

Cutaneous and oral comorbidities in patients with geographic tongue: a multicenter, multidisciplinary, cross-sectional, observational study

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Geographic tongue (GT) represents a localized type of psoriasis inversa and its burden of dermatological and oral comorbidities frequently conditions its severity and diagnosis. Currently, no epidemiological studies have evaluated GT muco-cutaneous comorbidities. We aimed to study oral and dermatological comorbidities in a large sample of GT patients. In this multicenter, cross-sectional study, involving 4 primary referral centers in Italy, we evaluated adult GT patients, who were assessed by board certified dermatologists and dentists for 5 months and collected demographics and medical history. GT was evaluated using Hume's classification together with Geographic tongue severity index (GTASI) to score its severity. The prevalence of oral and dermatological comorbidities was recorded. In the sample we enrolled 137 GT patients (M/F= 5:1) with a mean age of 48,2 ± 14,7 yoa and 33.6% had GT family history. The clinical evaluation found 96 (70.1%) GT type I, 7 (5.1%) type II, 13 (9.5%) type IIIa, 19 (13.9%) type IIIb, 2 (1.5%) type IV, following Hume's classification. The mean GTASI score was 23,7 ± 14,2 and the vast majority displayed a severe form of GT. Eighty-nine patients had oral comorbidities (burning mouth syndrome, caries, parulid and lichen planus) and 80 had dermatological concurrent conditions (plaque psoriasis, inverse psoriasis and atopic dermatitis). In GT patients, both dermatological and dental evaluation should be mandatory to identify previously undiagnosed mucocutaneous comorbidities.

Geographic tongue (GT) is a benign, common oral condition, also known as “benign migratory glossitis”, “*Erythema migrans*”, “*Annulus migrans*”, and “tongue

wandering rash”, with 1%-2.5% prevalence in the general population, affecting mainly females (M/F: 9/1) (1). Due to its immunological, histological and

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genetic similarities to psoriasis (2), GT is regarded as a clinical, localized variant of inverse psoriasis, a psoriasis that affects intertriginous areas and mucosa (i.e., lips or penis glans). Furthermore, psoriatic patients may experience more than one type of psoriasis (i.e., plaque psoriasis and inverse psoriasis) during their life, explaining the association between GT and psoriasis, often described in literature (3). Psoriasis is a systemic inflammatory disease (4) with a growing body of comorbidities, such as cardiovascular (5-7) and the recently evaluated respiratory (8-10) and digestive (11-13) ones, capable to detriment patients' psychological status (14), daily undermined by poor sleep (15), itch (16, 17) and social stigmatization (18).

Conversely, GT is often asymptomatic and displays a relapsing remitting behavior; occasionally it co-exists with burning mouth syndrome and deserves topical and/or systemic treatments (19). Thus, GT diagnosis may be challenged by the co-occurrence of other oral diseases and, at the same time, its severity may be influenced by other treatments prescribed for dermatological comorbidities (i.e., psoriasis). Remarkably, an extensive epidemiological study characterizing the dermatological and oral burden of GT comorbidities is still missing and may be useful in daily clinical practice for both dentists and dermatologists.

MATERIALS AND METHODS

Study design

In this cross-sectional study we enrolled adult patients with GT referred to both Dental and Dermatological Italian Units (A.O.U. Maggiore della Carità in Novara, IRCCS Istituto Ortopedico Galeazzi in Milan, IRCCS Cà Granda Ospedale Maggiore Policlinico in Milan, Azienda Ospedaliera San Donato Milanese in Milan) during the period between the 1st of September 2020 and 31st of January 2021. The study received approval for all Local Ethical Committees and all patients signed an informed consent form, in line with Helsinki Declaration principles and the Italian Health Care System (20-22).

All patients underwent both dermatological and dental evaluation by two board-certified specialists with more than 5 years of experience. Demographics together with clinical data and medical history were carefully collected.

Social index was calculated with Equivalent Economic

Situation Indicator (ISEE), patients then were divided in 9 classes based on yearly income: Class 1 (0 €-23,120.00 €), Class 2 (23,121.00 €-27,000.00 €), Class 3 (27,001.00 €-31,000.00 €), Class 4 (31,001.00 €-40,000.00 €), Class 5 (40,001.00 €-51,000.00 €), Class 6 (51,001.00 €-63,000.00 €), Class 7 (63,001.00 €-75,000.00 €), Class 8 (75,001.00 €-95,000.00 €), Class 9 (>95,000.00 €).

