Original Article

Relevance of patch testing in patients of chronic spontaneous urticaria and its correlation with serum IgE level

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ABSTRACT

Objectives: Chronic spontaneous urticaria (CSU) is defined as short lived (< 24h) wheals occurring spontaneously without any triggering factors, daily or almost daily for at least 6 weeks. Though CSU is mainly a Type 1 hypersensitivity reaction, earlier studies suggested contact allergy may have some role to play an important role in the etiopathogenesis of CSU. The objective of the study is to find out the relevance of patch test in the etiopathogenesis of and its correlation with serum IgE level.

Materials and Methods: Thirty-one patients of CSU were thoroughly evaluated for clinical and laboratory parameters. We conducted patch testing with Indian Standard Series (ISS) in all of them and tried to find out the relevance of every positive reaction. Relevant positive cases were asked to avoid exposure for 2 months and were maintained only in breakthrough antihistamines. Furthermore, correlation of positive patch test reaction with high IgE and eosinophil count were studied.

Results: Seventeen (55%) cases came positive for patch test. Potassium dichromate, lanolin, benzocaine, and fragrance mix were the most common offenders. Patients with very high IgE count had patch test positivity with multiple allergens. Seven of the fifteen patients who had relevant positive patch results could be followed up to remission; three were lost to follow-up.

Conclusion: Patch test with ISS may give important clue to in a subset of patients of CSU and thus may be considered an important part of routine investigations of CSU.

Keywords: Patch test, Chronic urticaria, Serum IgE level

INTRODUCTION

Chronic urticaria (CU) is defined as short lived (<24 h) wheals occurring daily or almost daily for at least 6 weeks. CU can be divided into chronic spontaneous urticaria (CSU) and chronic inducible urticaria.

Urticaria is mainly presumed to be a type I hypersensitivity reaction. Thus, IgE was suggested as a marker and is often found to be high in CU patients.[1]

Etiology of urticaria is very difficult to find in every patient and it is said to be associated with various factors such as drugs, food, and food additives, infections, infestations, heat, cold, water, stress, any systemic condition, or autoimmunity.[2] Though CSU is mainly a Type 1 hypersensitivity reaction, earlier studies suggested contact allergy may have some role to play an important role in the etiopathogenesis of CSU.

Sharma has done patch testing in CSU patients and found a high amount of positivity.[3]

Though the study opens a new dimension in the understanding and management of CSU, it falls short of establishing the role of contact sensitization as there was a lack of effort to find out the relevance of the positive allergens, and also there was no correlation done with disease activity. However, it raises a question that can CSU which is presumably a Type I hypersensitivity, may also have associated Type IV hypersensitivity attributes as suggested by positive patch test results? Thus we conducted a study on the role of patch testing and the relevance of positive allergens in CSU and its correlation with serum IgE level. We hypothesized that if positive and relevant patch test results may give us important clues regarding the possible etiology,

and therefore help in the management of this challenging condition.

MATERIALS AND METHODS

We conducted an institution-based observational cross-sectional study carried out from February 2011 to September 2011 to find out the role of patch testing in CU and its relationship with levels of serum IgE.

Thirty-one patients with CSU who had symptoms persisting for more than 6 weeks and active disease at presentation were evaluated after informed consent. Patients of CSU with angioedema or angioedema due to other causes such as ACI inhibitors were not included in the study. Patient who had any clinical history or rashes suggestive of atopic eczema or contact eczema were also excluded from the study. At the time of patch test, it was ensured that back of the patients was free of lesions and they have abstained from any antihistamines for at least 48 hours. Patients, who had individual lesions lasting for more than 24 h or any other clinicopathological features suggestive of urticarial vasculitis, were excluded from the study.

Detailed history and examination findings were entered in case record form. Routine blood and urine examinations including serum IgE were done. Patch testing was performed as per CODFI guidelines with Indian Standard Series (ISS) and readings were taken at 48 and 96 hours. Later patients were evaluated for the relevance of the positive allergens.

The relevance of patch testing is defined as the ratio between the response obtained in the reading and the patient's contact with the causative agent of the dermatosis. A particular test may also be relevant in relation to a previous contact, that is, a positive result refers to a contact that is unrelated to the current dermatosis.

