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Original Article

Graves' disease patients with iron deficiency anemia: serologic evidence of co-existent autoimmune gastritis

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Abstract: Background: Graves' disease (GD) has been associated with iron deficiency anemia (IDA). Atrophic gastritis leads to IDA and has been associated with autoimmune thyroid disease. This study prospectively determined the prevalence of atrophic gastritis markers and the relationship between these markers and markers of IDA in GD subjects. Methods: Newly diagnosed GD patients (90) and controls (41) were studied. Of the newly diagnosed GD patients, 65 were consecutively enrolled and identified with GD irrespective of anemia, 25 had GD and IDA. Thyroid function, hematologic indices, and atrophic gastritis markers [parietal-cell antibodies (PCab), *Helicobacter pylori* antibodies (*H. pylori* ab), mean serum gastrin levels] were examined. Results: GD patients presenting with IDA were twice as likely (64% vs. 32%, P=0.049) to harbor PCabs when compared to all other GD subjects. Unselected GD subjects (n=65) had significantly higher PCab (37% vs. 7%, P<0.001) compared to controls. Gastrin levels were significantly elevated in all GD subjects compared to controls (105 vs. 39 pg/ml, P<0.0001). This difference was magnified in PCab+ subjects (202 vs. 64 pg/ml, P=0.003). In all GD subjects, PCabs were associated with increased gastrin levels (202 vs. 75 pg/ml, P=0.0004) and lower ferritin levels (52 vs. 95, P=0.05). In GD anemic subjects, PCabs were associated with lower mean corpuscular volume (75 vs. 81, P=0.001). Gastrin levels correlated inversely with ferritin levels in all GD subjects and positively with TIBC in GD anemic subjects. Conclusions: A significant subset of patients presenting with GD may suffer from IDA due to concurrent autoimmune atrophic gastritis.

Keywords: Iron metabolism, iron deficiency anemia, autoimmune, Graves' disease, atrophic gastritis

Introduction

Autoimmune gastritis is a significant cause of unexplained iron deficiency anemia (IDA) and often goes undiagnosed [1-3]. Iron absorption is dependent on normal gastric acid secretion to solubilize and reduce dietary iron [4]. Iron absorption is therefore impaired by the achlorhydria associated with autoimmune atrophic gastritis [5]. Undiagnosed autoimmune atrophic gastritis can lead to consequences such as signs and symptoms of anemia, refractoriness to oral iron supplementation, and increased risk for gastric malignancy [1, 6]. Importantly, studies have shown that only half of patients with autoimmune gastritis have gastrointestinal symptoms [7]. Thus, awareness and early diagnosis of autoimmune gastritis is important.

Graves' disease (GD) is an autoimmune thyroid disease characterized by the presence of antithyroid abs [8]. Consequently, patients with GD are at higher risk than the general population of manifesting additional autoimmune diseases such as autoimmune gastropathy [9]. Approximately 30% of patients with Graves' disease exhibit anemia on presentation [10]. The majority of these patients exhibit 'GD anemia' [10]. As previously described, 'GD anemia' accounts for 67% of the anemic Graves' disease patients, has similar hematologic characteristics to the anemia of chronic disease and corrects with resolution of the hyperthyroidism on the order of 2.8 g/dl mean increase in hemoglobin levels [10]. The remaining 33% of anemic GD patients present with IDA which does not correct when euthyroidism is achi-

eved [10]. This subset of patients is the subject of this study.

It is recognized that a person with one type of autoimmune disease may harbor another autoantibody to a different tissue or organ, although the underlying pathogenesis is not well characterized [9]. In particular, previous studies have demonstrated a close association between autoimmune thyroid disease (AITD) and atrophic gastritis [9]. Atrophic gastritis can have an autoimmune or infectious (*Helicobacter pylori*) etiology [11-13]. Autoimmune atrophic gastritis, also known as Type A gastritis [9], is corpus predominant and characterized by auto-antibodies targeting the gastric parietal cell H^+K^+-ATPase (PCabs) [11, 12, 14]. *Helicobacter pylori (H. pylori)* is a gram-negative pathogenic bacterium that colonizes the gastric epithelium and leads to multifocal atrophic gastritis also known as Type B gastritis [11, 15-17]. Atrophic gastritis is characterized by chronic inflammation and destruction of gastric glandular cells resulting in achlorhydria and iron malabsorption [15]. Serum gastrin levels increase in autoimmune atrophic gastritis secondary to achlorhydria and the absence of acid inhibition of gastric antral G cell gastrin secretion [14, 18, 19]. Markers of chronic atrophic gastritis include the presence of PCabs, antibodies to *H. pylori* and elevated serum gastrin levels [15, 18].

