REVISTA BRASILEIRA DE REUMATOLOGIA

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SOCIEDADE BRASILEIRA DE REUMATOLOGIA

Original article

Autoimmune diseases and autoantibodies in pediatric patients and their first-degree relatives with immunoglobulin A deficiency

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ARTICLE INFO

Article history:
Received 23 January 2014
Accepted 6 October 2014
Available online 4 January 2015

Keywords:
IgA deficiency
Autoimmunity
Autoantibodies
Thyroiditis

ABSTRACT

Introduction: Clinical manifestations of Immunoglobulin A Deficiency (IgAD) include recurrent infections, atopy and autoimmune diseases. However, to our knowledge, the concomitant evaluations of autoimmune diseases and auto antibodies in a cohort of IgAD patients with current age >10 years and their relatives have not been assessed.
Objectives: To evaluate autoimmune diseases and the presence of auto antibodies in IgAD patients and their first-degree relatives.
Methods: A cross-sectional study was performed in 34 IgAD patients (current age >10 years) and their first-degree relatives. All of them were followed at a tertiary Brazilian primary immunodeficiency center: 27 children/adolescents and 7 of their first-degree relatives with a late diagnosis of IgAD. Autoimmune diseases and autoantibodies (antinuclear antibodies, rheumatoid factor, and anti-thyroglobulin, anti-thyroperoxidase and IgA class anti-endomysial antibodies) were also assessed.
Results: Autoimmune diseases ($n = 14$) and/or autoantibodies ($n = 10$, four of them with isolated autoantibodies) were observed in 18/34 (53%) of the patients and their relatives. The most common autoimmune diseases found were thyroiditis (18%), chronic arthritis (12%) and celiac disease (6%). The most frequent autoantibodies were antinuclear antibodies (2%), anti-thyroglobulin and/or anti-thyroperoxidase (24%). No significant differences were observed in the female gender, age at diagnosis and current age in IgAD patients with and without autoimmune diseases and/or presence of auto antibodies ($p > 0.05$). The frequencies of primary immunodeficiencies in family, autoimmunity in family, atopy and recurrent infections were similar in both groups ($p > 0.05$).
Conclusion: Autoimmune diseases and auto antibodies were observed in IgAD patients during follow-up, reinforcing the necessity of a rigorous and continuous follow-up during adolescence and adulthood.

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http://dx.doi.org/10.1016/j.rbre.2014.10.003

Doenças autoimunes e autoanticorpos em pacientes pediátricos e seus parentes de primeiro grau com deficiência de imunoglobulina

Palavras-chave:
Deficiência de IgA
Autoimunidade
Autoanticorpos
Tireoidite

RESUMO

Introdução: As manifestações clínicas da deficiência de imunoglobulina A (DIgA) incluem infecções recorrentes, atopia e doenças autoimunes. No entanto, para o nosso conhecimento, as avaliações concomitantes de doenças autoimunes e autoanticorpos em uma coorte de pacientes com DIgA com idade atual > 10 anos e seus parentes não foram feitas.
Objetivos: Avaliar doenças autoimunes e presença de autoanticorpos em pacientes com DIgA e seus parentes de primeiro grau.
Métodos: Estudo transversal feito em 34 pacientes com DIgA (idade atual > 10 anos) e em seus parentes de primeiro grau. Todos foram acompanhados em um centro terciário brasileiro para imunodeficiência primária: 27 crianças/adolescentes e sete de seus parentes de primeiro grau com diagnóstico tardio de DIgA. Doenças autoimunes e autoanticorpos (anticorpos antinucleares, fator reumatoide e antitireoglobulina, antitiroperoxidase e anticorpos antiendomísio da classe IgA) também foram avaliadas.
Resultados: Doenças autoimunes (n = 14) e/ou autoanticorpos (n = 10, quatro deles com autoanticorpos isolados) foram observadas em 18/34 (53%) dos pacientes e seus parentes. As doenças autoimunes mais comuns encontradas foram tireoidite (18%), artrite crônica (12%) e doença celíaca (6%). Os autoanticorpos mais frequentes foram anticorpos antinucleares (2%), antitireoglobulina e/ou antitireoperoxidase (24%). Nenhuma diferença significativa foi observada no sexo feminino, idade no momento do diagnóstico e idade atual em pacientes com DIgA com e sem doenças autoimunes e/ou presença de autoanticorpos (p > 0,05). As frequências de imunodeficiência de primárias na família, autoimunidade em família, atopia e infecções recorrentes foram semelhantes em ambos os grupos (p> 0,05).
Conclusão: Doenças autoimunes e autoanticorpos foram observadas em pacientes com DIgA durante o acompanhamento, o que reforça a necessidade de um acompanhamento rigoroso e contínuo durante a adolescência e a idade adulta.

Introduction

IgA deficiency (IgAD) is the most frequent primary immunodeficiency (PID). It is a defect which is caused due to terminal B lymphocyte differentiation, resulting in an insufficient production of serum and secretory IgA (SIgA).[1–4] SIgA has some protective functions on mucosa, neutralizing microorganisms and proteins.[5–8]

The clinical manifestations of IgAD patients range from asymptomatic to recurrent infections, allergic symptoms and autoimmune diseases,[9] with an increased autoantibodies production.[10] Of note, autoimmune diseases occur in 7–36% of IgAD patients and autoantibodies are observed in more than 40% of the patients.[10,11] The prevalence of IgAD is 1–4% in systemic lupus erythematosus (SLE) patients,[10] 2–4% in rheumatoid arthritis (RA)[10] and 2.6% in celiac disease (CD).[12] Furthermore, autoimmune diseases are frequently reported in relatives of IgAD patients. Among the first-degree relatives of IgAD patients, 10% had autoimmune diseases compared to 5% in general population.[11–15]

However, to our knowledge, the concomitant evaluation of autoimmune diseases and auto antibodies in a cohort of IgAD patients with current age greater than 10 years and their relatives with IgAD has not been studied.

Therefore, the aim of this study was to evaluate the occurrence of autoimmune diseases and auto antibodies in a cohort of IgAD patients with current age greater than 10 years and their respective first-degree relatives followed at a tertiary Brazilian reference center for pediatric PID.

Patients and methods

We selected 126 IgAD patients followed at a Brazilian pediatric reference center for PID in the last 30 consecutive years. Ninety-two of the IgAD patients who were diagnosed at childhood had current age lower than 10 years and were excluded from this study. IgA assessment was systematically performed in all first-degree relatives that presented any symptoms or signals of recurrent infectious and autoimmune diseases, and IgAD diagnosis was established in 7/62 (11%) of first-degree relatives. Therefore, a cross-sectional study was carried out in 34 IgAD patients: 27 IgAD patients (current age greater than 10 years) and their 7 first-degree relatives with a late diagnosis of IgAD. The study was approved by the Ethical Committee and the written informed consent was obtained from all participants.

A systematic clinical evaluation was performed and included the assessments of various autoimmune disorders, recurrent infectious episodes, atopic manifestations and current or past neoplasia in the IgAD patients and their respective families. IgAD was diagnosed according to Pan-American Group for Immunodeficiency and European