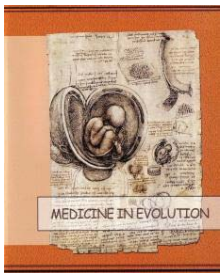
G Tongue In Adults And Children



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Abstract

Geographic tongue is a benign oral condition with a migratory pattern of the dorsal tongue. Aim and objectives: This paper aims to emphasize the etiology, epidemiology, pathogenesis and associated factors of geographic tongue, in an effort to improve the means of misdiagnosed and overtreated cases in adults and children. The variable clinical features of this condition are described. Moreover, geographic tongue can be an oral manifestation of psoriasis, thus further investigations are necessary. Recent data on oral microbiota, salivary changes and treatment strategy are also presented.

Keywords: Geographic tongue, migratory glossitis, oral psoriasis

INTRODUCTION

Geographic tongue (GT) is an oral condition with various names in the literature such as benign migratory glossitis, erythema migrans, annulus migrans, benign wandering glossitis, exfoliatio areata linguae, or transitory benign plaque of the tongue [1]. GT has a benign behavior and with an unknown etiology and pathogenesis. An inherited pattern may be involved [2]. Its clinical appearance is variable in size and location on the tongue surface (Figure 1, A-E). GT can be associated with fissured tongue in 50% of cases (Figure 1D, E, F). The onset time may be in the early age-first weeks or months of life [3]. It disappears over time (with adulthood) or reappears periodically **[4].**

The clinical lesions are observed on the tongue, mainly dorsal and lateral areas (Figure 1 E, F). These are red patches frequently limited by white areas represented by hyperplastic, regenerating filiform papillae, keratin and neutrophils [4]. These geographical map-like areas are multifocal and surrounded by normal areas of the mucosa. In evolution, GT changes its position on the tongue, healing without scars and then reappearing in another region (a migratory pattern). This explains the migratory term used as an alternative of GT. Being most oftenly asymptomatic, the condition only comes to attention by its spectacular clinical pattern. Thus, the aesthetic aspect may easily confuse patients and doctors.

