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Geographic tongue and atopy: Is there an association?

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Abstract

Objective: this systematic literature review aimed to find data to clarify a controversy about the association between geographic tongue and atopic diseases/atopy. With emphasis on the relationship between these conditions. **Material and Methods:** data extracted include information on age and sex, family and personal history of atopy, geographic tongue prevalence, immunoglobulin E (IgE) serum levels, and skin tests. **Results:** 08 articles were selected and read in full text and information in articles used in this study. During a review, there was difficulty in standardizing the findings due to lack of details in the diagnosis of atopy and geographic tongue; and the lack of separate analysis of the conditions of asthma, rhinitis or atopic dermatitis. Limitation: low number of publications on the subject. **Conclusion:** based on the literature, more data are available to confirm the relationship between geographic tongue, atopic diseases / atopy, new ones with larger sample sizes, adequate diagnosis of atopy / atopic diseases and geographic tongue, IgE serum levels determined simultaneously oral examination and skin tests.

Keywords: Atopic dermatitis; Asthma; Allergic rhinitis; Atopy; Geographic tongue.

Introduction

Allergic diseases are common in the general population and are usually associated with sensitivity to environmental allergens such as foods, pollen, mites, fungus, insects, and drugs.[1] The prevalence of these diseases has increased considerably in recent decades. Consequently, several theories have been proposed as a justification; however, no conclusive explanation for this phenomenon has been defined.[2] In this context, atopy, the hereditary predisposition of the immune system to immunoglobulin E (IgE)-mediated hypersensitivity reactions in response to common antigens, in intra- and extra-domiciliary environments is important.[3] In addition to interactions with the environment in genetically predisposed individuals, there are systemic variations and immunological abnormalities that make the pathogenesis of this condition quite complex.[4]

The main atopic disorders are asthma, rhinitis, and atopic dermatitis (AD). Asthma is a chronic inflammatory disease of the airways characterized by generalized but variable bronchial obstruction, partially reversible spontaneously or by pharmacological intervention. In allergic asthma, the inflammation is largely dependent on IgE sensitization.[5]

Allergic rhinitis is characterizing by inflammation of the nasal membranes, induced by exposure to allergens. It occurs in the form of intense nasal pruritus, sneezing, nasal obstruction, oral breathing, and decreased sense of smell, all resulting from the inflammatory process.[6]

AD is a chronic inflammatory, cutaneous disease, with outbreaks that occur more often in children in the first years of life but may persist until adulthood.[7] It is an itchy disease, but its clinical presentation depends on the age of the patient. It can be classified as either extrinsic AD, integrated with atopy, or intrinsic AD, considered only as a skin disease that may eventually be associated with respiratory diseases.[7] The earlier the appearance of AD in the child, the greater the child's propensity to develop atopic diseases in the future.

In addition to cutaneous lesions and respiratory diseases, patients with atopy may exhibit oral lesions. Thus, some studies have reported that patients presenting with allergic diseases, a personal or family history of atopy, and high IgE serum levels are more likely to present with geographic tongue (GT). One possible explanation for this is an acute inflammatory condition contribute to the emergence of both: atopy and GT.[8] Although not a specific feature of atopy, GT is a condition that may be associated with an atopic disorder and is often reported before other symptoms of atopy.[9]

GT, or benign migratory glossitis, is a recurrent condition characterized by the loss of the epithelium, particularly the filiform papillae, on the dorsum of the tongue (Figure 1).[10] The appearance of GT may vary, with stages of exacerbation and remission of the lesion.[11,12] It is an immunologically mediated condition associated with diseases such as psoriasis, as demonstrated in a recent literature review.[13]

