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Hypersensitivity to Standard Contact Allergens in Patients With Cutaneous Lichen Planus

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ABSTRACT

Aim: Lichen planus is a lymphocytic inflammatory disorder of unknown origin mediated by cellular immunity. The reports documenting contact hypersensitivity to certain antigens are increasing in number mainly in oral but also in cutaneous lichen planus as well. However, there are only a few studies questioning whether there is any alteration in contact hypersensitivity response in this patient group due to T-cell mediated changes.

Methods: The purpose of this study is to find out the prevalence of contact hypersensitivity to standard contact allergens in cutaneous lichen planus patients. In the present study 43 cutaneous lichen planus patients and 33 controls were patch tested by T.R.U.E test methodology.

Resulst: A positive patch test reaction was found in 11.6% of the lichen planus patients while the control group showed a percentage of 30.3%. Statistically, the difference between the two groups was not significant (Fischer test p=0.07).

Conclusions: This is the first study examining into the standard patch test positivity in cutaneous lichen planus patients the results showed no difference from the control.

Key words: contact hypersensitivity; lichen planus; cutaneous lichen planus; patch test; T.R.U.E. test

KÜTANÖZ LIKEN PLANUSTA STANDART KONTAKT ALLERJENLERE AŞIRI DUYARLILIK

ÖZET

Amaç: Liken planus, lenfositik enflamasyonla karakterize hücresel immün sistemin rol oynadığı nedeni bilinmeyen bir hastalıktır. Belirli antijenlere karşı kontakt aşırı duyarlılığın başta oral liken planus olmak üzere kütanöz liken planusta da bulunduğunu gösteren çalışmalar giderek artmaktadır. Buna karşın T hücre aracılı bu hastalıkta kontakt aşırı duyarlılık cevabında herhangi bir değişiklik olup olmadığını sorgulayan az sayıda çalışma mevcuttur.

Hastalar ve Yöntem: Bu çalışmanın amacı kütanöz liken planuslu hastalarda standart kontakt allerjenlere karşı oluşan aşırı duyarlılık reaksiyonlarının prevalansını saptamaktır. Bu çalışmada kütanöz liken planus tanısı konulan 43 kişilik hasta grubuna ve 33 kişilik kontrol grubuna T.R.U.E test metolojisi ile yama testi uygulanmıştır.

Bulgular: Hasta grubunda yama testi pozitifliği %11.6, kontrol grubunda %30.3 olarak bulunmuştur. İki grup arasındaki fark istatistiki olarak anlamlı değildir. (Fischer testi p=0.07).

Sonuç: Bu çalışma kütanöz liken planusta yama testi pozitifliğini araştıran ilk çalışmadır ve hasta grubunun kontrol grubundan farklı olmadığı sonucuna varılmıştır.

Anahtar sözcükler: kontakt aşırı duyarlılık, liken planus, kütanöz liken planus, yama testi, T.R.U.E test

Introduction

Lichen planus (LP) is an inflammatory dermatosis of skin and mucous membranes characterized by flat-topped, violaceous, shiny, pruritic papules on the skin and milky white lesions on the mucosa. Based on the lymphocytic inflammatory response, cell-mediated immunity is noted to play the major role in triggering the disease. Though the exact etiology is still unknown, clinical observations and anecdotal evidence point exposure to a number of exogenous agents. Up to date viruses, medications and contact allergens have been implicated in the etiopathogenesis (1-5). However, there are only a few studies questioning whether there is any alteration in contact hypersensitivity response in these patients. A literature survey displayed that contact hypersensitivity to standard allergens has been checked out in oral LP, but not in cutaneous LP before (6).

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In this study, it is aimed to investigate the prevalence of hypersensitivity to standard contact allergens in cutaneous LP patients and to contribute to the discussions on studies examining the causal relationship in between two entities..