Iron deficiency is usually exhibited by a microcytic anemia with low serum ferritin and normal/elevated total iron binding capacity (TIBC) [20]. Microcytosis is indicated by a mean corpuscular volume (MCV) below 80-82 mcg/dL in most laboratories and is reflective of smaller-sized red blood cells. Ferritin is a cellular storage protein of iron, and a ferritin level below 15 ng/mL, is 99% specific for making a diagnosis of iron deficiency [20]. It is important to note that ferritin is also an acute phase reactant important for cellular defense against oxidative stress and inflammation. TIBC is the capacity of transferrin, the transport molecule of iron, to bind with iron; transferrin saturation is the ratio of iron to TIBC and in iron deficiency, transferrin saturation is increased.

In this prospective study we determine the prevalence of PCabs, *H. pylori* abs and mean serum gastrin levels in our cohort of newly diagnosed GD subjects. This study is the first to examine the association between these markers of atrophic gastritis and markers of iron deficiency anemia in a large cohort of newly diagnosed patients with Graves' disease.

Methods

Study subjects

Patients who presented to the Harbor-UCLA Medical Center with newly diagnosed GD were enrolled after obtaining informed consent, as approved by the Institutional Review Board. The diagnosis of GD was established on the basis of standard clinical and laboratory criteria. Subjects were included if they were already treated with β-blockers but were excluded if thionamides or corticosteroid therapy had been initiated. Subjects taking proton pump inhibitors were excluded from the gastrin analysis. Ninety patients were enrolled and comprise the study group. Of these 90 subjects, 7 failed to undergo a complete blood count (CBC) and were therefore excluded from the anemia analyses. Of these 90 GD subjects, 65 were newly diagnosed and enrolled consecutively (denoted as unselected patients). The remaining 25 subjects were not consecutively enrolled, but were selected because they were newly diagnosed with both GD and anemia. These 25 patients were included if a diagnosis of anemia was established based on hemoglobin levels below the lower limit of the reference range for our assay (females 11.9-14.9 g/dl, males 13.9-16.9 g/dl). The study group was divided into those presenting with anemia (n=37) and those with normal hemoglobin (n=46). Euthyroidism was achieved with thionamide therapy alone or in combination with radioactive iodine treatment or surgical thyroidectomy followed by thyroid hormone replacement. Control subjects (30 females and 11 males) without hyperthyroidism or any known autoimmune disease were also recruited.

Laboratory investigation

Gastrin (Cat. #478X) levels were measured using an immunoassay by Quest Diagnositcs. *H. pylori* antibodies (Cat. #37695X) were also assayed by an immunoassay by Quest Diagnostics. PCabs (Cat. #15114X) were detected by an enzyme linked immunosorbent immunoassay by Quest Diagnostics (San Juan Capistrano, CA).

Table 1. Baseline characteristics of study subjects

Characteristic	All GD N=90	GD with anemia N=37	GD without anemia N=46	Control N=41	*P* value
Age (yr) (mean ± SD)	37 ± 11	39 ± 13	36 ± 10	39 ± 15	0.36
Female sex (%)	73.3%	67.6%	73.9%	73.1%	0.79
Hispanic (%)	66.7%	73.0%	65.2%	53.7%	0.15[a]
Non-hispanic (%)	33.3%	27.0%	34.8%	46.3%	
African American (%)[b]	46.7%	50.0%	37.5%	26.3%	
Asian (%)[b]	26.7%	30.0%	25.0%	36.8%	
White (%)[b]	26.7%	30.0%	31.3%	31.6%	
Other (%)[b]	0.0%	0.0%	6.3%	5.3%	

GD: Graves' disease. a. *P* value for % Hispanic among GD with anemia, GD without anemia, and control groups. b. Percentages may not total 100 because some subjects selected more than one race.

Table 2. Prevalence of parietal cell antibody, Helicobacter pylori antibody and mean gastrin levels (95% CI) in Graves' disease subjects versus controls

	GD	Controls	*P* Value
PCab[a]	24/65=37%	3/41=7%	0.001
H. pylori ab[a]	38/64=59%	16/40=40%	0.07
Gastrin (pg/ml)[b]	105 (82-133)	39 (32-46)	<0.0001

GD: Graves' disease, PCab: parietal cell antibody, *H. pylori* ab: *Helicobacter pylori* antibody. a. Prevalence data were obtained from consecutively enrolled subjects n=65. b. All GD study subjects n=90.

Statistical analysis

Percentages were compared between groups with Fisher's exact tests. All continuous measurements are summarized as mean ± standard deviation or 95% confidence intervals and compared between groups with 2-sided t-tests. The geometric means are given for ferritin and gastrin since these measures were analyzed on the log scale to resolve their skewed distributions. Pearson correlations were used to measure associations between continuous measurements. A level of P<0.05 was regarded as significant. For statistical analysis, we used SAS Version 9.3.