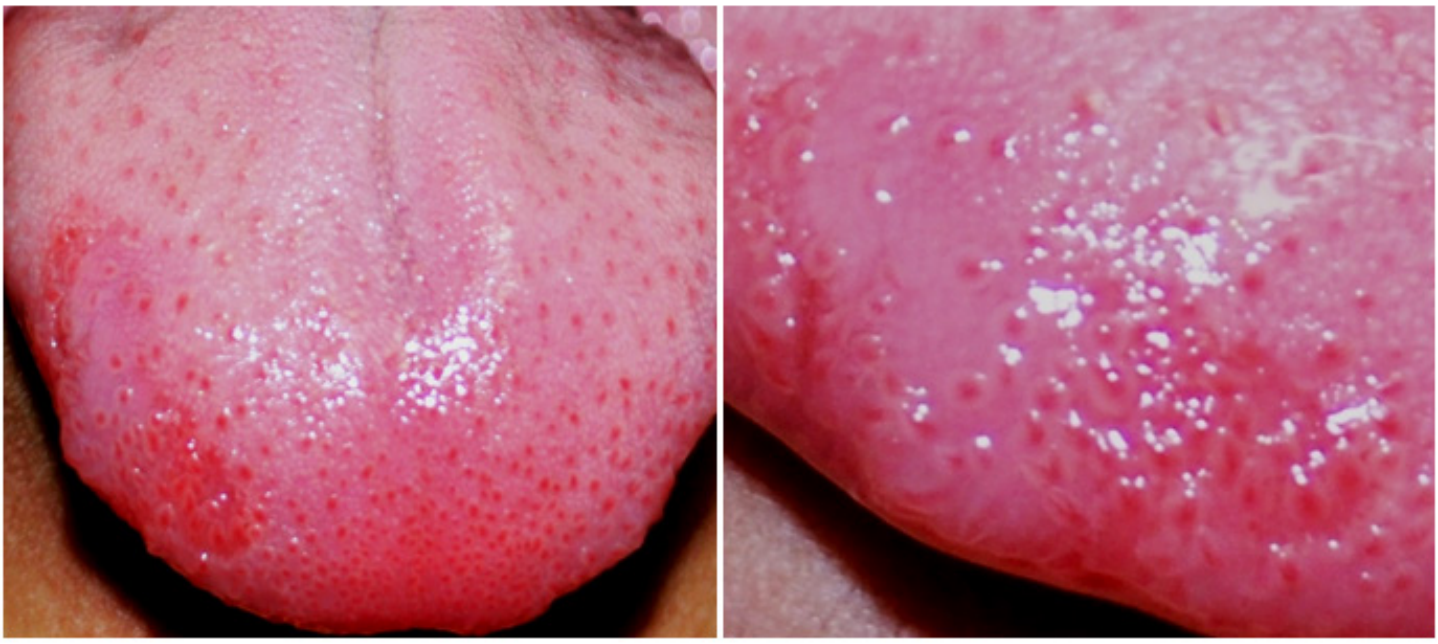

Figure 1. Clinical aspects of geographic tongue in a patient with atopic dermatitis

The association between GT and atopy is not very well defined. Some authors have affirmed this association, while others have denied it.[14,15] Furthermore, the number of clinical studies reporting adequate evidence for the definitive diagnosis of GT or atopy is limited. The GT frequently appears in atopic patients, being able to constitute a predecessor of the atopic disorder and gravity marker. Therefore, it is essential to resolve this controversy, for that the extraoral and intraoral thorough examination in atopic patients and in patients with geographic tongue should not be neglected so there is no loss of holistic assessment of the disease. Thus, the aim of this systematic literature review was to obtain supporting data to clarify this controversy, with particular emphasis on the relationship between atopy and GT.

Material and Methods

The systematic literature review reported here was performed according to the following steps:

1. After a thorough review of the literature and based on the authors' clinical experience, two guiding questions were formulated to be answered by the present study: What is the frequency of geographic tongue in patients with atopy? Did these findings were correlate with the IgE levels and skin tests?

