

Predisposition of allergy in patients with benign migratory glossitis

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Objective. The purpose of this study was to investigate the presence of allergy in patients with benign migratory glossitis (BMG) using patch and prick tests.

Patients and methods. Eighty patients (40 BMG and 40 healthy controls) received patch and prick tests. If at least one test result was positive, patients were considered to be allergic.

Results. The prick test was positive in 10 patients (25.0%) of the study group and in 4 patients (10.0%) of the control group. The patch test was positive in 12 patients (30.0%) of the study group and in 6 patients (15.0%) of the control group. When results of both tests were evaluated together, the study group showed a positive rate of 47.5% ($n = 19$), whereas the control group showed a positive rate of 22.5% ($n = 9$) ($P = .02$).

Conclusion. Our results revealed that a combination of prick and patch tests can significantly enhance the diagnostic accuracy of predisposition of allergy in patients with BMG. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;xx:xxx)

Benign migratory glossitis (BMG) is a recurrent condition characterized by loss of epithelium particularly of the filiform papillae on the dorsum of the tongue. The appearance is of multifocal, circinate, irregular erythematous patches bounded by a slightly elevated, white or cream-colored keratotic band or line. The central erythematous patch represents atrophy of the filiform papillae. The white border is composed of regenerating filiform papillae and a mixture of keratin and neutrophils.^{1,2}

The etiology of BMG remains unknown. Several related etiologic factors have been proposed; however, none of the suggested causes provide clear-cut evidence of a causal relationship. One of them is allergy or atopy.¹⁻²¹ It is difficult to diagnose allergy using a single criterion. This condition is mostly detected by the existence of abnormalities—such as asthma, eczema, or hay fever—personal or familial history, raised levels of serum immunoglobulin E (IgE), the presence of IgE against specific antigens, like tissue mast cells,

and positive patch or prick tests. In the literature, a relationship between BMG and allergy has been shown by history of patients in some studies,^{1,3-7,10,11,13} total serum IgE levels,¹⁴ HLA antigen,²⁰ and prick tests.^{2,12}

More recently, the role of cellular immunity in allergic diseases has been emphasized. For instance, the pathogenesis of atopic dermatitis formerly highlighted the role of type 1 reactions and IgE; however, more recent evidence also suggests cellular immunity (particularly T-cell) involvement.^{22,23} To evaluate these distinct arms of immunity, the prick test is a method that measures the coexistence of type 1 allergic reaction, atopy, and IgE, whereas the patch contact test is a method for measuring delayed cellular hypersensitivity (type 4 reaction). As there is lack of information in the literature on BMG and these immunological mechanisms, we sought to investigate the role of contact allergens in BMG by using both the prick and patch tests.

PATIENTS AND METHODS

The study began with 107 patients. Excluded were patients who used any medication (mainly steroid, antihistamine, and antidepressant), patients with atopic dermatitis or any diagnosed allergic problems (such as allergic rhinitis, asthma, and hay fever), children younger than 5 years, pregnant patients, and patients who did not take into account warnings about the applying allergen. The final sample study group was 40 dental patients (25 female and 15 male; mean age: 25.6 ± 11.2) diagnosed with BMG. Another 40 dental patients without BMG lesions (25 female and 15 male; mean

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age: 24.1 ± 12.7) were selected as the control group. These 2 groups were compared in terms of age and gender. This study was approved by the ethical committee and informed consent was obtained from all patients.

To minimize variability in the present study, the diagnosis of BMG was determined jointly by the first (postgraduate doctor) and third (associate professor) authors of the article. Clinical protocols were applied according to World Health Organization (WHO) guidelines.²⁴ A lesion was classified as BMG when (1) there was a localized absence of filiform papillae; (2) the affected area was irregularly shaped; and (3) the area changed location over time.

Allergy tests of the study and control groups were performed in the Ataturk University Faculty of Medicine, in the Dermatology Department. The evaluation and performance of both tests were made by the second (postgraduate doctor) and fourth (professor) authors of the article. If at least one test result was positive, patients were considered to be allergic. The differences among the authors in both evaluation of allergy tests and diagnosis of BMG were resolved by consensus.

Patch test

Twenty-three allergens of the European standard patch test series²⁵ prepared by Stallergenes (Antony, Cedex, France) were used (1. potassium dichromate, 2. neomycin sulfate, 3. thiuram mix, 4. parafenilendiamin hydrochloride, 5. cobalt chlorite, 6. benzocaine, 7. formaldehyde, 8. klofan, 9. quinoline mix, 10. Peru balsam, 11. isopropyl fenil 0.1% parafenilendiamin [IPPD], 12. lanolin alcohols, 13. merkaptio mix, 14. epoxy resin, 15. paraben mix, 16. butyl phenol formaldehyde resin, 17. fragrance mix, 18. quaternium, 19. nickel sulfate, 20. cloro metyl izotiozolinon, 21. mercaptobenzothiazole, 22. sesquiterpene lactone mix, and 23. primin), put into the small finn chambers via plastic syringes, and fixed to the backs of patients. After the numbering of allergens, patients were advised to keep their skin dry and avoid sun and sports activities that cause perspiration. Test results were evaluated by the doctor after 48, 72, and 96 hours. The test panel was removed and it was analyzed and recorded as follows: if no reaction (–); erythema (+/–); erythema and infiltration (+); erythema, infiltration, papillae, and vesicle (++); and erythema, infiltration, bulla (+++), according to the International Contact Research Dermatitis Groups (ICRDG).²⁶

