COMMUNICATION

Prevalence of autoantibodies in a group of hereditary angioedema patients *

Prevalência de autoanticorpos em uma população com angioedema hereditário

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Abstract: Hereditary Angioedema is a dominantly inherited disease. Routine screening of autoantibodies (AAB) is not recommended for individuals with Hereditary Angioedema; however, prevalence of these antibodies in Hereditary Angioedema patients is not well documented. We aim to determine the prevalence of AAB so that individuals at risk of developing autoimmune diseases can be identified. Fifteen patients with Hereditary Angioedema attended at Clementino Fraga Filho University Hospital accepted to participate in this study. Prevalence of AAB was 40%. Our data indicate high prevalence of AAB in patients with Hereditary Angioedema. Large-scale studies should be considered to determine the significance of these AAB in the follow-up care of patients with Hereditary Angioedema.
Keywords: Angioedemas, hereditary; Autoantibodies; Hereditary angioedema type III; Hereditary angioedema types I and II; Prevalence

Resumo: O Angioedema Hereditário é uma doença autossômica dominante. A pesquisa de rotina para autoanticorpos não é recomendada para pacientes com Angioedema Hereditário; entretanto, a prevalência desses anticorpos em pacientes com Angioedema Hereditário não está bem documentada. Objetivamos determinar a prevalência de autoanticorpos para identificar indivíduos sob risco de desenvolver doenças autoimunes. Quinze pacientes com Angioedema Hereditário atendidos no Hospital Universitário Clementino Fraga Filho aceitaram participar do estudo. A prevalência de autoanticorpos foi de 40%. Nossos dados indicam alta prevalência de autoanticorpos em pacientes com Angioedema Hereditário. Estudos de maior escala deveriam ser considerados para determinar a significância desses autoanticorpos no acompanhamento clínico de pacientes com Angioedema Hereditário.
Palavras-chave: Angioedemas hereditários; Angioedema hereditário tipos I e II; Angioedema hereditário tipo III; Auto-anticorpos; Prevalência

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Hereditary Angioedema (HAE) is a dominantly inherited disease that affects about 1:50000 persons. It has been reported in all races, and there is no sex bias in its forms (types I, II and III). Type I is a result of a quantitative defect in the plasma inhibitor of the first component of complement (C1INH). Type II results from a functional defect in C1INH. The third form occurs in people with quantitatively and functionally normal C1INH activity, and is related to estrogenic activity.

An increased frequency of several autoimmune diseases in patients with HAE has been reported. These diseases include glomerulonephritis, Sjögren syndrome, thyroiditis, and lupus. There are several reports of patients, with both deficiencies (type I and II), who developed lupus, including that of twins with HAE who presented a kind of "familial" lupus. [1-6] HAE has also been described in association with glomerulonephritis.[7-9]

Circulating autoantibodies are diagnostic markers for a variety of autoimmune diseases. Routine screening of immune-mediated antibodies is not recommended for people with HAE; however, the prevalence of these antibodies in HAE patients is not well documented.

This study was designed to determine the prevalence of autoantibodies so that any individual at risk of developing autoimmune diseases can be identified.

It's a cross-sectional study in which patients with Hereditary Angioedema attended at the Clinical Immunology Service of Clementino Fraga Filho University Hospital (HUCFF – UFRJ) from July 2009 to July 2010 were followed. Institutional review board approval was obtained, and all patients participating in the study or their parents/guardians (when patients were younger than 18 years old) gave us their written informed consent. Therefore, it is an intentional sample. Eligibility criteria included previously or newly diagnosed HAE, regardless of the type.

Patients were treated according to the attending immunologist's preference. Treatment options included observation alone, attenuated androgens and observation plus estrogen avoidance (the latter in type III HAE patients).

All the laboratory evaluations were performed according to standard methods used at HUCFF – UFRJ attending Laboratory. Laboratory tests included antithyroid peroxidase antibody (antiTPO), antithyroglobulin antibody (ATG), rheumatoid factor (RF), antinuclear antibody (ANA), anti deoxyribonucleoproteins antibody (anti-DNA), venereal disease research laboratory (VDRL), anti cardiolipin antibodies IgM and IgG.

Binominal was the statistical analysis method used. A *P* value of less than 0.05 was considered to indicate a statistically significant difference among the groups compared.