2. Search strategies: the chosen descriptors were previously identified in published articles on the theme in question and they were registered in the MeSH of PubMed. The following virtual databases have been accessed: PubMed, Scientific Electronic Library Online (SciELO) and Latin American and Caribbean Health Sciences (LILACS). They were searched using combinations of the descriptors with the help of the Boolean operator AND: geographic tongue, benign migratory glossitis, atopic dermatitis, asthma, immediate hypersensitivity, allergic rhinitis, and hay fever. A temporal interval was not established in order to obtain as many publications as possible.

3. Inclusion and exclusion criteria: Articles were select if they to be relate to the research theme through the reading of titles and abstracts. Duplicate publications, publications for whom the full article could not be accessed, and publications written in languages other than Portuguese, English and Spanish were excluded (Figure 2).

4. Analysis: Extracted data included information about the age and gender of the participants, atopy, prevalence of GT, IgE levels, and skin tests.

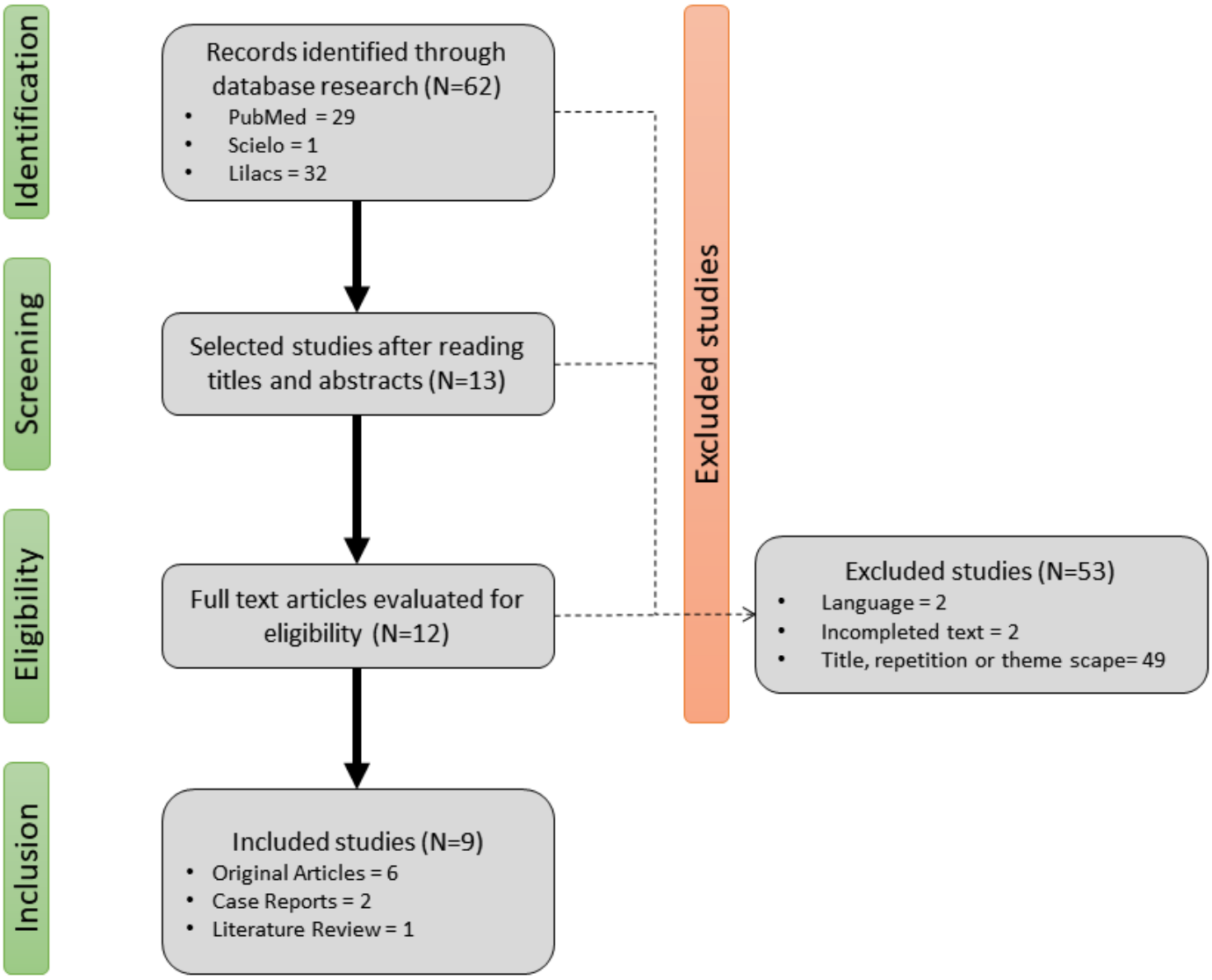

Figure 2. Study selection flowchart

Results

The research resulted in 29 articles in PubMed, 1 article in SciELO and 32 articles in LILACS. Some articles were excluded either based on the title or because of being a repetition, two were excluded based on language (Chinese and French), and two were excluded as the full text could not be obtained for them. Ultimately, only 08 articles were selected and read in full text, and information from these articles was used in this study.

The 07 publications comprise the literature between 1979 and 2015, of which 6 are original articles, 1 case reports, and 1 a literature review. The majority involved both male and female patients, ranging in age from 3 to 83 years. Although females were more prevalent in the studies, this did not seem significant to the authors. Not all articles described the average ages of the participants, but when described it was around 30 years.

In relation to atopy, three articles were related to asthma, rhinitis, and AD; three to asthma; two to AD; and one to asthma and rhinitis. In the only original article, that considered exclusively asthma, the research group concluded that the frequency of GT in 100 asthmatic patients was 10%, which was higher than that in the control group (2%).