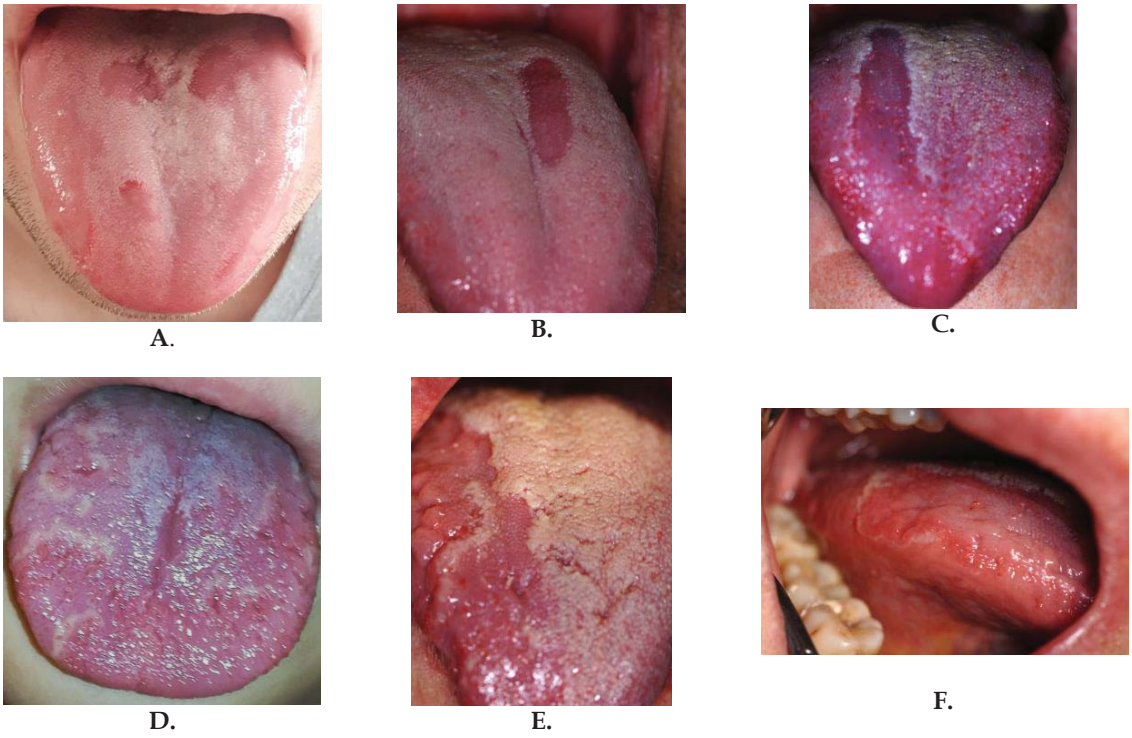

Figure 1. Different types of geographic tongue: A, B mild, C moderate, D severe, E, F moderate GT dorsal and lateral tongue of the same patient

In some cases a spectacular clinical pattern (Figure 1D) or the absence of the serpiginous white areas (Figure 1 A, B) can raise diagnostic difficulties.

In most of the cases GT is an asymptomatic condition and does not require medical intervention. But there are some patients with disturbing symptoms who need therapy. The treatment options vary from recommendations to avoid spicy, salty foods and acid beverages to medication and laser interventions [1]. The general treatments used are antihistamines, anxiolytics, corticosteroids and nutritional supplements. The topical therapeutic options

include ointments or rinses with anesthetics, antihistamines, corticosteroids, vitamins [5]. But a systematic review analysing the GT treatment in adults and children concluded that there is no clinical evidence for a specific treatment option in symptomatic GT [5].

Aim and objectives

The paper aims to emphasize the possible causative and associated factors of geographic tongue in adults and children, in an effort to improve the means of misdiagnosed and overtreated cases.

MATERIALS AND METHODS

Epidemiology

The benign geographic tongue is reported to appear in a percentage of 1 to 2.5 and even 3% of the population [2,4]. A Spanish study shows the prevalence of this oral mucosa variation had risen in time, from a value of 1-3% before 2002, to 4.9% and 9.08% in studies from different regions of Brazil in 2004[3]. More recently, between 2004 to 2016, several studies showed that the migratory glossitis has a prevalence of 2.15% in Europe, 1.62% in Africa and 2.79% in the American Regions (South, Central and North), meaning a higher prevalence in the American territory than anywhere else [6].

Concerning age and gender, it is affirmed by some authors that this tongue condition is more frequent in female subjects, in childhood or puberty [7], whereas other authors report an increased prevalence in adults, demonstrating its persistence [8]. According to J. Banoczy the gap between the prevalence of different age groups suggests that the etiology of the benign migratory glossitis might actually not be genetic, but a multifactorial cause. A few studies note that in almost 1 out of 2 cases, the geographic tongue is usually associated with fissured tongue, also known by the name of scrotal tongue[4].Analysing the prevalence of oral mucosal conditions in children in the latest World Workshop on Oral Medicine, geographic tongue results of 17 clinical studies had an overall relative frequency of 1.29% and a pooled relative frequency of 2.08%[6].

Etiology and pathogenesis

The main assumptions related to the etiology of this variation of lingual mucosa include local factors, genetic factors, hormonal disturbances(pregnancy), allergic conditions, systemic diseases, psychological factors, nutritional deficiencies and a special association with psoriasis [9]. Other correlations between GT are done with Down syndrome, diabetes mellitus, Reiter's syndrome, and medications such as oral contraceptives and lithium carbonate [10].

The genetic implication is one of the most popular theories, supported by several scientists. Eidelman and Redman suggest a polygenic mode of heredity based on the fissured tongue association in 50% of cases [2]. Another study which proves this theory reports a higher prevalence of GT among first degree relatives of the GT group and among the study group and general population [9].

Hormonal disturbances might also be a causative agent. The present theory is demonstrated by a study of GT patients and oral contraceptives medication, which determined that the lesions were most severe on the 17th day of the cycle [11].

