ORIGINAL ARTICLE

Autoserum skin tests in allergic patients, and in autistic patients and their mothers

Pruebas dermatológicas con autosuero en pacientes alérgicos y en pacientes autistas y sus madres

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ABSTRACT

Introduction: Allergies are frequently found among patients with autism and autism shows an increased frequency among the allergic patients.
Objective: To demonstrate that allergies and autism share some similar immunological patterns.
Methods: The autoserum skin test (ASST) was used to demonstrate the presence of anti-IgE and/or anti-IgE receptor antibodies (FcεRIα).
Results: The ASST demonstrated similar frequency, positives/positives and negatives/negatives, considering allergic and autistic patients. These similarities didn't exist when comparing with the control group. A positive correlation had been found with the results of autistic patients and their mothers.
Conclusions: Autistic and allergic patients share some immunological similarities. Both differ from normal controls. It is not uncommon autistics with allergic symptoms and allergic patients with autism. If the immunological findings represent a clinical bridge between both processes, it is under discussion. Also it was demonstrated a possible genetic correlation between the patients with autism and their mothers.

Key words: Allergy; autism; anti-IgE receptor; anti-IgE; IgE; skin test.

RESUMEN

Introducción: las alergias se encuentran con frecuencia en pacientes autistas y asimismo el autismo muestra una gran presencia entre los pacientes alérgicos.

Objetivo: demostrar que las alergias y el autismo comparten algunos patrones inmunológicos similares.
Métodos: la prueba dermatológica con autosuero se utilizó para demostrar la presencia de anti-IgE y/o de anticuerpos de receptores de Ig/E (FcεRIα).
Resultados: la prueba ASST confirmó la frecuencia similar de positivos/positivos y de negativos/negativos en pacientes alérgicos y en pacientes autistas. Estas similitudes no existieron cuando se realizó la comparación con el grupo control. Se había hallado una correlación positiva con los resultados obtenidos en pacientes autistas y sus madres.
Conclusiones: los pacientes autistas y los pacientes alérgicos comparten ciertas similitudes inmunológicas. Ambos se diferencian del grupo de controles sin estas condiciones. Resulta frecuente encontrar pacientes autistas con síntomas alérgicos y pacientes alérgicos con signos de autismo. Es motivo de análisis si los hallazgos inmunológicos representan un puente clínico entre ambos procesos. Asimismo se mostró una posible correlación genética entre los pacientes con autismo y sus madres.

Palabras clave: alergia; autismo; receptor de anti-IgE; anti-IgE; IgE; prueba dermatológica.

INTRODUCTION

Infantile autism was first described by Leo Kanner (1894-1981) in 1943.[1] It is defined by DSM-IV criteria as a childhood behavioral and neurological disorder with onset prior to three years of age.[2] In 1978 in the United States 0.01 % of the children showed autistic symptoms.[3] In 2008 this percentage increased to 0.88 %.[4,5]

The history of allergies comes about two thousand years ago. As to autism, its frequency is rising. Food allergies, for example, have increased about 1,2 percentage point per decade.[6]

This paper attempts to demonstrate some immunological aspects common in the autism and in the allergies.

We studied the presence of anti-IgE and/or anti-IgE receptor antibodies in both groups) through ASST procedure technique.[7-9]

METHODS

A cross-sectional study was conducted with 251 residents of Brasília, Brazil, between 2012 and 2014. These individuals were divided in four groups.

The allergic patients were a group of patients from a private clinic, all with respiratory allergic processes (asthma and/or rhinitis) associated with cutaneous processes (atopic derrmatitis). The patients or their parents who arrived at the clinic with the mentioned symptoms were asked if they would like to participate in the study. This group contains 104 individuals, ages between 5 and 74 years, 50 males and 54 females.

The control group were the non-allergic companion of allergic patients, medicine students and some internal collaborators who volunteered to participate in the research. The group was composed of 63 people, aged between 4 and 71 years, 20 males and 43 females. The autistic patients were referred through groups of autistic relatives in Brasília, DF. These patients with autism without allergy were 42, all males, ages between 3 and 14 years.