[16] IgE serum levels were reported in only three articles (Table 1) in which 200 patients had GT.[8,14,16-20,31-33] In the first and second articles, all atopic diseases were considered within the same group. In the first article, of 100 participants with GT, 28% presented with IgE total serum levels ≥ 200 units/mL against 18% of those in the control group. In another article with 95 participants with GT, 24.2% presented high IgE total serum levels, but the control group was not mentioned. In the third article where mainly participants with AD were studied, IgE was cited but the result was not used for comparison with GT.

Table 1. Atopy, tests performed, age, gender and category of study evaluated in articles

Author	Year	Category of study	Gender	Age (years old)	Atopy	IgE serum dosing	Skin test	Prevalence of GT in the control group	Prevalence of GT in the study group
Marks & Simons	1979	Original	Both	3-77	Rhinitis, Asthma and AD	Present	Absent	Absent	100%
Marks & Tait	1980	Original	Both	No	Rhinitis, Asthma and AD	Present	Absent	Absent	100%
Marks & Czarny	1984	Original	Both	3-72	Rhinitis, Asthma and AD	Absent	Prick Test	24%	46%
Kang & Tian	1987	Original	Both	0-12	Atopic dermatitis	Present	Prick Test	Absent	6%
Sigal *et al*.	1992	Case report	Female	3	Asthma	Absent	Absent	Absent	100%
Bascones -Martínez et al.	2005	Literature review	No	No	Atopic dermatitis	Absent	Absent	Absent	Absent
Shulman & Carpenter	2006	Original	No	>18	Asthma and Rhinitis	Absent	Absent	Absent	1,9%
Goswami *et al*.	2012	Case report	Female	11	Asthma	Absent	Absent	Absent	100%
Ghapanchi *et al*.	2015	Original	No	12-83	Asthma	Absent	Absent	2%	10%

The use of the prick test reported in only two articles, and the result used only for the evaluation of atopy. In one of those articles, among 70 patients with AD and/or respiratory allergy, 41 (58%) showed positive prick test results to an extract of *Dermatophagoides farinae* compared with 3 of 39 (7.7%) non-atopic persons. However, the relationship between GT and a positive prick test result was not discussed in this article (Table 2).[8,18,31] At the same time, in another study of 102 atopic participants with prick test result positive to common inhalant allergens, mixed-grass pollens, and house dust mites, 46 (45%) presented with GT. Of 164 participants in the control group, 38 (23%) showed positive prick test results. Of these 38 participants, 12 (31%) presented with GT. These findings led the authors to conclude that there is a possible association between allergic conditions and the presence of GT.