An allergic mechanism is allegedly at cause for this condition in the studies of Marks and Miloglu that have found a higher prevalence of GT in patients with asthma, allergic rhinitis and high levels of immunoglobulin E (86% of the patients presented geographic tongue) versus patients unaffected by the mentioned diseases (37% of the control group)[11]. Akdis's theory also supports the allergenic mechanism associated with patients with personal or family history of atopic dermatitis such as allergic rhinitis and asthma, these patients have an immunological alteration that causes an IgE-mediated sensitization with the dysfunction of the epithelial barrier [12].Moreover, Marks and Simons found that the prevalence of the

HLA antigen B15 was significantly elevated in cases with geographic tongue when compared to a normal population [9]**.** Furthermore, Mclendon and Jaeger show a significant percentage of patients with cow's milk allergy (true milk allergy and not just lactose intolerance) presented geographical tongue. Even though there is a certain relationship between allergies, atopy and migratory glossitis, there are not enough reasons to consider that these diseases are the etiological cause of GT.

Geographic tongue and psoriasis association

Although much more common as a skin condition, psoriasis can sometimes have oral manifestations. These are clinical lesions very similar in appearance to migratory glossitis. Oral psoriasis often goes undiagnosed because the clinical signs may go unnoticed without careful examination. Thus, compared to the cutaneous manifestation of the disease, which presents a characteristic picture with red erythematous plaques, covered with pearly white scales located mainly on the scalp, elbows or knees, oral psoriasis requires further investigation for a correct diagnosis [13]**.**

Regarding oral psoriasis, at present, in the literature the opinions are contradictory. While some authors deny its existence mainly due to histopathological non-confirmation of most reported cases, there are others who argue that, although oral involvement is rare, it cannot be denied [13,14]. Usually, oral forms of psoriasis have been observed especially in the context of skin subtypes such as pustular or erythrodermic psoriasis [15]. The first documentation of a case of oral psoriasis, diagnosed on clinical and histopathological criteria, was mentioned in 1903 by Oppenheim. Since then and so far over 60 other fully investigated cases have been reported in the European medical literature [13].

From a clinical point of view, oral psoriasis is often polymorphic, and because of the similarity to other oral conditions the diagnosis is quite difficult. The presence of skin lesions guides the clinician in establishing the therapeutic strategy. Oral manifestations may be in the form of erythematous plaques, with diffuse edges and white-gray outlines. Sometimes mixed clinical forms may be observed with vesicular or ulcerative lesions. Clinical lesions change their aspect and location carrying a course of periods of remission and exacerbation. The evolution of oral lesions is consistent with that of skin lesions. The most common location is the buccal and lingual mucosa. The hard palate and gingiva are only exceptionally interested. Extralingual lesions are frequently observed and are named migratory stomatitis, ectopic geographical language or erythema circinata migrans [15]. There are also situations in which the oral manifestation of psoriasis is reduced, in the form of limited lesions of migratory glossitis. These are integrated in the general pathological context of mucocutaneous psoriasis or may go unnoticed in the absence of a complete history of the patient's medical history [13]. They are discovered by chance because most of the time they are asymptomatic, producing only transient discomfort and burns when eating sour foods [15,16].

Although the first clinical observations on GT were mentioned by Reiter in 1831, even to this day its pathogenesis has not been clarified. The association with psoriasis has been reported in many studies. Thus, research has shown that GT is the most common oral manifestation in psoriasis, and between the two pathological entities, there are many similarities in etiological, clinical, and histopathological aspects. The existence of a common genetic marker, HLA-Cw6 [17], was also proven.

The characteristic clinical picture in the context of skin lesions and sometimes family history are suggestive elements that guide the clinician to the diagnosis of oral psoriasis. The clinical and histopathological similarities between psoriasis and geographical language are arguments that support that there are indisputable correlations between the two. However, histopathological examination reveals important elements to support the clinical diagnosis. This is important for the complete assessment of the disease and to exclude other similar conditions. The histopathological criteria are slightly different in the cutaneous location from the oral one. Thus, for psoriasis with oral involvement, no clearly histopathological criteria

are defined. The varied aspects of clinical lesions and cyclical evolution are factors that make the diagnosis difficult [18].

As a differential diagnosis, oral psoriasis must be distinguished from other oral conditions with a similar clinical appearance. Of these, various inflammatory or infectious diseases are most often involved.