The mothers of the autistic patients were those of the children who participate the study, 42, ages between 25 and 62 years.

When the evaluation of the autistic and their mothers was considered concluded, the evaluations of the allergic ones were finished.

Drugs that might interfere with the ASST results were not used for seven days before and on the day of the test.

The procedure (ASST) was the following:[1,8] 0.05 mL of the patient's own serum was intradermally injected in the forearm skin; 0.05 mL of saline was used as control. The papule diameters were measured 15 minutes after injections. The result was considered positive when the serum papule diameter was at least 3.0 mm or greater than the diameter obtained with the saline. The ASST is a routine procedure with the patients evaluation in allergy clinics. It is in accordance with ethical standards.

The diagnosis of allergy was established through the history, clinical, and routine laboratorial findings. With the autistics the diagnosis was clinical and based on the criteria for autistic disorder as defined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV).[10]

For statistical evaluation, the chi-squared and the Fisher's method were used based on the number of the patients in the groups and the variables studied. The variable used in the study was the results of the ASST test, positive or negative, in each of studied groups.

RESULTS

The first hypothesis to be tested is whether the presence of anti-IgE and/or anti-IgE receptor antibodies in autistic patients is independent from the presence of these antibodies in their non-autistic mothers (table 1).

Table 1. The presence of the antibodies in autistics and normal mothers

Autistics	Normal mothers					
	PA		NA		Total	
	No.	%	No.	%	No.	%
PA	30	93.8	2	6.2	32	100
NA	4	40	6	60	10	100
Total	34	81	8	19	42	100

PA: presence of antibodies (positive test); NA: absence of the antibodies (negative test).

The chance of autistic patients with the presence of the antibodies (positive test) having mothers with the same antibodies is 15.12, and the chance of autistic patients without the presence of the antibodies (negative test) having mothers with no antibodies is 1.5. Positive autistic patients are 22.5 times more likely to have positive mothers than autistic patients without these antibodies (negative).

Table 2 shows the results of chi-squared (X^2) and Fisher's exact test. The null hypothesis is that when one data set is independent from other data set. In other words, we are testing if there is no association between the presence of antibodies in autistic patients, normal subjects, and in their mothers.

Table 2. Independence test results

Test	Statistic test	P-value	Degrees of freedom
Chi-square	11.0023	0.0091	1
Fisher	19.84	0.0091	1

According to the chi-square test and Fisher's exact test, assuming a 95-percent level of reliability, the variables are dependent: negative autistic patients are associated with negative mothers and positive autistic patients are associated with positive mothers.

The second hypothesis test verifies if the presence of antibodies distribution is homogeneous in three groups. It verifies if the presence of the antibodies depends on the type of pathology. Table 3 shows the proportions in the three groups analyzed: control group with no disease; autistic patients group; and allergic patients group.

Table 3. Pathology and the presence of the antibodies

	IgE anti-receptor		
Pathology	Positive	Negative	Total
Control group	22 (57.9 %)	16 (42.1 %)	38 (100 %)
Autistics	32 (76.2 %)	10 (23.8 %)	42 (100 %)
Allergic	74 (71.2 %)	30 (28.8 %)	104 (100 %)
Total	128 (69.6 %)	56 (30.4 %)	184 (100 %)

Table 4. Homogeneity chi-square test results

Test	Test statistic	P-value	Degrees of Freedom
χ^2(chi-square)	26,64	$1,65.\ 10^{-6}$	2

Table 4 shows the result of the chi-square test for homogeneity. The test verifies if groups with some pathology-autism or allergy-differ from the control group.

Based on the X^2 test, the hypothesis of similarity between groups was rejected. It is thus possible to affirm that the presence of antibodies occurs heterogeneously among autistic and allergic patients, and the control group.

DISCUSSION

The conexion of autism with allergies is an up to date discussion. In this paper it will be tried to find an immunological bridge between both pathologies.

