Atopik dermatit otoimmün bir hastalık mıdır?

Is Atopic Dermatitis an Autoimmune Disease?

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Abstract
Background: IgE-type autoantibodies against self proteins have been detected in serum of the patients with atopic dermatitis (AD). The role of this IgE autoantibodies involved in the pathogenesis of AD remain unclear. The autologus serum skin testing is applied to both AD patients and healthy control and the results are evaluated in our study.
Methods: Autologous serum and normal saline are applied to the volar surface of right forearm of all the study groups.
Results: The autologous serum skin testing is evaluated positive in 70% of the AD patients and 16.7% of the control group. The test was 67.7% positive in AD patients with a history of atopy whereas 65.5% postive in patients with a negative atopy history. The moderately severe AD patients according to SCORAD scoring system showed 72% positivity on the other hand the test was positive in 60% of the mildly severe AD patients. Test was positive in 72.7% of patients with high serum IgE and 66.7% in patients with low serum IgE.
Conclusion: We detected 70% positive autologus serum skin testing in AD patients and test positivity was found higher in patients with atopy history, moderately severe disease calculated by SCORAD index and high serum IgE levels.
Key words: Autologous serum skin testing, atopic dermatitis, IgE autoantibodies

Özet
Amaç: Atopik dermatitli hastaların serumlarında, kendi proteinlerine karşı IgE tabiatında otoantikorlar saptanmıştır. IgE otoantikorların, atopik dermatit'in patogenezindeki rolleri tam olarak bilinmemektedir. Çalışmamızda, atopik dermatitli hastalar ile sağlıklı bireylere otolog serum deri testi uygulandı ve sonuçlar değerlendirildi.
Materyal ve Metod: Atopik dermatitli hastalar ve kontrol grubundaki sağlıklı bireylerin sağ önkol fleksör yüzlerine otolog serum ve serum fizyolojik uygulandı.
Bulgular: Atopik dermatitli hastaların %70'inde ve kontrol grubunun %16,7'sinde otolog serum deri testini pozitif olarak saptadık. Atopi anamnezi olan atopik dermatitli hastaların %67,7'sinde otolog serum deri testini pozitif olarak tespit etik. Atopi anamnezi olmayan atopik dermatitli hastalarda bu oran %65,5 düzeyindeydi. SCORAD indeksine göre orta şiddetteki atopik dermatitli hastaların %72'sinde otolog serum deri testini pozitif olarak saptanırken hafif şiddetteki atopik dermatitli hastaların %60'ında otolog serum deri testini pozitif olarak saptadık. Serum total IgE düzeyleri yüksek olan atopik dermatitli hastaların %72,7'sinde otolog serum deri testi pozitif olarak gözlenirken, serum total IgE düzeyleri düşük olan atopik dermatitli hastaların %66,7'sinde otolog serum deri testini pozitif olarak gözlemlendi.
Sonuç: Çalışmamızda otolog serum deri testini atopik dermatitli hastaların %70'ninde otolog serum deri testini pozitif olarak saptadık. Atopi anamnezi bulunan atopik dermatitli hastalar, SOCRAD indeksine göre orta şiddetteki hastalar ile serum total IgE düzeyleri yüksek olan atopik dermatitli hastalarda otolog serum deri testinin pozitifliğini yüksek olarak tespit ettik.

Anahtar kelimeler: Otolog serum testi, atopik dermatit, IgE otoantikorları
Conclusions: Late admission of patients and retroperitoneal area injury are responsible for high morbidity and mortality in blunt and penetrating abdomen injuries. If Damage Control Surgery tecniques are applied early and dynamical in critical cases, this may reduce mortality.
Key words: Blunt and penetrating abdomen injury, risk factors, morbidity, damage control surgery

Introduction

Atopic dermatitis (AD) is a chronic recurrent skin disease, with an increasing prevelance which affects 5-20% of children and 1-3% of adults (1). The pathogenesis of atopic dermatitis is not fully understood, but the disease is thought to occur as a result from interactions between susceptibility genes, the host environment, skin barrier defects, infections and immunological factors (2, 3).

Recently, autoreactive IgE antibodies against self-proteins or environmental antigens were detected in AD patients (4-6). These autoantigens are defined in different tissues and cell types whose complementary DNA coding sequences are detected at molecular levels. IgE autoimmunity can play a pathologic mechanism in AD which is revealed in paradigmatic models (7). Furthermore, it has been shown that the levels of IgE autoantibodies are associated with severity of disease. The determination of these antibodies in AD patients can be of importance, providing benefit in prognosis determinance and treatment selection.

Autologus serum skin testing (ASST) is a simple in vivo screening test used to detect autoreactivity. A wheal and flare response after intradermal injection of autologous serum with a diameter $\geq$ 1.5mm as compared to saline is a positive ASST. Detection of a positive ASST in AD patients can be a supporting data for the existence of autoreactive IgE antibodies in the serum of patients. This study is conducted with sixty AD patients and thirty control groups. ASST is performed to both groups then the results are evaluated.

Methods

The Clinical Research Ethics Committee Scientific Research Project supported our study, which started in January 2010 and ended in June 2010. The study protocol was approved by the Helsinki Declaration of ethical guidelines and all patients gave informed consent prior to participation in the study. Sixty AD patients (25 males and 35 females) and 30 healthy individuals (13 males and 17 females) are carefully examined by means of clinical history, medications, clinical symptoms and signs. AD patients are diagnosed according to the criteria of Hanifin and Rajka (8). The SCORAD index is used to determine the severity of the eczema. The patients showing evidence of any other disease are not included to our study. No drug was allowed fourteen days prior to the test, including antihistamines and steroids.