Material and methods

In the present study 50 consecutive cutaneous LP patients who were treated at the dermatology clinic and 40 age and sex matched controls at the physical therapy and rehabilitation ward treated for sports injuries, spinal discopathies, fractures and who were free of any inflammatory dermatologic lesions, were patch tested with T.R.U.E. Test methodology. (Pharmacia & Upjohn Hillerod AS, Hillerod, Denmark) Patients with a diagnosis of connective tissue disease and inflammatory dermatologic diseases were not included in the control group. Verbal informed consent was taken from all the participants. All enrolled patients had histologically proven LP and both the patients and the controls were questioned and examined before test procedure. Type of LP, the duration of the disease, the presence of mucosal involvement and active lesions, previous treatments before testing, dental amalgams and metal prostheses if present, were recorded.

T.R.U.E. Test is a ready-to-use patch test system for diagnosis of allergic contact dermatitis containing individual allergens or allergen mixes released onto the skin after applying the patches (7). The T.R.U.E. Test panels used in this study contained 24 allergens (12 in each); consisting of nickel sulphate, wool alcohols, neomycin sulphate, potassium dichromate, caine mix, fragrance mix, colophony, epoxy resin, quinoline mix, balsam of Peru, ethylenediamine dihydrochloride, cobalt chloride, p-tert-butylphenol formaldehyde resin, paraben mix, carba mix, black rubber mix, Cl+Me-isothiazolinone, quarternium-15, mercaptobenzothiazole, p-phenylenediamine, formaldehyde, mercapto mix, thiomersal and thiuram mix.

Since steroids may suppress a positive test reaction, patients on systemic or topical steroids within previous 2 weeks were excluded from the study. The tests were applied, only to healthy skin to prevent misinterpretation of the test results. Patients returned for reading the patch test results at the 48th and 96th hours after the application. The interpretation was made according to the following description. A doubtful reaction was interpreted if there is only faint macular erythema, a weak positive reaction was recorded if there are erythema, infiltration and possible papules, and a strong positive reaction was indicated if there are vesicles in addition to the lesions listed above.

Fisher's exact test was used for statistical analysis. A p value of 0.05 was defined as the level of significance.

Results

After withdrawals due to noncompliance with the instructions during either test procedure or reading period, 43 biopsy proven cutaneous LP patients (28 women, 15 men) age range 19 to 68 years, (mean 44) and 33 controls (21 women, 12 men) age range 18 to 68, (mean 43.2) were evaluated in this study. Of the 43 LP cases 30 were generalized LP, 8 were localized LP, 3 were lichen hypertrophicus, and the remaining two were cases of a lichen planopilaris and a lichen planus pemphigoides. In the patient group the duration of the disease ranged from 1 week to 5 years (mean 9.6 months), mucosal involvement was present in 32.5% (14/43) of the patients. During testing, active lesions were recorded in 62.7% (27/43) of the patients. Of the 43 patients 19 (44%) did not take any treatment before patch testing, while the other 23 were on either systemic or topical therapy. Among the 23 patients, 7 had had completed enoxaparin treatment before testing with an average of 6.4 months (range 4-9.5 months); 6 had received metronidazole and stopped treatment with a mean of 66.6 days ago (range 3 days-3.5 months). A total of 8 who had been on topical corticosteroids had given up therapy more than 2 weeks ago, a patient who had been given systemic steroids had completed the therapy one month ago. The last case had completed a course of PUVA treatment 6 months ago.

In the LP group a positive patch test reaction was found in 11.6% (5/43) of the patients. These were found to be nickel sulphate in 2 patients, which were weak positive, cobalt chloride in 2 patients that were both strong positive and formaldehyde in the last one with a weak positive reaction. One of the patients was known to be allergic to nickel before the test and one of the cobalt positive patients was involved as a manufacturer in the automotive sector. Other patients did not give a history clarifying the positive patch test reactions.