Fifteen patients from 12 to 57 years old, with a mean age of 33 years, participated in the study. Thirteen of them were diagnosed as type I HAE (87%) and 2 as type III HAE (13%). Ten females and 5 males were enrolled.

Among these 15 patients, six (46%) had positive autoantibodies dosage, all of them were type I HAE. The prevalence of autoantibodies in the group tested was 40%. The autoantibodies identified among the patients in this group were ANA and anticardiolipin antibodies IgM and IgG.

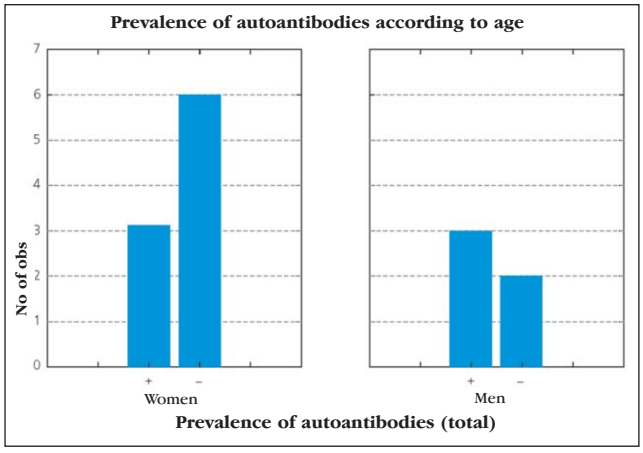
ANA is an AAB present in more than 98% of the patients diagnosed with Systemic Erythematosus Lupus. ANA low titers can also be found in about 10% of normal people. Two patients (13%) presented ANA in low titers.

Although prevalence of AAB in men (60%) was twice greater than in women, we found no significant difference in the likelihood of testing positive for autoantibodies between genders. (Graph 1)

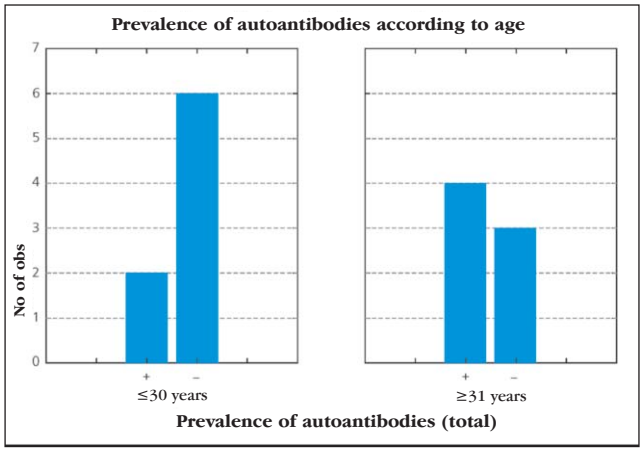
Considering age, prevalence of AAB in patients older than 30 years (57%) is greater than in younger ones (23%). (Graph 2) However, no significant difference in the likelihood of testing positive for autoantibodies was found. The limited sample size could have masked small differences.

Our data suggest that patients with type I HAE tend to have serologic autoimmune abnormalities. Whether this portends later expression of autoimmune disease or not is unknown. If it were possible to predict an autoimmune disease, different treatment strategies could be employed earlier in the course of the disease. The purpose of this study has been to determine the prevalence of different kinds of autoantibodies in a group of patients diagnosed with HAE.

Although none of the patients exhibited overt thyroid or connective tissue disease, 46% of the patients tested demonstrated an abnormal antibody



Graph 1: Autoantibodies prevalence according to sex. +: positive autoantibodies; -: negative autoantibodies



Graph 2: Autoantibodies prevalence according to age. +: positive autoantibodies; -: negative autoantibodies

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Typically, autoantibody testing is not obtained from people presenting with HAE. Further studies are necessary to determine whether it is reasonable or cost-effective to perform those dosages. The significance of positive autoantibodies and the development of later disease is not known, but the presence of a positive test may indicate the need for follow-up and early detection of symptoms for a treatable and life-threatening entity such as thyroid storm. Large-scale studies should be developed to determine the significance of these abnormalities in the long-term follow-up care of these patients.

As autoantibodies can be found in healthy people, large-group trials would be necessary to establish the real correlation between autoantibodies positivity and HAE, considering sex and age. ❑

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