Table 2. Correlation between GT, atopy and IgE serum levels

Year	Author	Control Group (n)	Participants with atopy (n)	Atopy + GT (n)	Atopy + *high IgE serum dosing (n)	GT + *high IgE serum dosing (n)	Control Group + *high IgE serum dosing
1979	Marks & Simons	255	66	66	21	28	46
1980	Marks & Tait	586	95	63	absent	23	absent
1987	Kang & Tian	213	372	22	65	absent	absent

*High IgE serum dosing ≥ 200 u/ml

The diagnosis of GT was considered when the following conditions were present: papillary atrophy (reported in six articles), "white halo" (reported in two articles), and lesion migration (reported in two articles). In only one study, there was a differential diagnosis with candidiasis, a principal diagnostic differential for GT. Further assessment was hampered by variations in the description of the lesion among the studies.

Discussion

Atopy is the hereditary predisposition of the immune system to IgE-mediated hypersensitivity reactions in response to common environmental antigens. In addition to environmental interaction in genetically predisposed individuals, there are systemic variations and immunological abnormalities that make the pathogenesis of this condition quite complex. The presence of oral lesions in atopy remains controversial, with GT considered the most frequent lesion. Some studies have shown this relationship through the patient's clinical history, total IgE serum levels, human leukocyte antigens, and prick test results.[18-21] Many other associations between GT and systemic diseases have already been described, with psoriasis being the disease that presents the most significant clinical, histopathological, and genetic relationship.[13,22]

Several studies have shown that GT has no gender preference and usually occurs in the third decade of life.[23,24] Our results regarding the prevalence of GT revealed no differences between the genders. Jainkittivong *et al*.[25] showed that GT is more prevalent in women than in men (1.5:1), attributing this frequency to female hormones, which can intensify the condition, facilitating the diagnosis. In relation to age, corroborating our findings in the literature, we observed that in atopic individuals, GT is more frequent before the age of 40 years. In patients with psoriasis, GT is associated with early disease, whereas some studies have reported that GT may represent a predilection for future disease.[26-28] Thus, it is extremely important to identify the age at lesion onset and to monitor patients for the early diagnosis of atopy or other diseases.

The association between GT and atopy was first described in 1979, where Marks and Simons[8] demonstrated the increased frequency of atopy (asthma, rhinitis, and dermatitis) in patients with GT. GT was directly related to high IgE serum levels and occurred at levels > 200 μ/mL. The authors concluded that there is a relation between GT and atopy, raising the hypothesis that these conditions are similar in pathogenesis.[8] Both conditions (GT and atopy) are recurrent and inflammatory and can get initiated by contact with external environmental irritants. Although the authors have determined such an association, their work does not report in detail how the diagnosis of atopy was made or the variations in the frequency of GT in each condition: asthma, rhinitis, or AD. Although this association was reported more than 30 years ago, few additional studies have been performed. In addition, the existing studies were clinical, without distinction between atopy and atopic diseases. The only study investigating the association of oral lesions with asthma found a high frequency of GT in asthmatic patients, but the authors did not describe how the diagnosis of both conditions was made and did not affirm that GT is a manifestation associated with asthma.[16]

Shulman & Carpenter[20] evaluated the presence of atopy, with emphasis on cutaneous manifestations, in 279 cases of GT and 16.554 control individuals and found no relation between these conditions. Further, despite emphasizing cutaneous manifestations, there was no dissociation between intrinsic and extrinsic ADs, which hinders the correlation between AD and GT.[20] In addition, the assessment of the presence of GT is often inaccurate in cross-sectional studies because the patient may not present with the lesion in that examination and may be unaware of its presence. Gonzaga & Consolaro [29] reported that the prevalence of GT in some diseases, such as psoriasis, would be much higher than that reported due to the fact that, as a rule, patients are not routinely subjected to a thorough oral examination, which would yield results that are helpful in the resolution of this divergence. New studies with a larger sample size and diagnostic criteria for atopic diseases and GT are necessary.

