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ORIGINAL ARTICLE

Anemia and hematinic deficiencies in anti-gastric parietal cell antibody-positive and -negative recurrent aphthous stomatitis patients with anti-thyroid antibody positivity

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Pernicious anemia;
Vitamin B12 deficiency

Background/Purpose: Serum anti-gastric parietal cell (GPCA), anti-thyroglobulin (TGA), and anti-thyroid microsomal antibodies (TMA) can be found in some recurrent aphthous stomatitis (RAS) patients. This study mainly assessed whether serum GPCA, TGA, TMA and RAS itself played significant roles in causing anemia and hematinic deficiencies in TGA/TMA-positive RAS patients with GPCA positivity (GPCA+/TGA/TMA/RAS patients) or negativity (GPCA −/TGA/TMA/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 the four groups of 15 GPCA+/TGA/TMA/RAS patients, 69 GPCA−/TGA/TMA/RAS patients, 240 all autoantibodies-negative RAS patients (Abs−/RAS patients), and 342 healthy control subjects.

Results: GPCA+/TGA/TMA/RAS patients had significantly lower mean Hb (for men only) and vitamin B12 levels as well as significantly greater frequencies of Hb, iron, and vitamin B12 deficiencies than healthy control subjects. GPCA+/TGA/TMA/RAS patients had lower serum vitamin B12 level and higher MCV as well as a significantly greater frequency of vitamin B12 deficiency than GPCA−/TGA/TMA/RAS patients. Furthermore, both GPCA−/TGA/TMA/RAS and Abs−/RAS patients did have significantly lower mean Hb, MCV, and iron levels as well as

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significantly greater frequencies of Hb, iron and vitamin B12 deficiencies than healthy control subjects. There were no significant differences in blood data between GPCA−/TGA/TMA/RAS and Abs−/RAS patients

Conclusion: Both serum GPCA positivity and RAS itself are the contributing factors causing anemia and hematinic deficiencies in GPCA+/TGA/TMA/RAS patients. RAS itself but not TGA/TMA positivity plays a significant role in causing anemia and hematinic deficiencies in GPCA−/TGA/TMA/RAS patients.

Introduction

Recurrent aphthous stomatitis (RAS) is a common oral mucosal disease characterized by recurrent and painful ulcerations on the movable and nonkeratinized oral mucosae. The prevalence of RAS is 10.5% in the general population in Taiwan.[1]

The exact causes of RAS are still not very clear, although several etiological factors have been shown to be related to RAS.[2,3] The finding of a mononuclear cell infiltrate in the subepithelial connective tissue of RAS specimens favor the role of cell-mediated cytotoxicity in the immunopathogenesis of RAS.[3] In addition to dysregulation of immune function, 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] GPCA can induce destruction of gastric parietal cells, resulting in failure of intrinsic factor production.[5,6] Intrinsic factor deficiency may cause insufficient absorption of vitamin B12 that finally leads to the status of pernicious anemia (PA).[7,8] 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 TGA-positive and/or TMA-positive (TGA/TMA-positive) RAS patients with GPCA positivity (GPCA+/TGA/TMA/RAS patients) or negativity (GPCA−/TGA/TMA/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, anti-nuclear antibody (ANA), anti-smooth muscle antibody (SMA), anti-mitochondrial antibody (AMA), GPCA, TGA, and TMA levels were often examined to evaluate whether these patients have anemia, hematinic deficiencies and serum ANA, SMA, AMA, GPCA, TGA, or TMA positivity.[3,4,9–25] Our previous studies discovered that 16.1%, 20.2%, 16.1% and 4.0% of 124 GPCA-positive patients (75 AG and 49 BMS patients), and 16.3%, 14.2%, 6.3% and 1.1% of 190 TGA/TMA-positive patients (83 AG and 107 BMS patients) have Hb, serum iron, vitamin B12, and folic acid deficiencies, respectively.[14,17] To assess whether the serum GPCA, TGA, and TMA as well as the disease of RAS itself played significant roles in causing anemia and hematinic deficiencies in GPCA+/TGA/TMA/RAS patients or GPCA−/TGA/TMA/RAS patients, 15 GPCA+/TGA/TMA/RAS patients without ANA, SMA, and AMA positivities, 69 GPCA−/TGA/TMA/RAS patients without ANA, SMA, and AMA positivities, and 240 all six aforementioned autoantibodies-negative RAS patients (Abs−/RAS patients) were collected and included in this study. 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. The purposes of this study were to study the anemia statuses and hematinic deficiencies in these 15 GPCA+/TGA/TMA/RAS patients and 69 GPCA−/TGA/TMA/RAS patients and to further clarify the roles of the serum GPCA, TGA, TMA and/or the disease of RAS itself in the final development of anemia and hematinic deficiencies in our GPCA+/TGA/TMA/RAS and GPCA−/TGA/TMA/RAS patients.

Materials and methods

Subjects

This study included 84 (18 men and 66 women, age range 26–83 years, mean age 54.5 ± 13.7 years) TGA/TMA/RAS patients, 240 (78 men and 162 women, age range 18–90 years, mean 50.9 ± 16.3 years) Abs−/RAS patients, and 342 healthy control subjects (104 men and 238 women, age range 20–89 years, mean 52.7 ± 14.7 years). The 84 TGA/TMA/RAS patients were further divided into 15 (3 men and 12 women, age range 47–71 years, mean age 61.2 ± 8.0 years) GPCA+/TGA/TMA/RAS patients and 69 (15 men and 54 women, age range 26–83 years, mean age 53.1 ± 14.3 years) GPCA−/TGA/TMA/RAS patients. 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-

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