJ, Bonilla FA. Pathogenesis, diagnosis, and management of primary antibody deficiencies and infections. Clin Microbiol Rev 2009;22:396-414.
7. Mamishi S, Eghbali AN, Rezaei N, et al. A single center 14 years study of ınfectious complications leading to hospitalization of patients with primary antibody deficiencies. Braz J Infect Dis 2010;14:351-5.
8. Ballow M. Primary immunodeficiency disorders: antibody deficiency. J Allergy Clin Immunol 2002;109:581-91.
9. https://esid.org/Working-Parties/Registry-Working-Party/Diagnosis-criteria acess date 15.12.2018
10. Habahbeh ZM, Abu-Shukair ME, Almutereen MA, et al. Primary antibody deficiencies at Queen Rania Children Hospital in Jordan: single center experience. Iran J Immunol 2014;11:49-58.
11. Yorulmaz A, Artaç H, Kara R, et al. Primer İmmün Yetmezlikli 1054 Olgunun Retrospektif Değerlendirilmesi. Astım Allerji Immünoloji 2008;6:127-34.