The ASST is performed on the basis of EAACI recommendations (9). Samples of 5 ml of venous blood were collected in sterile Vacutainers© without a clotting accelerator, assigned properly and allowed to clot at room temperature for 30 minutes. Later, serum was centrifuged at 500g for 10 minutes. Samples of 0.05 ml of centrifuged undiluted serum and 0.9% sterile normal saline were injected intradermally into the volar aspect of the right forearm with a gap of 5 cm between injection sites. Wheal and flare response was measured after 30 minutes. ASST is accepted positive if serum-induced wheal is red with diameter wider by $\geq$1.5 mm than the saline-induced response. The diameter is measured via digital calliber measuring device (Figure 1) (10).

Besides, total IgE levels (3G Allergy®–various allergens RAST testing) are measured by chemiluminescent immunoassay system method followed through Immulite 2000 device.

Statistical analysis

Statistical analysis are performed by SAS® 9.22 software. In the beginning, introductory statistics for the variables are calculated. Later, ASST test results are compared in AE patients and control group as well as the relationship of atopic history, disease severity and total IgE levels in atopic patients is evaluated, by two-proportion test. P-value <0.05 is regarded statistically significant.

Results

The mean age of AD patients and the control group was 16.15±13.69 and 13.07±10.56, respectively. An atopy history (asthma, allergic rhinitis etc) is stated by 51.7% (n=31) of the AD patients. The mean SCORAD indices of AD patients were calculated as 24.250±7.098, of which 83.3% (n=50) is moderately severe and 16.7% (n=10) is mild. Serum total IgE level is found high in 55% (n=33) of AD patients.

The ASST positivity was 70% in AD group, whereas it was 16.7% in control group. The difference in ASST positivity ratios between two groups was statistically significant (p=0.001) (Table 1). The test was positive in 67.7% of AD patients with an atopy history, whereas 65.5% in patients with negative history, indicating a statistically insignificant relation (p=0.464) (Table 2).

The fifty moderately severe AD group evaluated by SCORAD index showed 72% positivity. Six out of ten mild AE group tested positive, meaning 60% test positivity. This was not remarkable (p= 0.474) (Table 2).

Thirty-three patients with high serum IgE levels revealed 72.7% positivity in test and the twenty-seven patients with low IgE levels showed 66.7% positivity. The difference between high level IgE patients and low level IgE patients were not significant (p=0.612) (Table 2).

Discussion

It has long been known that AD is often associated with high serum IgE levels and sensitization against a variety of environmental allergens. On the other hand, the exacerbations on the course of AD are sometimes observed without a relation to an offending exposure. Some molecular homology between self proteins and these environmental allergens are described with the progress of the molecular biology methods, indicating these self antigens may be a contributing factor in exacerbations (11). So far, a broad spectrum of at least

140 autoallergens associated with AD are identified, the majority of which are intracellular proteins including the transcription factor LEDGF/DSF70, ribosomal P2 protein, cyclophilin, thiredoxin, Hom S1–5 secreted by keratinocytes and the manganese superoxide dismutase (MnSOD). The latter is sensitized by Malassezia sympodialis and well known as it can elicit an eczema reaction in normal skin of AD patients in atopy patch tests (5, 7, 12-17). IgG type autoantibodies such as anti-nuclear antibodies were also detected in some patients with AD (15). Altrichter et al investigated serum IgE autoreactivity against both human epithelial cell line A431 and the keratinocytes, in 192 AD patients by western blotting technique (1). They revealed 28% IgE autoreactivity in AD patients whereas no autoreactivity achieved in healthy controls, pointing the usefulness of detection in treatment and prognosis of disease. Mothes et al suggested autoIgE antibodies produced in the first years of life. But these IgE antibodies are detected only in 25% of the adult (18, 19).

The serum levels of IgE antibodies found to correlate with the severity of the disease (1). In severe disease, antigens found in epithelial cells and many histologically different cell types act as a trigger in exacerbations. The hallmarks of severe illness is early-onset, intense pruritus, history of atopy, recurrent bacterial skin infections, and high serum IgE levels (7). In our study, the ASST positivity was 70% in AD group and the test positivity increased in relation to atopy history, disease severity and high serum IgE.

The itch-scratch cycle via injury to keratinocytes expose intracellular protein molecules extracellularly which share some homology with foreign antigens of the normal flora such as Malassezia, inducing production of IgE autoantibodies (13). These autoallergens elicit T cell or IgE mediated immune response, the cause of tissue injury in patients with AD (20).

In our study, a higher rate of positivity of ASST in AD patients than the control group is demonstrated. So we can comment that ASST which is used to show autoimmune process in chronic urticaria can be a useful tool in defining autoımmunity in AD. The higher positive results achieved in patients with a atopy history, severe disease and high serum IgE levels may have benefits in determination of prognosis and treatment modality (systemic treatments) especially in treatment resistant cases. More studies should be conducted to support this data.

Table 1: Comparison of positive ASST in atopic dermatitis patient and control group

Groups	Positive ASST	P value
Atopic dermatitis group	%70	0.001
Control group	%16.7	

Table2 : Positive ASST in atopic dermatitis patients in relation to atopy history, clinical severity evaluated by SCORAD index and serum total IgE levels

Atopic dermatitis group	Positive ASST	P value
Atopy		
Positive atopy (n=31)	%67.7	0,464
Negative atop y (n=29)	%65.5	
SCORAD index		
Moderate (n=50)	%72	0,474
Mild (n=10)	%60	
Total IgE level		
High total IgE level (n=33)	%72.7	0,612
Low total IgE level (n=27)	%66.7	

Yazarlarla ilgili bildirilmesi gereken konular (Conflict of interest statement) : Yok (None)

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