Geographic tongue (GT) evaluation

To clinically classify GT, we used the classification by Hume (23):

- Type I: GT limited to the tongue;
- Type II: GT with involvement of other oral structures (GT plus geographic stomatitis);
- Type III: GT with clinically atypical lesions:
 - a) fixed with non-migratory recurrent lesions,
 - b) abortive with a white alopec rapidly regressing without mucosa erosions;
- Type IV: Geographic stomatitis without GT
- Two cases of GT type I are shown in Fig. 1 and 2.

To assess GT severity, we used Geographic tongue severity index (GTASI) (24), after Italian translation and validation. GTASI is a severity score (0-54 points) that divides the tongue in four topographic areas (apex, borders, lingual bells and dorsum), calculating in each one erythema (0-4 points: 0=absence, 1=mild, 2=moderate, 3=marked, 4=severe), white halo (0-4 points: 0=absence, 1=thin, 2=moderate thick, 3=thick, 4=very thick), fissures (0-1 point: 0=absence, 1=presence), and lesions extension (0-6 points: 0=0%, 1=<10%, 2= 10%-29%, 3= 30-49%, 4=50-69%, 5=70-89%, 6=90%-100%). GTASI score classified patients in mild (<7 points), moderate (7-12 points) and severe (>12 points).

Statistics

Categorical data were expressed as absolute counts and percentages, whilst continuous variables were expressed as mean value \pm standard deviation. All statistical analyses were conducted by means of the commercial software "Statistical Package for Social Sciences" (SPSS for Windows, version 24, IBM, Armonk, NY, USA).

RESULTS

Demographics

We enrolled 137 GT patients (M/F= 5:1) with

a mean age of 48.2 ± 14.7 years. Thirteen (9.5%) patients were Africans, whilst the other ones were Caucasians (90.5%). Evaluating marital status, 89 (65.0%) patients were married, 30 (21.9%) separated/divorced, 12 (8.8%) singles and 6 (4.4%) widows. Patients display different levels of scholaryity without statistically significant differences for gender: 24 (17.5%) finished middle school, 83 (60.6%) high school, 17 (12.4%) had a bachelor's degree, 7 (5.1%) had a master's degree and 6 (4.4%) had a Doctorate/MBA or even Postdoctoral degree. Thirty-nine (28.5%) patients were in Class-1, 45 (32.8%) in Class-2, 15 (10.9%) in Class-3, 10 (7.3%) in Class-4, 5 (3.6%) in Class-5, 8 (5.8%) in Class-6, 9 (6.6%) in Class-7, 5 (3.6%) in Class-8 and 1 (0.7%) in Class-9 of the Equivalent Economic Situation Indicator.

Interestingly, 78 (56.9%) patients smoked only cigarettes ($10,4 \pm 6,1$ pack/year), 13 (9.5%) smoked

only e-cigarettes and 8 (5.8%) smoked both cigarettes and e-cigarettes. Alcohol consumption was quantified with Alcohol Use Disorders Identification Test (AUDIT) and clustered 11 (8.0%) patients as "Low Risk" (<7 points), 91 (66.4%) as "Medium Risk" (8-15 points), 23 (16.8%) as "High Risk" (16-19 points) and 12 (8.8%) as "addiction likely" (20-40 points points).

GT evaluation

Remarkably, 36 patients had a new diagnosis of GT. Forty-six (33.6%) had GT family history and 13 (9.5%) had more than one family member with GT. Following Hume's classification, in our sample we found 96 (70.1%) GT type I, 7 (5.1%) type II, 13 (9.5%) type IIIa, 19 (13.9%) type IIIb, 2 (1.5%) type IV. The mean GTASI score was 23.7 ± 14.2 with 21 (15.3%) patients classified as "Mild", 27 (19.7%) as "Moderate" and 89 (65.0%) as "Severe". We calculated also the GTASI score interobserver agreement with Fleiss' kappa between 4 dermatologists, 4 dentists and 4 dermatologists together with 4 dentists (0.68; 0.73; 0.80).