Hypothesis to explain the autism are multiples. Increased gut permeability has been considered. It facilitates a direct or an undirect aggression by microorganisms For example, the measles virus cross-reacts with the cell junction filaments affecting the intestinal mucosa's integrity and cell to cell communication, thereby producing a leaking effect and disfunction in intestinal absorption. This provokes the absorption of undesirable substances, such as phenolic amines, which are known to be deleterious for the autistics.[11,12]

The innoculation with pertussis toxin can produce a separation of the G-alpha protein from the retinoid receptor which the consequent increasing in the autism symptoms.

Autistic patients strongly react to inflammatory processes. Vaccines, such as measles, pertussis and rubella can trigger strong reactions in the form of fever, urticaria, angioedema and lethargy, which can last for more than 24 hours. Some authors considered the use of these vaccines as a precipitant factor of autistic symptoms.[13]

The influence of agrochemicals has been considered. Diets can influence the autistic behaviour. As so, gluten and casein, which are important allergens, have been incriminated for triggering autistic symptoms once they form opioids that cause a disruption both of neuroregulation and brain development.[14] By other way, some foods which can help autistics can also help the allergics. For example, the camel milk improves the autistic behaviour and ameliorates allergic symptoms.[15-17]

Genetic transmission can be considered in autism. When the HLA is HREs, DR3, DR43 or DR5 there is the possiblity that the disease will be more severe.[18] In this paper we show a significant statistical correlation between mothers and their autistic children (table 1) 47.6 % of autistic patients present allergies, mainly skin and food allergies.[19,20] Changes in the gut barrier, microorganisms, foods, environment (hygiene hypothesis), autoimmunity, etc., need to be considered in the physiopathology of allergies and autism.

Allergies are more frequent in autistic than in non-autistic patients. The allergy's severity is proportional to the degree of autism. Sixty-one percent of severe autistics have allergies, while 25 percent of moderately autistic children show less severe allergies.[21]

With the allergic patients, the immunological pattern Th1/Th2 tends to go to Th2 with the consequent increasing of IgE, IL-4, IL-5, IL-9, IL-13 and eotaxin-3 with an attendant increase in eosinophil and mast cell survival. There is also an increase of C4B null allele, a reduction of TCD4+ lymphocytes. Most of these findings are found also in autistic patients.[4.22]

Autoimmunity plays part in allergies and autism.[23] Antibodies against neuronal cells, anti-MBP (myelin basic protein) and anti-MAG (myelin associated glycoprotein) are found in both groups. Anti-measles, herpes virus and *Chlamidia pneumoniae* antibodies or streptococcal M protein are more elevated in the autism associated with allergies than in non-allergic autistic patients.[24]

Allergic and autistic patients show a sort of immunological disruption. Repeated infections, mostly ear and upper respiratory tract infections, prolonged course of illnesses, and multiple drug reactions take part in the pathological day-by-day of them. Chronic infections predispose the sensitization to food proteins. Increased TNF-α associated with a reduction of counter regulatory cytokines helps the development of gut problems, with attendant adverse reactions to environmental factors.[23]

In the allergic diseases, as in chronic allergic urticaria, it is usual to detect an increased presence of anti-IgE and anti-IgE receptors antibodies. In this paper an identical proportion of these antibodies in autistic and in the allergic patients is demonstrated and also a correlation between ASST results in autistic patients and their mothers, which can mean a genetic correlation between them (table 3).

Based on the analysis of our data it is possible to conclude that the presence of the anti-IgE and/or anti-receptor IgE antibodies in autistic patients is strongly associated with the presence of the same antibodies in their mothers. This may indicate that in autism genetics, the presence of these antibodies may be a marker of heredity, which may also be a marker of autism.

The similarity of results in positive non-autistic allergic patients (71.1 %) and positive autistic patients (76.1 %) shows that the presence of the antibodies may be a common factor in the two conditions. Furthermore, the results showed evidence that the presence of the antibodies in autism and allergy occurs differently in the control group (table 4).

Is there a link between autism and allergy? When it is observed similar clinical and immunological findings in autistic and allergic individuals this just meaning a coincidental ocurrence? These are questions to be answered with further studies.

CONFLICTS OF INTEREST

No potential conflict of interest was reported.

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