Unlike skin forms, the treatment of oral psoriasis has different directions depending on the severity of the symptoms accused by patients. Many of the oral manifestations are a little annoying and often do not require treatment. For symptomatic forms, depending on the extent of the lesions, local treatment with corticosteroids, immunosuppressants such as tacrolimus, or retinoids may be recommended. They have favorable effects and relieve painful symptoms and functional disorders. In extended or refractory cases, local treatments are useful and systemic medication imposes [15,17].

Although at present the cutaneous psoriasis knowledge, as well as the general concern about its treatment are at a high standard, for oral manifestation data are limited. Responsible for this is the epidemiological context, namely the low frequency of oral psoriasis, and the fact that often the lesions have a transient nature and reduced symptoms. However, there is a need for interdisciplinary studies to investigate this topic and draw the attention of clinicians to the oral manifestations of psoriasis. Thus, patients diagnosed with cutaneous psoriasis will need to be examined for oral lesions, even reduced oral psoriasis [15]. Also, patients with GT need a referral to a dermatologist. The anamnesis information on the family history of psoriasis is recommended. Recent studies have shown that there is a close association between the fissured tongue and GT, on the one hand, and psoriasis [16]. Some authors even claim that the GT could be an oral manifestation of psoriasis and also an index of its severity, imposing the need to include oral changes in clinical diagnostic criteria. Thus, more and more lately, GT is considered the most common oral lesion in psoriasis, because histopathological, immunohistochemical, and genetic similarities were observed between the two diseases [17].

Regarding the association of psoriasis in children with or without GT, it has been observed that psoriasis children with GT have an earlier onset, a severe form of the disease and present a family history of psoriasis [19].

Microbiota

The oral cavity is one of the richest human regions in the presence of microorganisms. It contains more than 500 to 1,000 different types of bacteria. In patients with low oral hygiene over 100 million bacteria are found on a single tooth surface [4]. Amal Dafar, from Sweden, has studied the differences between the microbiota of patients with GT (microbiota on the lesions and surrounding the lesions) versus a control group of subjects without this condition. This cross-sectional case-control study included 35 GT subjects and 22 control group subjects. Patients with oral lesions such as aphthous ulcers, oral lichen planus or under antibiotic treatment, use antibacterial oral rinses or consume tobacco were not included in the study. The anamnestic data of these patients (19 males and 16 females) revealed 5 hypertension and 4 associated psoriasis cases. The samples were taken in pairs, from the healthy surface of the tongue and from the erythematous area. The samples were used for DNA extraction, polymerase chain reaction and sequencing, sequence analysis and statistical analyses (univariate analyses of the relative abundance, the overall richness, and the Shannon and Simpson diversity indexes and multivariate analyses) [20]. The results showed that *Sphingomonas, Acinetobacter*, and *Delftia* (part of Proteobacteria phylum) are far more prevalent in both lesional and healthy areas of GT than in the control group. The greatest prevalence of Firmicutes (*Mogibacterium* and *Catonella*), Actinobacteria, Bacteroidetes *(Capnocytophaga)* was detected in the control group. Comparing the microbiota of the same patient in different tongue regions, the red areas presented higher levels of *Mogibacterium* and a significantly increased prevalence of the phylum Spirochaetes than in the healthy regions of the tongue [20]. The major finding of this study shows higher richness (more bacterial taxa) but not

higher bacterial density in the lesional sites than in the healthy sites of the migratory glossitis. This could be explained by the naturally protected niches at the papillae base pole which increase the bacterial density by preventing the bacteria from being removed by the salivary flux. Conversely, in the erythematous areas, the loss of filiform papillae is a direct cause of the dysbiotic states of tongue microbiota causing chronic inflammation. Dysbiosis is caused by three mechanisms: loss of beneficial bacteria, expansion of pathogenic bacteria, and changes in the diversity of the microbiota [21]. The constant variations of the regions affected by this condition make it difficult to re-establish a normal ecology of the microbiota, thus emphasizing the difficulties of finding the right treatment for this mucosal behaviour.