Oral evaluation

Dental prosthesis was present in 61 (44.5%) patients with a mean duration of $8 \pm 3,5$ years; 11 (8.0%) had a peri-mucositis and 8 (5.8%) a peri-implantitis. 89 (65.0%) GT patients had at least one oral comorbidity: 13 (9.5%) had burning mouth syndrome, 5 (3.6%) a parulid, 12 (8.8%) single or multiple papillomas, 21 (15.3%) oral lichen planus, 6 (4.4%) oral erosive lichen, 4 (2.9%) dyshomogeneous verrucous leucoplakia, 4 (2.9%) oral allergic syndrome, 2 (1.5%) hemangiomas, 2 (1.5%) erythroplakia. Twenty-one (15.3%) patients had caries and 65 (47.4%) declared to undergo less than 3 dental hygiene per year.

Dermatological evaluation

After a dermatological assessment 80 (58.4%) patients had at least a dermatological comorbidity; in particular, 28 (20.4%) had plaque psoriasis, 8 (5.8%) inverse psoriasis, 2 (1.5%) pustular psoriasis, 21 (15.3%) atopic dermatitis, 9 (6.6%) lichen planopilaris, 6 (4.4%) prurigo nodularis, 3 (2.2%) lichen sclerosus et atrophicus, 3 (2.2%) granulomatous rosacea.



Fig. 1. A typical GT pattern is evident in the right proximal border of the tongue.



Fig. 2. A GT pattern is visible around the tip of the tongue.

DISCUSSION

GT patients displayed a high burden of mucocutaneous comorbidities that was not previously evaluated. In line with Ching et al., we found a high prevalence of burning mouth syndrome in GT patients (25), but our patients did not experience dysgeusia in contrast with cases reported by Su et al. (26).

Our study confirmed the epidemiological association between plaque psoriasis and GT (27, 28), and further enforce the anecdotal association with pustular psoriasis, both generalized (28, 29) and acrodermatitis continua of Hallopeau (30). Furthermore, our two patients with pustular psoriasis had palmo-plantar variant, not previously report in association with GT. Interestingly, in our cohort we found higher prevalence of inverse psoriasis than pustular one and this aspect has never been described.

In literature, is also described that psoriatic patients may exhibit more than one psoriasis type (i.e. plaque and inverse) (31) due to the disease itself or as a paradoxical reaction to biological and not biological anti-psoriatic drugs (32). Thus, due to the epidemiological (27), immunological, genetic and histological similarities (1), GT may be considered a form of inverse psoriasis. Recently, Baron treated a 42-year-old woman with acrodermatitis continua of Hallopeau and GT with secukinumab, an anti-IL-17, and the patients resolved both condition in 5 days (33). Unfortunately, no data are available in regard of the patient's follow up. Despite the therapeutic positive outcome of this case's results need to be further verified in a larger cohort (34-36), patients with GT and psoriasis may benefit from the use of IL-17 blockers.

Interestingly > 6% of GT patients had an inflammatory peri-implantitis, clinically undistinguishable from the psoriasis-related one (37,38). In fact, psoriatic patients had high level of S100A8 in the gingival crevicular fluid and this marker is related to psoriasis severity, suggesting an oral-skin axis (39). Psoriasis systemic inflammation influenced both skin and oral microbiome triggering local dysbiosis (40,41), the hypothesized *Primum movens* in inflammatory periodontitis (i.e. psoriasis-related) (42). Preus et colleagues sustained the

previous concept by proving that psoriatic patients had more missing teeth and higher bone loss that sex- and age-matched healthy controls (43).

Since psoriasis is regarded as a complex disease in which clinically susceptible individuals manifest psoriasis upon certain triggers or exposures, exposome studies should also be performed in GT patients to further understand GT triggers. Interestingly, in psoriatic patients, diet (44-46), vaccines (47) and other preventive strategies (48, 49) act as disease modifiers, but their effects on GT occurrence and severity still remain understudied. Thus, data are mandatory to establish evidence-based clinical and therapeutic evaluation and follow up in GT patients.

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