Journal of the Formosan Medical Association (2016) xx, 1–6

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfma-online.com

ORIGINAL ARTICLE

Antigastric parietal cell and antithyroid autoantibodies in patients with recurrent aphthous stomatitis

Yang-Che Wu [a,b], Yu-Hsueh Wu [a,b], Yi-Ping Wang [a,b,c], Julia Yu-Fong Chang [a,b,c], Hsin-Ming Chen [a,b,c], Andy Sun [a,b,*]

[a] *Graduate Institute of Clinical Dentistry, School of Dentistry, National Taiwan University, Taipei, Taiwan*
[b] *Department of Dentistry, National Taiwan University Hospital, College of Medicine, National Taiwan University, Taipei, Taiwan*
[c] *Graduate Institute of Oral Biology, School of Dentistry, National Taiwan University, Taipei, Taiwan*

Received 22 September 2016; accepted 30 September 2016

KEYWORDS
antigastric parietal cell antibody;
antithyroglobulin antibody;
antithyroid microsomal antibody;
atrophic glossitis;
recurrent aphthous stomatitis

Background/Purpose: Anti-gastric parietal cell antibody (GPCA), anti-thyroglobulin antibody (TGA), and anti-thyroid microsomal antibody (TMA) have not yet been reported in patients with recurrent aphthous stomatitis (RAS). This study mainly assessed the frequencies of the presence of serum GPCA, TGA, and TMA in different types of RAS patients.
Methods: Serum GPCA, TGA, and TMA levels were measured in 355 RAS patients of different subtypes and in 355 age- and sex-matched healthy control individuals.
Results: We found that 13.0%, 19.4%, and 19.7% of 355 RAS patients, 16.7%, 23.3%, and 21.7% of 60 major-typed RAS patients, 12.2%, 18.6%, and 19.3% of 295 minor-typed RAS patients, 18.1%, 20.0%, and 21.9% of 160 atrophic glossitis-positive RAS (AG+/RAS) patients, and 8.7%, 19.0%, and 17.9% of 195 AG-negative RAS (AG−/RAS) patients had the presence of GPCA, TGA, and TMA in their sera, respectively. RAS, major-typed RAS, minor-typed RAS, AG+/RAS, and AG −/RAS patients all had a significantly higher frequency of GPCA, TGA, or TMA positivity than healthy control individuals (all $p < 0.001$). Of 65 TGA/TMA-positive RAS patients whose serum thyroid-stimulating hormone (TSH) levels were measured, 76.9%, 12.3%, and 10.8% of these TGA/TMA-positive RAS patients had normal, lower, and higher serum TSH levels, respectively.
Conclusion: We conclude that approximately one-third RAS patients may have GPCA/TGA/TMA positivity in their sera. Because some GPCA-positive patients may develop pernicious anemia,

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

* Corresponding author. Department of Dentistry, National Taiwan University Hospital, Number 1, Chang-Te Street, Taipei 10048, Taiwan.
E-mail address: andysun7702@yahoo.com.tw (A. Sun).

http://dx.doi.org/10.1016/j.jfma.2016.09.008

autoimmune atrophic gastritis, and gastric carcinoma, and some TGA/TMA-positive patients may have thyroid dysfunction such as hyperthyroidism and hypothyroidism, these patients should be referred to doctors for further management.

Introduction

Recurrent aphthous stomatitis (RAS) is a common oral mucosal disease characterized by recurrent and painful ulcerations on the nonkeratinized oral mucosa. The prevalence of RAS varies from 5% to 20% depending on the population evaluated.[1] In Taiwan, the prevalence of RAS is 10.5% in the general population.[2]

Although several etiological factors have been proposed, the exact cause underlying RAS remains unclear.[3] The study results on tissue infiltrated mononuclear cells favor the role of cell-mediated cytotoxicity in the immunopathogenesis of RAS.[4] In addition to immune dysregulation, multiple nutritional deficiencies including deficiencies of vitamins B_1, B_2, B_6, and B_{12}, folate, iron, and ferritin are found to be the possible etiologies of RAS.[4] Although several different types of antibody or autoantibody have already been reported in RAS patients,[5–9] the organ-specific autoantibodies such as anti-gastric parietal cell antibody (GPCA), anti-thyroglobulin antibody (TGA), and anti-thyroid microsomal antibody (TMA) have not yet been reported in RAS patients.