Prick test

The prick test was used for a mixed test of Stallergen's respiratory series.²⁷ The forearm region was cleaned with alcohol. Twelve points, on the inside of

Table 1. Comparison of study and control groups with respect to allergen tests

	Study group		Control group		χ^2	P value
	n	%	n	%		
Patch test						
Positive	12	30.0	6	15.0	2.58	.11
Negative	28	70.0	34	85.0		
Prick test						
Positive	10	25.0	4	10.0	3.12	.08
Negative	30	75.0	36	90.0		
Total						
Positive	19	47.5	9	22.5	5.49	.02
Negative	21	52.5	31	77.5		

the forearm, were marked at approximately 2-cm distance from each other and as 2 rows, bilateral and sub-bottom. Later, 1 drop of each allergen was placed onto marked fields and pricked with a lancet: 1. serum saline (negative control), 2. histamine (positive control), 3. *Dermatophagoides farinae*, 4. *Dermatophagoides pteronyssinus*, 5. Betulaceae (609-615-649-619), 6. Salicaceae (659-669), 7. mixture of 4 cereals, 8. mixture of 5 grasses, 9. mixture of 12 grasses, 10. composite, 11. feathers mixture, and 12. cat hair. In the evaluation after 20 minutes, skin induration of 3 mm or more was considered a positive response.

Patients with positive tests were recommended to take antihistaminic medications advised by their dermatologist and to avoid responsible allergens for 10 days. These patients were later reevaluated.

Statistical analysis

The variables were analyzed using the Statistical Package for Social Sciences (SPSS 16.0; Chicago, IL) program. The Pearson chi-squared test was used to determine potential differences in the distribution of allergens. A P value of less than .05 was considered statistically significant.

RESULTS

The results of the patch and prick tests in each group are reported in Table 1. Thirty-two (40%) of the 80 patients tested showed 1 or more relevant positive patch and prick test reactions. The prick test was positive in 10 patients (25.0%) and negative in 30 patients (75.0%) in the study group. In the control group, the prick test was positive in 4 patients (10.0%) and negative in 36 patients (90.0%). This difference of positive prick test responses between the study and control groups was not significant ($P = .08$). The patch test was positive in 12 patients (30.0%) and negative in 28 (70.0%) in the

Table II. Distribution of detected allergens in study and control groups with respect to prick and patch tests

<i>Prick test</i>							
<i>Names of allergens</i>	<i>Dermatophagoides farinae</i>	<i>Dermatophagoides pteronyssinus</i>	<i>Salicaceae</i>	<i>Mixture of 4 cereals</i>	<i>Mixture of 5 grasses</i>	<i>Mixture of 12 grasses</i>	<i>Composite</i>
Study group	++++	++++	+	++	++++	+++	+++
Control group	–	–	–	+++	++	++	–
<i>Patch test</i>							
<i>Names of allergens</i>	<i>Parafenilendiamin hydrochloride</i>	<i>Peru balsam</i>	<i>Butyl phenol formaldehyde resin</i>	<i>Fragrance mix</i>	<i>Nickel sulfate</i>	<i>Quaternium</i>	<i>Mercaptobenzothiazole</i>
Study group	+	+	+	+	+++++	–	–
Control group	+	–	+++	–	–	+	+

+, 1 positive response; ++, 2 positive responses; +++, 3 positive responses; +++++, 4 positive responses; ++++++, 5 positive responses; –, no or negative response.

study group. In the control group, the patch test was positive in 6 patients (15.0%) and negative in 34 patients (85.0%) ($P = .11$). Both patch and prick tests were positive in 3 patients in the study group and 1 patient in the control group. When the results of both tests were evaluated together, predisposition of allergy was significantly increased in the study group as compared with the control group ($P = .02$). The study group showed a positive rate of 47.5% ($n = 19$), whereas the control group showed a positive rate of 22.5% ($n = 9$).

