Journal of the Formosan Medical Association (2017) xx, 1–7

Available online at www.sciencedirect.com

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journal homepage: www.jfma-online.com

ORIGINAL ARTICLE

Anemia and hematinic deficiencies in gastric parietal cell antibody-positive and -negative oral mucosal disease patients with microcytosis

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Received 25 January 2017; accepted 3 February 2017

KEYWORDS
anemia;
gastric parietal cell antibody;
iron;
vitamin B12;
homocysteine;
thalassemia trait

Background/Purpose: Microcytosis is defined as mean corpuscular volume (MCV) $<$ 80 fL. This study assessed the anemia statuses and hematinic deficiencies in 30 patients with gastric parietal cell antibody-positive microcytosis (GPCA+/microcytosis) and 210 patients with GPCA-negative microcytosis (GPCA−/microcytosis).
Methods: We measured and compared the mean red blood cell (RBC) count, MCV, and RBC distribution width (RDW), as well as blood levels of hemoglobin, iron, vitamin B12, folic acid, and homocysteine among the aforementioned patient groups and 240 healthy controls.
Results: Compared with GPCA−/microcytosis, the positive counterparts presented with a lower mean serum vitamin B12 level (marginal significance), significantly higher mean RDW and serum homocysteine level, and significantly greater frequencies of vitamin B12 deficiency and high homocysteine level. GPCA−/microcytosis patients had significantly greater frequencies of hemoglobin, iron, vitamin B12, and folic acid deficiencies and of RBC count $> 5 \times 10^{12}$/L than healthy controls. Moreover, 19 of 30 GPCA+/microcytosis patients and 143 of 210 GPCA−/microcytosis patients had anemia, with iron deficiency anemia being the

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

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http://dx.doi.org/10.1016/j.jfma.2017.02.001

most common type, followed by thalassemia trait-induced anemia and microcytic anemia due to other causes.
Conclusion: We conclude that GPCA in microcytosis patients' sera may have caused significantly lower mean vitamin B12 level as well as significantly higher mean RDW and serum homocysteine level in our GPCA+/microcytosis patients than in GPCA−/microcytosis patients. Herein, iron deficiency anemia was the most common type of anemia in anemic GPCA+/microcytosis and GPCA−/microcytosis patients.

Introduction

Microcytosis is defined as mean corpuscular volume (MCV) $<$ 80 fL.[1–5] Hemoglobin (Hb) deficiency leads to abnormally small size of red blood cells (RBCs). Heme (composed of iron and protoporphyrine IX), α-globin, and β-globin form Hb, and severe deficiency of any of these results in microcytic anemia (defined as MCV $<$ 80 fL, Hb $<$ 13 g/dL for men, and Hb $<$ 12 g/dL for women).[1–5] The causes of microcytic anemia are lack of iron delivery to the heme group (iron deficiency anemia), lack of α-globin or β-globin synthesis (thalassemia minor or major), restricted iron delivery to the heme group (anemia of inflammation), and defects in the synthesis of the heme group (sideroblastic anemias).[1]

Gastric parietal cell antibody (GPCA) can induce destruction of gastric parietal cells, resulting in failure of intrinsic factor and hydrochloric acid production.[6,7] Lack of hydrochloric acid may disturb iron resorption and cause iron deficiency anemia (IDA).[8] However, lack of an intrinsic factor may lead to vitamin B12 deficiency and macrocytic anemia.[9–11] Therefore, it is interesting to know the changes of blood data in serum GPCA-positive microcytosis (GPCA+/microcytosis) patients.

In our oral mucosal disease clinic, we frequently encounter patients with atrophic glossitis (AG), burning mouth syndrome (BMS), oral lichen planus (OLP), recurrent aphthous stomatitis (RAS), oral submucous fibrosis, and other oral mucosal diseases.[2–5,8–25] In these patients, complete blood count, serum iron, vitamin B12, folic acid, and homocysteine levels are frequently examined to check for anemia or hematinic deficiencies.[2–5,8–25] In this study, 240 oral mucosal disease patients with microcytosis who visited our oral mucosal disease clinic were included and divided into two groups: GPCA+/microcytosis patients (n = 30) and GPCA-negative microcytosis (GPCA−/microcytosis) patients (n = 210). 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 240 healthy controls. The main purposes of this study were: (1) to study the anemia statuses and hematinic deficiencies in these 30 GPCA+/microcytosis and 210 GPCA−/microcytosis patients; (2) to assess the differences in blood data between 30 GPCA+/microcytosis and 210 GPCA−/microcytosis patients; and (3) to find out the most prevalent anemia types in these 30 GPCA+/microcytosis and 210 GPCA−/microcytosis patients.

Materials and methods

Patients

In this study, we included 30 GPCA+/microcytosis patients (6 men and 24 women; age range, 23–88 years; mean age, 57 ± 15 years) and 210 GPCA−/microcytosis patients (40 men and 170 women; age range, 20–88 years; mean age, 52 ± 15 years) who visited the oral mucosal disease clinic of the National Taiwan University Hospital (NTUH), Taipei, Taiwan. For comparisons, 240 age- (±2 years of each patient's age) and sex-matched healthy controls (46 men and 194 women, age range 20-88 years, mean age 53 ± 14 years) were also included in this study. All microcytosis patients and controls were seen consecutively, diagnosed, and treated in the Department of Dentistry, NTUH from July 2007 to July 2016. The diagnoses of OLP,[2,12] RAS,[3–5,13,14] AG,[15,16] and BMS[17,18] were described previously. Microcytosis 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, malignancy, or recent surgery were excluded. In addition, we excluded all microcytosis patients with serum creatinine levels indicative of renal dysfunction (i.e., men, $>$131 μM; women, $>$115 μM) and those with a history of stroke, heavy alcohol use, or diseases of the liver, kidney, or coronary arteries.[26] Healthy controls had dental caries, pulpal disease, malocclusion, or missing teeth but did not have any oral mucosal or systemic diseases. Microcytosis patients who had taken any prescription medications for AG, BMS, OLP, or RAS within 3 months before entering the study were excluded.

The 30 GPCA+/microcytosis patients included 12 with AG, eight with BMS, eight with OLP, and two with both RAS and AG. Moreover, 210 GPCA−/microcytosis patients included 69 with AG, 64 with BMS, 26 with OLP, 15 with RAS, 33 with both RAS and AG, and three with both RAS and OLP. The blood samples were drawn from all microcytosis patients and healthy controls for measurement of complete blood count, serum iron, vitamin B12, folic acid, homocysteine levels, and serum GPCA titer. All patients and

Please cite this article in press as: Lin H-P, et al., Anemia and hematinic deficiencies in gastric parietal cell antibody-positive and -negative oral mucosal disease patients with microcytosis, Journal of the Formosan Medical Association (2017), http://dx.doi.org/10.1016/j.jfma.2017.02.001