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ORIGINAL ARTICLE

Hematinic deficiencies and anemia statuses in antigastric parietal cell antibody-positive erosive oral lichen planus patients with desquamative gingivitis

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Background/purpose: Erosive oral lichen planus (EOLP) patients with desquamative gingivitis (DG) are sometimes encountered in our oral mucosal disease clinic. This study assessed hematinic deficiencies and anemia statuses in antigastric parietal cell antibody (GPCA)-positive EOLP patients with DG ($GPCA^+/DG^+$/EOLP patients).

Methods: The blood hemoglobin, iron, vitamin B12, folic acid, and homocysteine concentrations and serum GPCA levels in 92 $GPCA^+/DG^+$/EOLP patients and 184 age- and sex-matched healthy controls were measured and compared between the two groups.

Results: We found that 27 (29.3%), 16 (17.4%), and 27 (29.3%) of 92 $GPCA^+/DG^+$/EOLP patients had hemoglobin (men $<$ 13 g/dL and women $<$ 12 g/dL), iron ($<$ 60 μg/dL), and vitamin B12 ($<$ 200 pg/mL) deficiencies, respectively. Moreover, 37 (40.2%) of 92 $GPCA^+/DG^+$/EOLP patients had an abnormally high blood homocysteine level ($>$ 12.1μM). $GPCA^+/DG^+$/EOLP patients had a significantly higher frequency of hemoglobin, iron, or vitamin B12 deficiency and an abnormally high blood homocysteine level than healthy control individuals (all $p < 0.001$). Of 27 anemic $GPCA^+/DG^+$/EOLP patients, 13 (48.2%) had pernicious anemia, five (18.5%) had iron deficiency anemia, one (3.7%) had thalassemia trait, and the remaining eight (29.6%) had normocytic anemia. Moreover, of the 92 $GPCA^+/DG^+$/EOLP patients, 24 had macrocytosis, and only 13 (54.2%) of these 24 patients had pernicious anemia.

Conclusion: We conclude that $GPCA^+/DG^+$/EOLP patients may have vitamin B12 deficiency, iron deficiency, and an abnormally high blood homocysteine level. In addition to pernicious

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

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anemia, GPCA$^+$/DG$^+$/EOLP patients may sometimes have normocytic anemia or iron deficiency anemia.

Introduction

Desquamative gingivitis (DG) presents mainly as painful erosions or ulcerations of the attached and free gingivae. It is now recognized to be a manifestation of several diseases, principally mucocutaneous autoimmune disorders such as oral lichen planus (OLP), mucous membrane pemphigoid, and pemphigus vulgaris.[1–3] Our recent study found that 455 (91%), 40 (8%), and five (1%) of 500 DG patients were associated with erosive oral lichen planus (EOLP), pemphigus vulgaris, and mucous membrane pemphigoid, respectively.[4]

Our previous study found that 84 (26.3%) of 320 OLP patients were antigastric parietal cell antibody (anti-GPCA) positive.[5] Our recent study also showed a GPCA-positive rate of 39.6% in 455 EOLP patients with DG (DG$^+$/EOLP patients).[4] The GPCA may induce destruction of gastric parietal cells and, in turn, result in failure of intrinsic factor production.[6,7] A lack of intrinsic factor may lead to vitamin B12 deficiency. Vitamin B12 plays an important role in hemoglobin (Hb) and DNA synthesis and cell division. Patients with vitamin B12 deficiency may have Hb deficiency and macrocytosis [mean corpuscular volume or (MCV) $\geq$ 100 fL] that finally causes pernicious anemia.[8,9] Vitamin B12 deficiency may also be due to an inadequate intake of vitamin B12-containing foods, vitamin B12 malabsorption, biologic competition including bacterial overgrowth and tapeworm infestation, and transcobalamin II deficiency.[9] As multiple causes are involved in vitamin B12 deficiency and macrocytosis, it is interesting to know the frequencies of vitamin B12 deficiency, macrocytosis, and macrocytic anemia in GPCA-positive DG$^+$/EOLP patients (GPCA$^+$/DG$^+$/EOLP patients).

Our previous studies demonstrated that some patients with oral mucosal diseases such as OLP, burning mouth syndrome, and atrophic glossitis may have autoantibodies in their sera. Thus, we frequently examined the presence of different types of autoantibodies such as GPCA, antithyroglobulin antibody (anti-TGA), and antithyroid microsomal antibody (anti-TMA, also known as antithyroid peroxidase antibody) in the sera of oral mucosal disease patients, especially the DG$^+$/EOLP patients.[4,5,10–16] In this study, we recruited 92 GPCA$^+$/DG$^+$/EOLP patients from the oral mucosal disease clinic of National Taiwan University Hospital (NTUH). For these GPCA$^+$/DG$^+$/EOLP patients, complete blood count, serum iron, vitamin B12, folic acid, homocysteine, TGA, and TMA levels were checked to assess whether these patients had microcytic, normocytic, or macrocytic anemia; thalassemia; deficiencies of hematinics; and serum TGA or TMA positivity. These data were further compared with the corresponding data of 184 age- and sex-matched healthy control individuals without oral mucosal and systemic diseases to evaluate whether GPCA$^+$/DG$^+$/EOLP patients had higher frequencies of anemia, vitamin B12 deficiency, macrocytosis (MCV $\geq$ 100 fL), abnormally high blood homocysteine level, and TGA or TMA positivity than with healthy control individuals.

Materials and methods

Patients

In this study, 92 (14 men and 78 women, age range 29–87 years, mean age 58 $\pm$ 12 years) GPCA$^+$/DG$^+$/EOLP patients were enrolled. For each GPCA$^+$/DG$^+$/EOLP patient, two age- ($\pm$2 years of each patient's age) and sex-matched healthy control individuals were selected. Thus, the normal control group consisted of 184 healthy individuals (28 men and 156 women, age range 29–87 years, mean age 57 $\pm$ 11 years). All the patients and healthy control individuals who were seen consecutively, diagnosed, and treated in the oral mucosal disease clinic of NTUH from July 2007 to May 2015 were selected for the study. DG was diagnosed when patients had painful erythematous lesions, erosions, or ulcerations on at least one-quarter of the total maxillary and mandibular gingivae.[1,2] OLP was diagnosed according to the criteria described previously.[5,16] However, all GPCA$^+$/DG$^+$/EOLP patients with areca quid chewing habit, autoimmune diseases (such as systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome, pemphigus vulgaris, and cicatricial pemphigoid), inflammatory diseases, recurrent aphthous ulcerations, malignancy, or recent surgery were excluded. In addition, all GPCA$^+$/DG$^+$/EOLP patients with serum creatinine concentrations indicative of renal dysfunction (men $>$ 131μM, women $>$ 115μM) and those who reported a history of stroke, heavy alcohol use, or diseases of the liver, kidney, or coronary arteries were also excluded.[17] Healthy control individuals had dental caries, pulpal disease, malocclusion, or missing of teeth, but did not have any oral mucosal or systemic diseases. None of our GPCA$^+$/DG$^+$/EOLP patients had taken any prescription medication for malignancies, epilepsy, diabetes mellitus, infection, inflammation, DG, or EOLP at least 3 months before entering the study.

The blood samples were drawn from all GPCA$^+$/DG$^+$/EOLP patients and healthy control individuals for measurement of complete blood count, blood iron, vitamin B12, folic acid, and homocysteine concentrations, as well as serum GPCA, TGA, and TMA levels. All the patients and healthy control individuals signed the informed consent forms before entering the study. This study was reviewed and approved by the Institutional Review Board of NTUH.