Ethical considerations

This study was approved by the institutional review board at the Lundquist Institute (Ref. Num. 10678-05). All participants were provided written consent to participate in the study prior to entering the study. Patients could withdraw consent and participation from this study at any time. All procedures were performed in accordance with the ethical standards of the institutional review board.

Results

Baseline characteristics of the study subjects can be seen in **Table 1**. Of the 90 subjects comprising the study group, 65 were unselected and consecutively enrolled.

Prevalence of parietal cell antibodies, H. pylori antibodies, and mean gastrin levels in subjects newly diagnosed with Graves' disease

The 65 unselected and consecutively enrolled GD subjects were used to establish the antibody prevalence in our population. Subjects with GD had a significantly higher prevalence of PCab (37% vs. 7%, P<0.001) and a substantially but non-significantly higher prevalence of *H. pylori* antibodies (59 vs. 40%, P=0.07) compared to controls (**Table 2**). Of note, when the whole cohort of GD subjects (n=90) was examined the antibody prevalence was similar; 34% PCab and 59% *H. pylori* antibody respectively (data not shown). Similarly, as shown in **Table 2** (geometric mean) gastrin levels were significantly elevated in GD subjects (n=90) compared to controls (105 vs. 39 pg/ml, P<0.0001) and this difference in mean gastrin levels (GD vs. controls) was magnified in PCab positive subjects (202 vs. 64 pg/ml, P=0.003). Gastrin levels did not correct after achieving euthyroidism regardless of anemia status (data not shown).

Association between parietal cell antibodies and mean gastrin levels

We next examined the association between PCabs and serum gastrin levels. As shown in

Table 3. Association between mean gastrin levels (pg/ml) and parietal cell antibodies in all subjects and those with Graves' disease

	PCab (+)		PCab (-)		*P* Value
	N	Mean (95% CI)	N	Mean (95% CI)	
All subjects	31	181 (115-283)	92	56 (48-67)	<0.0001
H. pylori ab (-)	12	244 (91-649)	44	40 (32-51)	0.002
Graves' disease	28	202 (125-326)	55	75 (60-94)	0.0004
H. pylori ab (-)	11	281 (100-786)	22	52 (36-76)	0.005

PCab: parietal cell antibody, *H. pylori* ab: *Helicobacter pylori* antibody.

Table 3, PCabs were associated with increased gastrin levels in all study subjects (181 vs. 56 pg/ml, P<0.0001) and this relationship was magnified (244 vs. 40 pg/ml, P=0.002) when the subjects with *H. pylori* abs were excluded. Similarly, when only GD subjects were examined, mean gastrin levels were found to be significantly elevated (202 vs. 75 pg/ml, P=0.0004) in those with PCabs compared to those without (**Table 3**). When GD subjects lacking *H. pylori* abs were examined, the association between PCab and gastrin levels was further magnified (281 vs. 52 pg/ml, P=0.005). Lastly, we compared serum gastrin levels between subjects taking and those not taking β-blockers and found almost identical mean gastrin levels (P=0.95).

Association between H. pylori antibodies and mean gastrin levels

We proceeded to examine the association of *H. pylori* abs and mean serum gastrin levels in our cohort. Serum gastrin levels were found to be only modestly increased (93 vs. 59 pg/ml, P=0.02) in all subjects with *H. pylori* abs and this association was unchanged when subjects with PCabs were excluded (76 vs. 40 pg/ml, P=0.0001). *H. pylori* abs were not associated with anemia or any hematologic indices (data not shown).

Association between parietal cell antibodies and markers of iron deficiency

We next evaluated the association of PCabs with anemia and markers of iron deficiency. We examined GD subjects, stratified on the diagnosis of anemia. We examined markers of iron deficiency including serum ferritin, MCV and TIBC. Subjects with Graves' disease and PCabs were found to have lower (geometric mean) ferritin levels (52 vs. 95 ng/ml, P=0.04) when compared to those without PCab (**Figure 1A**). When this analysis was performed on the GD subjects with anemia, a substantial trend (41 vs. 95 ng/ml, P=0.08) between PCabs and serum ferritin was found (**Table 4**). Additionally, PCabs were found to be statistically significantly associated with lower MCV (74 vs. 81, P=0.001) in GD anemic subjects (**Table 4**). No association was found between PCabs and TIBC in GD subjects with or without anemia (**Table 4**).