Treatment strategies

Although defined as an asymptomatic inflammatory disorder with unknown aetiology, in some cases, GT is disturbing. In non-symptomatic cases, no treatment is needed. Some patients complain of pain, burning sensation and a specific sensibility against garlic and all products containing garlic. Also taste reduction while ingesting spicy or sour foods, carbonated drinks, citrus fruits and derivatives can be present. In these cases, treatment is necessary in order to soothe the discomfort, but no curative treatment has been found.

The first step is to evaluate the mycological infection. If Candida infection is detected, the antifungal treatment is needed. Topical steroids, retinoic acid, cyclosporine, antihistamine, tacrolimus, immune system regulators, vitamin B and Vitamin D supplements are used in proposed treatment plans for GT. Until present, no treatment proved specific for this tongue condition. Najafi of Tehran University concludes in a study that the combination of triamcinolone and retinoic acid was not shown more effective than triamcinolone alone in symptomatic GT [22]. In another Japanese study, topical corticosteroid ointments to reduce strong pain in GT lesions was proven ineffective, on the other hand, applying topical tacrolimus the lesions have healed and improved course [23]. Helfman also reported GT improvement with tretinoin and partially improved state with vitamin A therapy [24]. Although their efforts, the results do not prove the therapy efficacy, not detecting the difference between the natural course of the condition (the migratory feature) and the actual improvement induced by the medication. It is important to remember that GT is a non-pathogenic condition of the dorsum tongue mucosa, with no significant damage to the general or local health of the patient, being mostly asymptomatic. Several authors have reported mouth rinsing with a topical anaesthetic soothes the discomfort for the symptomatic GT [9] as well as properly educating the patients about their condition and suggesting them to avoid ingesting sensitizing foods (spicy, sour, acid, hot, heavily salted). Another possibility for symptomatic GT is phototherapy by use of a laser. It was reported effective for GT with pain or burning sensation but there is still a lack of long term evidence of stable results [25].

DISCUSSIONS

The most frequent condition with which GT is misdiagnosed is oral candidiasis. There are clinical differences between these disorders: oral candidiasis has 2 two main forms: pseudomembranous and erythematous. Moreover, in candidiasis the lesions are painful and cause more discomfort compared to GT. Limited forms of oral yeast infection may involve hard palate, dorsal tongue, angular areas. In case of unclear differential diagnosis, one simple method is the mycological exam. Candida species can be isolated in about 50% of healthy persons [26] without clinical signs of infection (Candida carriage). It was encountered in a variable percentage between 20% [27] to 40% of GT patients [26].

Another oral disease which can raise misdiagnosis with GT is burning mouth syndrome. This condition is described as a persistent, burning sensation of the oral mucosa in the absence of visible lesions. It affects mainly the tongue. Its diagnosis and therapeutic approach is complex and includes a general and local evaluation. It can be associated with GT but the pain features are distinct [4].

Because of this frequent misdiagnosis, patients are prescribed antifungal treatment. More complicated cases are noticed in children with no complaints. Parents observe the atypical aspect of the GT and they refer to general practitioners or to the dentist.

Vitamin B12 and iron deficiency can play an important factor in the epithelial homeostasis, probably associated with formation of filiform papillae. As the atrophy of lingual filiform papillae is present in GT, Khayamzadeh et al. investigated the salivary level of zinc in GT patients. They found lower values in GT patients compared to controls but in zinc serum level no difference. Regarding vitamin B12 there were no differences between GT group and controls [28].

Analysing the levels of calprotectin and IL-8 in the whole saliva of both GT patients and controls, a recent study determined that there was a significant and positive correlation [24].

A recent research detected that the salivary level of alpha-amylase in GT patients was slightly, but not significantly, higher than that of controls (non GT patients) [10]. Same study investigated the anxiety levels in GT patients and found a slightly increased level when compared to controls, but not statistically significant [10].

CONCLUSIONS

Geographic tongue is a benign oral condition with various aspects and self-limited evolution. Its etiology is still unknown. There are differences in oral microbiota and salivary content. Although it is an asymptomatic condition, in cases with persistent complaints a treatment can be used, but it is not specific. Moreover, migratory glossitis is considered the most common oral lesion in psoriasis, because histopathological, immunohistochemical, and genetic similarities were observed between the two diseases.

Conflict of interests statement

All the authors declare that they have no financial or other conflict of interests regarding the present study and the data and devices involved in this article.

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