Findings were then evaluated statistically by 'Fishers exact probability test' using a software Statistics.

RESULTS

Of the total 31 patients, 19 were female and 12 were male. The age of presentation ranged from 6 to 56 years. Most patients (18, 58%) were young adults in the age group of 20–40 years. Duration of the disease ranged from 6 months to 5 years where most (19, 61%) of the patients had the disease for 3–5 years. The cases were graded with UAS7 scores, and out of the 31 patients, 16 patients had moderately severe urticaria (UAS7= 16–27) and 15 patients had severe urticaria (UAS7 = 28–42) at the time of presentation. However, no correlation could be found between the severity of the urticaria and patch test positivity.

Aggravating factors were found in 22 (71%) patients. Most common of them was sun exposure (7 patients), followed by pressure (6 patients) and cold (6 patients). Three other patients had a history of aggravation with heat or stress.

Eighteen patients (58%) had some associated conditions. Dermographism (9 patients) was most common amongst them followed by angioedema (8 patients), arthralgia (7 patients), pain abdomen (3 patients), headache (3 patients), syncope (2 patients) and photosensitivity (1 patient) [Table 1].

Serum IgE levels were categorized as <200 (normal), 200–500 (mildly elevated), 500–1000 (moderately elevated), >1000 mg/dl (significantly elevated). Thirteen patients (42%) had their IgE values below 200, 6 patients (19%) between 200 and 500, 7 patients (23%) between 500 and 1000 and 5 patients (16%) had more than 1000 mg/dl [Table 2].

Absolute eosinophil count was normal in 29 of the 31(94%) patients.

Patch test positivity was seen in 17 patients (55%). Out of these, seven were positive to 1-2 allergens, 7 were positive to 3-5 allergens, while three patients were allergic to more than 5 allergens. Out of these, 14 patients (45%) showed relevant positive results [Table 3].

The allergens found positive included potassium dichromate (9, 53%), followed by PPD (6, 35%), fragrance (4, 24%), lanolin (4, 24%), Paraben (3, 18%), black rubber mix (3, 18%), 4C3C (2, 12%), benzocaine (2, 12%), nickel (3, 18%). Other less common allergens showing positive reaction were CCH, balsam of Peru, epoxy resin, 4-tBP, gentamicin sulphate (2, 12% each).

On correlating the patch test positivity with serum IgE, it was seen that 12/14 patients who were patch test negative had normal Serum IgE levels. On the contrary, of the 17 patients with patch test positivity, 15 had their Serum IgE levels above normal. Of these, four patients had values > 1000 IU/ml and all four of them were positive to multiple allergens.

Similarly, relevant patch test positivity also correlated with levels of serum IgE.

The findings of correlation with IgE with patch test positivity and relevant patch test positivity were found to be significant ($P < 0.001$) when evaluated statistically using Fishers exact probability test [Tables 4 and 5].

Table 1: Epidemiology of chronic urticaria- comparison with previous studies.

	Our Study	Barlow *et al.*[4]	Kaplan[5]	Kulthanan and Wachirakaphan[6]
Age	Young adult	Young adult	Young adult	Young adult
Sex	F>M	F>M	F>M	F>M
Most common Associations	DG, Angioedema	Angioedema	-	Angioedema, DG
Aggravating factors	Sun exposure	Drugs, food, infection	Contact, food, infection	-

DG=Dermatographism

DISCUSSION

The demographic data of our study was comparable with the other studies [Table 1].[4-6]

We found 58% of our patients to have elevated levels of IgE which was much higher than the finding of Kessel *et al*.[1] [Table 2] However, majority (94%) of our patients had normal absolute eosinophil count.

While evaluating the relevance of patch testing in CU, we found that 55% of our patients showed positive patch test results in contrast to Sharma[3] (19%) & Guerra *et al*.[7] (41%). [Table 3] We tried to find out the relevance of the positive results and found a significantly large number of patients (48%) had relevant positive results. Twelve (39%) of our patients had positivity to multiple reagents. This number is significantly high in comparison to previous studies (0–2%).[3,7]

We tried to correlate patch test results with the level of serum IgE and found significant association of the level of serum IgE with both positive patch test results and relevant positive

results. This data suggests that as the level of IgE rises, patients become more prone to contact sensitization, especially to multiple allergens [Tables 4 and 5].