Table II shows the allergens causing positive results. The positive response in the prick test was observed in 4 patients to *D. farinae*, 4 patients to *D. pteronyssinus*, 1 patient to Salicaceae, 2 patients to mixture of 4 cereals, 4 patients to mixture of 5 grasses, 3 patients to mixture of 12 grasses, and 3 patients to composite in the study group. In the control group, 3 patients reacted to a mixture of 4 cereals, 2 patients to a mixture of 5 grasses, and 2 patients to a mixture of 12 grasses. In the patch test, allergic skin reactions were observed in 1 patient to parafenilendiamin hydrochloride, 1 patient to Peru balsam, 1 patient to butyl phenol formaldehyde resin, 1 patient to fragrance mix, and 9 patients to nickel sulfate in the study group. In the control group, reactions were detected in 1 patient to parafenilendiamin hydrochloride, 3 patients to butyl phenol formaldehyde resin, 1 patient to quaternium, and 1 patient to mercaptobenzothiazole. During patch testing, 5 weak positive reactions (erythema and infiltration), 6 strong positive reactions (erythema, infiltration, papillae, and vesicle), and 1 severe positive reaction (erythema, infiltration, bulla) were observed in the study group. In the control group, 4 weak positive reactions and 2 strong positive reactions were detected.

DISCUSSION

We investigated the relationship between BMG and allergy using patch and prick tests in a young study

population in which a history of allergic conditions and children younger than 5 years were excluded. In this study, we used both the patch and prick tests because both tests examine different mechanisms associated with allergy, i.e., the skin prick test measures specific IgE antibodies in serum and is used to indicate sensitization. It has diagnostic utility regarding the patient's medical history. This test is important in the diagnosis of early sensitization, but the diagnosis is more problematic for late type of allergic manifestation. The patch test, which consists of applying the suspected allergen to the skin, is an informative and reliable diagnostic method to determine delayed-type allergic reactions. This method is based on T-cell-specific response to the application of allergens.^{22,23} Evidence is accumulating that the patch test may provide further diagnostic information in addition to the skin prick test and serum Ig E values for allergy diagnosis.^{28,29} Our results confirm the importance of both tests performed in combination for improving the diagnostic efficacy of predisposition of allergy patients with BMG.

There are several studies of the relationship between BMG and allergy. Marks¹⁵ stated that BMG was the common stigma of allergy usually associated with food allergy in children and adults. Similarly, McLendon and Jaeger²¹ reported a series of children with milk allergy and stated that BMG occurred in a significant proportion of these patients. Ullmann¹⁹ found a significantly increased frequency of atopy among patients with BMG as compared with the general population. Järvinen et al.¹⁰ pointed out that, according to the patient's history, patients with BMG seemed to have a stronger tendency toward allergy than subjects with other tongue lesions and control groups. We also emphasized the relationship between BMG and allergies based on the history of patients in our previous study.¹ Marks and Simons¹⁴ found a raised total serum IgE in patients with BMG compared to a control population and stated that BMG was a sign of atopy in some

patients. An increased frequency of HLA antigen B15 and a decreased frequency of HLA B40 in patients with BMG who were atopic compared with the controls has also been reported.²⁰

Although Marks and Czarny¹² found a high prevalence of BMG in atopic patients with extrinsic asthma and rhinitis (study group) compared with nonatopic and healthy patients, they found no differences compared with nonatopic patients with asthma and rhinitis. All atopic patients in the study group were prick-test positive. They also found that BMG occurred with the same frequency between the atopic and nonatopic symptomatic populations. From this point, they suggested that BMG was a sign common to those patients who had recurrent inflammatory diseases such as asthma and rhinitis, whether they are atopic or not. We also did not include individuals with this type of disease in our study considering such a possibility.

Shulman and Carpenter² performed allergy skin reactivity tests (prick tests) on 2455 patients for white oak, cat, mite, alternaria, rye grass, peanut, Russian thistle, German cockroach, Bermuda grass, and ragweed and found a higher prevalence of BMG in patients who had negative responses to these tests. According to their findings, there was no relation between BMG and allergy. The prick test we used was different from the test used by Shulman and Carpenter² in terms of allergens contained and the sensitivity to prick tests in our study group was higher than the controls, in contrast to Shulman and Carpenter's findings. However, these differences were not statistically significant in both studies.

There are no previous investigations of patch testing in BMG subjects in the current literature. Therefore, this was the first study that performed patch testing to detect the relationship between BMG and allergy. In the patch testing, a 22.5% rate of positive response against nickel was observed in the BMG patients. Although reports by the North American Contact Dermatitis Group have consistently ranked nickel as the number one allergen in frequency of positive patch test reactions,³⁰ there was no relation between nickel allergy and BMG in the literature. However, some researchers^{31,32} suggested a high frequency of oral symptoms—such as stomatitis, gingivitis, and burning mouth—in addition to lichenoid tissue lesions in individuals with positive test results against some metals like nickel. We did not examine the oral cavity for evidence of any of the allergens and the presence of amalgam restorations in our patients. Thus, this was a limiting factor in our study.

In conclusion, this is the first study to investigate the relationship between BMG and allergy using patch and prick tests together. Our results revealed that this rela-

tion was significant when these tests were evaluated together for predisposition of allergy in patients with BMG. From this view point, it may be beneficial to advise patients of the potential for a predisposition to allergy. However, it should be considered that diagnostic differences of BMG, different allergy tests, and the criteria of patient and method selection may cause diverse results. Thus, additional research that includes comprehensive allergens and larger sample sizes are needed.

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