In the control group 10 of the 33 cases were using some kind of treatment including antiinflammatories, muscle relaxants, antibiotics, antihypertensives, thyroid hormones, vitamins, antidepressants which have not been found to have a notorious effect on contact hypersensitivity reactions. As a result, 30.3% (10 of the 33) of the controls

was found to have positive patch test reactions. These were nickel sulphate in 3 cases, wool alcohols and paraben mix together in one case, Cl+Me-Isothiazolinone in 2 cases and colophony, thiomersal, potassium dichromate, epoxy resin each in one patient. All the patch test reactions were weak positive except 3 strong positives of nickel sulphate, epoxy resin and thiomersal in sequence. Among 10 patch test positive controls 3 gave a history relevant of the clinical reaction. Dental metal compounds were found in 62.7% (27/43) of the LP patients while it was 46.1% (12/26) in the control group. The difference between the two was not significant (p=0.21).

Discussion

In this study a positive patch test reaction was found in 11.6% of the LP patients while the control group showed a percentage of 30.3%. The positive patch test reaction of 11.6% which was presumed to show a difference at first sight did not result in a statistically significant variation to be considered under scrutiny. (p= 0.0787).

Standard screening series test only statistically frequent allergens that have been implicated in the etiology of allergic contact dermatitis. Since there have been reports of LP implicating contact with certain substances including color film developers, latex antioxidant, epoxy resin, nickel salts, copper, mercury and metacrylic acid esters and dental metal compounds (2-5,8,9), a higher rate of patch test positivity could be assumed among these patients. In this respect, there is just one study arguing for decreased delayed type hypersensitivity response to dinitrochlorobenzene in 17 typical LP patients. Furthermore, the authors of this study suggested a primary immune defect in this group of patients (10). Our results showed that delayed type hypersensitivity response was same as the control group which is a totally different result from the latter study.

The patch test positivity of 30.3% found in the control group is in accordance with rates reported in general populations from different countries. Unfortunately, as standard patch test screening in general Turkish population is not available, we could only compare our results with that obtained from predetermined patient populations. In a retrospective study comprising 3017 adult patients, Ertam et al. found a patch test positivity of 31.3% (11) while in a pediatric population of 360, Önder et al. obtained a result of 32% (12). However, it should be noted that in both of these studies, the individuals had a pre-diagnosis of contact dermatitis and the numbers should be lower in the general population. Anyway studies on the prevalence of contact sensitization in the general population from Germany and Australia also showed high frequencies of 40% and 35% respectively (8,13). It is known that the prevalence of patch test positivity increases with age even in the absence of dermatitis (14). The mean age was about 44 in our study, compatible with the aforementioned statement. Comparison of relevant sensitivities was also similar in these two groups.

The patch test is a biologic test and like any other such test has the potential of some interpretation errors. The drugs that have been used during testing period may alter the contact hypersensitivity reaction. In this study 20 of the 43 LP patients had not been given any drugs while 23 had taken some treatment namely enoxaparin (n=7), metronidazole (n=6), topical steroids (n=8), systemic steroids (n=1), and PUVA (n=1). Apart from steroids and PUVA, enoxaparin and metronidazole are known to cause inhibition of contact hypersensitivity (15-17). In our patient group the duration between completion of the treatments and the test was sufficient to remove the effects of the drugs. Furthermore, the timing of the patch test with respect to disease activity is another important factor modifying the results. In other words, the chance of getting a positive response increases in active disease (18). In our patients active LP lesions were present in 62.7% while the positive patch test reaction was only 11.6%. It is thought that the activity of the disease in the majority of our patients is a favorable condition for examining a possible interaction between either positive or negative.

In conclusion, this is the first study questioning the prevalence of delayed type hypersensitivity against standard patch test allergens in cutaneous LP and it was shown to be 11.6%. Contrary to the concepts so far, our data indicated that in cutaneous LP contact hypersensitivity response does not seem to change. Finally, we are aware of the need for further research in larger study groups to draw reliable and firm conclusions.

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