Earlier workers had followed up patients for 1 month after avoidance of the suspected allergen and had found variable number (35–100%) of patients showing remission. Hession and Scheinman also studied role of contact sensitization on a small sample size without a control group, they also challenged the patients with the proven contact allergen only to have remission of urticaria which again resolved after avoidance of the allergen concluding contact sensitization to be helpful in the evaluation of CU patients.[8] On the other hand, In a recent study by Magen *et al*. performed retrospectively, authors found similar responses to the avoidance of the positive allergens for a month in three groups; CU with a positive patch test, CU with negative patch test, and control group. And thus they concluded to be no relationship between avoidance of allergen and course of CSU.[9] However, they did not find the relevant positive allergens for the patient.

We followed 12 patients with relevant positive patch test results for 2 months. Of them, 7 (58%) showed remission. We conclude that the lack of remission in five of our patients may be due to two reasons mostly. First, due to multiple allergen positivity, the elimination of all the possible allergens

Table 2: Serum IgE levels- Comparison with similar previous study.

	Our Study	Kessel *et al.* (Israel)
Serum IgE above normal	18/31 (58%)	69/203 (34%)

Table 3: Comparison of results of patch testing with previous studies.

	Our Study	Sharma[3]	Guerra *et al.*[7]
Patch Test positive	17/31 (55%)	11/57 (19%)	50/121 (41%)
Multiple allergen	12/31 (39%)	1/57 (2%)	-
Relevance	15/31 (48%)	-	-
Remission after avoidance of allergen	7/12 (58%) (3 lost in follow-up) (2 months)	9/11 (82%) (1 month)	All (100%) (1 month)

Table 4: Descriptive statistics of numerical variables of serum IgE and positive patch results. (*n*=31).

	Mean	Minimum	Maximum	Standard Deviation	Standard Error
IgE	570.19	18.00	2295.00	609.12	109.40
Number of Positive Patches	1.68	0.00	6.00	2.02	0.36
Both these variables are non-parametric i.e., not normally distributed					

Table 5: Strength of correlation of positive patch test and relevant positive patch test result with serum IgE level.

Quality of Patch Test Positive Number	Spearman	P-level	Comment
Correlation of IgE level with Positive Patch result	0.57	<0.001	This indicates good (but not strong) correlation
Correlation of serum IgE level with maximum Patch testing severity	0.71	<0.001	This indicates strong correlation.
Correlation of serum IgE level with Patch test relevant positive number	0.61	<0.001	This indicates good (but not strong) correlation

might have been incomplete. Second, it may be that contact sensitization in CU may not be a primary event, rather secondary to long-term mast cell stimulation. Hence, the elimination of sensitizers may not be able to stop the primary pathologic events.

However, the question remains that how does CU, which is primarily a type I hypersensitivity reaction, leads to patch test positivity. We propose that long-term mast cell stimulation may alter cytokine profile leading to T cell activation and Type IV hypersensitivity.

CONCLUSION

Patch test with ISS may give important clue to in a subset of patients of CU and thus may be considered as an additional investigation of CSU, especially in the refractory cases. We found that as the level of IgE rises, patients become more prone to be positive patch test, especially to multiple allergens. Thus, patient with high IgE level may consider as ideal candidate for patch testing. We suggest if detected relevant patch test positivity all patients should be enquired about the lifestyle and vocational exposure and give suggestions for limited such exposures. A PPD free hair color was suggested in our patients who were positive to PPD.

Complete avoidance of specific allergens and long-term follow-up is necessary to make conclusive statement regarding the temporary association between contact sensitizer and course of CSU. However, further studies with larger sample size, appropriate control groups are required to substantiate our hypothesis. Being a pilot study, small sample size and lack of control group are major drawbacks of our study.

Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

Conflicts of interest

There are no conflicts of interest.

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