Some studies have reported a significant increase in the frequency of GT associated with an increased frequency of elevated IgE serum levels. The authors suggested that GT probably represents a reaction pattern of the tongue to several different diseases, especially in the active and severe phases of those diseases.[8,19] Singh *et al*.[28] and Picciani *et al*.[30] demonstrated that psoriatic patients with GT presented a severe form of the cutaneous disease and concluded that this oral lesion represents a marker of psoriasis severity.

The role of cellular immunity, type 1 and type 4 reactions, in atopy has been evaluated for both the prick and patch tests. The immunological mechanisms of GT are not well described, and some studies have shown an increase in this lesion in atopic patients. These tests were used to investigate the role of allergens in GT.[19,27] The authors showed an increase in the positivity of these tests in GT patients, concluding that there is a predisposition to allergy in individuals with GT, thus, supporting the hypothesis that GT correlates with allergic conditions.[27] However, because the studies used skin tests for diagnosis, the clinical history of the participants was not described in detail, which makes it difficult to associate GT with some atopic diseases.

Although atopic diseases and GT are recurrent and inflammatory conditions, the immunopathogenesis of these conditions is distinct. While in the atopic diseases, the Th2

pathway involving IL-4 and IL-13 cytokines and IgE production, in GT the response is mediates by CD3 / CD4 / CD8 T lymphocytes. For this reason, there is an association between psoriasis and GT, whereas the association with atopic diseases remains uncertain.[4,5,13]

During the literature review, only 08 articles correlated the presence of GT with some atopy. In addition, in many cases, the characteristics of lesions such as papillary atrophy, the presence or absence of "white halo," and lesion migration were not reported, making it difficult to associate and characterize GT in atopy. It is important that Pap screening be routinely performed to detect the presence of atypical lesions because the primary differential diagnoses include candidiasis, which can be easily detected using cytopathology.

During the review, we found it difficult to standardize the findings because of a lack of detail in the diagnoses of atopy and GT; a lack of separate analyses of asthma, rhinitis, or AD conditions; and primarily, few publications on the subject. For this reason, the 08 publications related to the theme were included regardless of the type of study, i.e., a literature review, a case report, or an original article. Therefore, new research is needed for a better understanding of GT in atopy.

Conclusion

Based on the scarce literature on this subject, we conclude that there are still insufficient data to confirm the relationship between GT and atopy. Although not able to confirm this relation, some authors affirm that GT frequently appears in atopic patients, being able to constitute a predecessor of the atopic disorder and gravity marker. Therefore, it is essential to carry out a thorough oral examination and follow up patients with GT without atopic diseases. Besides that, new studies are need with larger sample sizes, adequate diagnoses of atopy and GT, IgE serum levels determined simultaneously with the oral examination, and skin tests.

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Mini Curriculum and Author's Contribution

1. Thaylla Núñez Amin Dick – DDS. Contribution: conception, drafting, review, and final approval.
2. Thays Teixeira-Souza – DDS and MSc. Contribution: participated in the data collection, review, and final approval.
3. Sueli Carneiro – MD and PhD. Contribution: data interpretation, review, and final approval.
4. Daniella Moore – MD and PhD. Contribution: data interpretation, review, and final approval.
5. Dennis de Carvalho Ferreira – DDS and PhD. Contribution: data interpretation, review, and final approval.
6. Simone Pestana – MD and MSc. Contribution: data interpretation, review, and final approval.
7. José Laerte Boechat – MD and PhD. Contribution: conception, drafting, review, and final approval.
8. Adrianna Milagres – DDS and PhD. Contribution: data interpretation, review, and final approval.
9. Bruna Picciani – DDS and PhD. Contribution: conception, drafting, review, and final approval.

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