In our oral mucosal disease clinic, patients with atrophic glossitis (AG), burning mouth syndrome (BMS), oral lichen planus (OLP), RAS, oral submucous fibrosis (OSF), and other oral mucosal diseases are frequently encountered.[4,10–24] For AG, BMS, OLP, RAS, and OSF patients, complete blood count, serum iron, vitamin B_{12}, folic acid, homocysteine, GPCA, TGA, and TMA levels are frequently examined to assess whether these patients have anemia, hematinic deficiencies, and serum GPCA, TGA, or TMA positivity.[4,10–21,25] The serum GPCA, TGA, and TMA levels were evaluated because patients with GPCA are more likely to have pernicious anemia and to develop autoimmune atrophic gastritis, which may subsequently progress to gastric carcinoma,[26,27] and patients with TGA or TMA may develop autoimmune thyroid disease and finally result in thyroid dysfunction.[10,28] For early diagnosis and treatment of subsequent diseases, it is very important to evaluate whether RAS patients have GPCA, TGA, and TMA in their sera.

In this study, the serum autoantibodies including GPCA, TGA, and TMA were measured in 355 RAS patients and 100 healthy control individuals. The purposes of this study were to assess whether a certain percentage of RAS patients might have GPCA, TGA, and TMA in their sera; to evaluate whether RAS patients might have a significantly higher frequency of GPCA, TGA, or TMA positivity than healthy control individuals; and to find whether TGA-positive and/or TMA-positive (TGA/TMA-positive) patients might have thyroid dysfunction.

Methods

Participants

The study group consisted of 355 RAS patients (106 men and 249 women; age range, 18–90 years; mean age, 52.8 ± 15.9 years). The normal control group consisted of 355 age- (± 2 years of each patient's age) and sex-matched healthy control individuals (106 men and 249 women; age range, 20–89 years; mean age, 53.1 ± 14.7 years). All RAS patients and control individuals were seen consecutively, diagnosed, and treated in the Department of Dentistry, National Taiwan University Hospital (NTUH; Taipei, Taiwan) from July 2007 to July 2016. Patients were diagnosed as having RAS when they had at least one episode of oral ulcerations on movable oral mucosa per month since childhood.[4] RAS were further divided into major-typed RAS ($n = 60$) when patients had recurrent oral ulcerations with a diameter more than 1 cm and minor-typed RAS ($n = 295$) when patients had recurrent oral ulcerations with a diameter less than 1 cm.[4] In this study, 160 RAS patients had concomitant partial or complete atrophic glossitis (AG), which was defined as partial or complete absence or flattening of filiform papillae on the dorsal surface of the tongue, respectively.[12] Thus, RAS patients could be further divided into AG-positive RAS (AG+/RAS) patients ($n = 160$) and AG-negative RAS (AG−/RAS) patients ($n = 195$). RAS patients with betel quid chewing habit or autoimmune diseases (such as systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome, pemphigus vulgaris, and cicatricial pemphigoid) were excluded. Moreover, patients with traumatic ulcers or with aphthous-like ulcers associated with systemic disorders including Behcet's syndrome, celiac disease, gluten-sensitive enteropathy, inflammatory bowel diseases, human immunodeficiency virus infection, and cyclic neutropenia were also excluded.[29] In addition, RAS patients with serum creatinine concentrations indicative of renal dysfunction (i.e., men, >131 μmol/L; women, >115 μmol/L), and who reported a history of stroke, heavy alcohol use, or diseases of the liver, kidney, or coronary arteries were also excluded.[30] Healthy control individuals had either dental caries, pulpal disease, malocclusion, or missing of teeth but did not have any oral mucosal or systemic diseases. None of the RAS patients had taken any prescription medication for RAU or AG at least 3 months prior to entering the study.

The blood samples were drawn from all RAS patients and healthy control volunteers for measurement of serum GPCA, TGA, and TMA levels. All RAS patients and healthy control individuals signed the informed consent

Please cite this article in press as: Wu Y-C, et al., Antigastric parietal cell and antithyroid autoantibodies in patients with recurrent aphthous stomatitis, Journal of the Formosan Medical Association (2016), http://dx.doi.org/10.1016/j.jfma.2016.09.008