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ORIGINAL ARTICLE

Anemia and hematinic deficiencies in anti-gastric parietal cell antibody-positive or all autoantibodies-negative recurrent aphthous stomatitis patients

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Background/Purpose: Approximately 13% of recurrent aphthous stomatitis (RAS) patients have serum anti-gastric parietal cell antibody (GPCA) positivity. This study assessed whether serum GPCA or RAS itself was a significant factor causing hematinic deficiencies and anemia statuses in GPCA-positive RAS (GPCA+/RAS) and all autoantibodies-negative RAS (Abs−/RAS) patients.
Methods: The mean corpuscular volume (MCV) and mean blood hemoglobin (Hb), iron, vitamin B12, and folic acid levels were measured and compared between any two of three groups of 31 GPCA+/RAS patients, 240 Abs−/RAS patients, and 342 healthy control subjects.
Results: GPCA+/RAS patients had significantly lower mean Hb and serum iron level (for women only) as well as significantly greater frequencies of Hb, iron, and vitamin B12 deficiencies than healthy control subjects. Moreover, GPCA+/RAS patients had a significantly higher MCV and a significantly greater frequency of vitamin B12 deficiency than Abs−/RAS patients. Furthermore, Abs−/RAS patients did have significantly lower mean Hb, MCV, iron, and folic acid levels and significantly greater frequencies of Hb, iron, vitamin B12, and folic acid deficiencies than

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healthy control subjects. Of 31 GPCA+/RAS patients, 3 (9.7%) had PA, 6 (19.4%) had vitamin B12 deficiency, and 3 (9.7%) had macrocytosis. Moreover, normocytic anemia (54.0%) and iron deficiency anemia (26.4%) are the two more common types of anemia in our RAS patients.
Conclusions: We conclude that serum GPCA plays a significant role in causing vitamin B12 deficiency and high MCV in GPCA+/RAS patients. RAS itself does play a significant role in causing anemia and hematinic deficiencies in both GPCA+/RAS and Abs−/RAS patients.

Introduction

Recurrent aphthous stomatitis (RAS) is a common oral mucosal disease characterized by recurrent and painful ulcerations on the nonkeratinized oral mucosae such as labial, buccal, alveolar, and ventral tongue mucosae. In Taiwan, the prevalence of RAS is 10.5% in the general population.[1]

Although several etiological factors have been proposed, the exact causes of RAS are still not very clear.[2] Previous studies of tissue infiltrated mononuclear cells in RAS specimens favor the role of cell-mediated cytotoxicity in the immunopathogenesis of RAS.[3] In addition to immune dysregulation, multiple nutritional deficiencies including deficiencies of vitamins B1, B2, B6, and B12, folate, iron, and ferritin are reported to be the possible etiologies of RAS.[3] Our previous studies showed that 57 (20.9%), 55 (20.1%), 13 (4.8%) and 7 (2.6%) of 273 RAS patients have deficiencies of hemoglobin (Hb), iron, vitamin B12, and folic acid, respectively.[3] We also demonstrated that 13.0%, 19.4%, and 19.7% of 355 RAS patients had the presence of anti-gastric parietal cell (GPCA), anti-thyroglobulin (TGA), and anti-thyroid microsomal autoantibodies (TMA) in their sera, respectively.[4] It is well known that GPCA can induce destruction of gastric parietal cells, resulting in failure of intrinsic factor production[5,6] and vitamin B12 deficiency that finally leads to the status of pernicious anemia (PA).[7,8] Vitamin B12 deficiency may also be due to insufficient intake of vitamin B12-containing foods, vitamin B12 malabsorption, and transcobalamin II deficiency.[8] Because multiple factors are involved in Hb deficiency (anemia) in RAS patients, it is interesting to know what factors are most important for the development of anemia or hematinic deficiencies in GPCA-positive RAS (GPCA+/RAS) patients and all autoantibodies-negative RAS (Abs−/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.[3,4,9–28] For AG, BMS, OLP, RAS and OSF patients, complete blood count, serum iron, vitamin B12, folic acid, homocysteine, serum anti-nuclear autoantibody (ANA), anti-smooth muscle autoantibody (SMA), anti-mitochondrial autoantibody (AMA), GPCA, TGA, and TMA levels were frequently examined to assess whether these patients have anemia, hematinic deficiencies, and serum ANA, SMA, AMA, GPCA, TGA, or TMA positivity.[3,4,9–25] To assess the roles of GPCA positivity and the disease of RAS itself in the development of anemia and hematinic deficiencies in GPCA+/RAS and Abs−/RAS patients, 31 GPCA+/RAS patients without ANA, SMA, AMA, TGA and TMA positivities and 240 Ab-/RAS patients were collected. Their complete blood counts as well as serum iron, vitamin B12, folic acid, and homocysteine levels were examined and compared with the corresponding data of 342 healthy control subjects without ANA, SMA, AMA, GPCA, TGA and TMA positivities. The purposes of this study were to evaluate the hematinic deficiencies and anemia statuses in these 31 GPCA+/RAS patients and 240 Abs−/RAS patients and to clarify the roles of the serum GPCA and/or the disease of RAS itself in the final development of anemia and hematinic deficiencies in our GPCA+/RAS and Abs−/RAS patients.

Materials and methods

Subjects

In this study, 31 (10 men and 21 women, age range 24–90 years, mean age 63.3 ± 12.9 years) GPCA+/RAS patients and 240 (78 men and 162 women, age range 18–90 years, mean age 50.9 ± 16.3 years) Abs−/RAS patients were collected from the oral mucosal disease clinic of National Taiwan University Hospital (NTUH). For comparisons, 342 healthy control subjects (104 men and 238 women, age range 20–89 years, mean age 52.7 ± 14.7 years) were also collected and included in this study. All RAS patients and control subjects were seen consecutively, diagnosed, and treated in the Department of Dentistry, NTUH 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.[3] 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

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