Association between mean gastrin levels and markers of iron deficiency

We next examined the association of serum gastrin levels with serum ferritin, MCV and TIBC. Gastrin levels were strongly inversely correlated with ferritin levels (r=-0.3, P=0.01) in all GD subjects (**Table 5**) and as shown in **Figure 1B**, this correlation was magnified in subjects with PCabs (r=-0.4, P=0.05). Similar inverse correlations were found in anemic Graves' disease subjects (r=-0.26, P=0.16) including those with PCabs (r=-0.42. P=0.17) (**Table 5**). Additionally, gastrin levels were positively correlated with TIBC (+0.4, P=0.03) in GD anemic subjects (**Table 5**). No statistical significance was found between serum gastrin and MCV in GD subjects, irrespective of anemia status (**Table 5**).

Prevalence of parietal cell antibody positivity amongst Graves' disease subjects presenting with iron deficiency anemia

GD subjects presenting with a combination of hematologic indices (mean ± SD) consistent with a clinical diagnosis of iron deficiency anemia [ferritin (14.4 ± 12 ng/ml), TIBC (415.6 ± 79.1 mcg/dl), MCV (71.9 ± 5.6)] were twice as likely (64% vs. 32%, P=0.049) to harbor PCabs when compared to all other anemic and non-anemic GD subjects (**Figure 2**).

Discussion

GD is an autoimmune thyroid disease characterized by the presence of anti-thyroid abs [8]. As such, patients with GD are at higher risk than the general population of manifesting

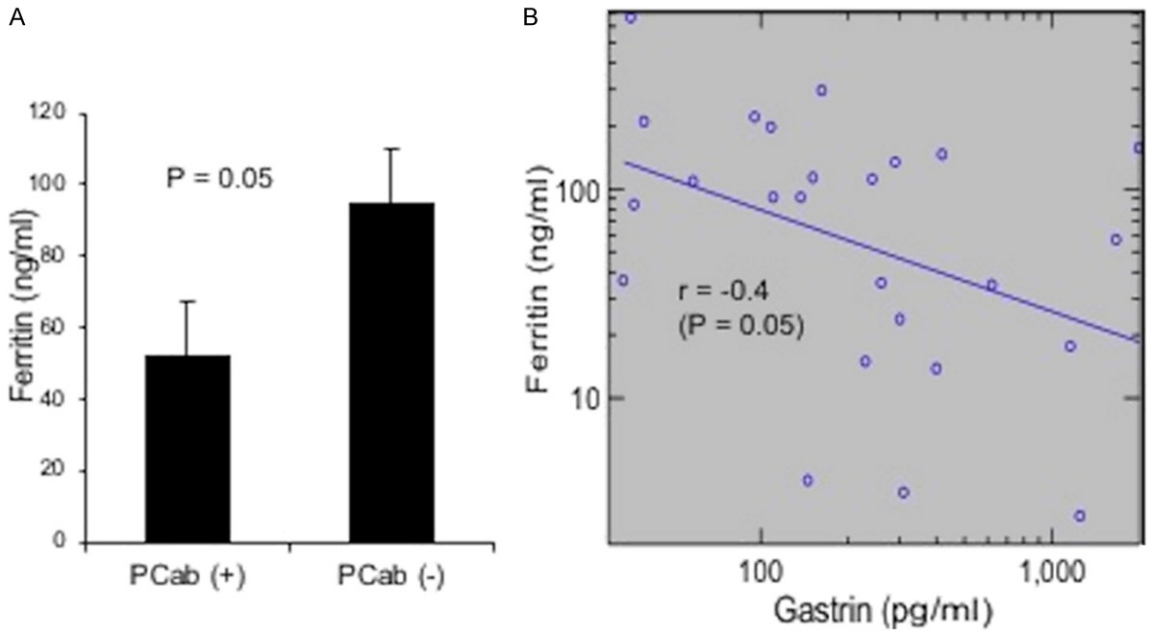

Figure 1. A. Relationship of serum ferritin to parietal cell antibodies (PCabs) in Graves' disease (GD) subjects. B. Correlation between serum ferritin and gastrin levels in GD subjects with PCabs.

Table 4. Association between parietal cell antibodies and markers of iron deficiency in all Graves' disease

	Graves' disease			Graves' disease with anemia		
	PCab (+) N=31	PCab (-) N=59	*P* Value	PCab (+) N=14	PCab (-) N=23	*P* Value
Ferritin (ng/ml)	52 (31-88)	95 (69-130)	0.05	41 (18-93)	95 (53-168)	0.08
MCV (fL)	79 (76-82)	81 (80-83)	0.12	75 (71-79)	81 (79-84)	0.001
TIBC (mcg/dl)	343 (309-376)	320 (302-339)	0.23	338 (276-401)	292 (263-322)	0.17

PCab: parietal cell antibody, MCV: mean corpuscular volume, TIBC: total iron binding capacity.

Table 5. Correlation between mean gastrin levels and markers of iron deficiency in all Graves' disease subjects and those with anemia according to parietal cell antibody positivity

	Graves' disease				Graves' disease with anemia			
	All		PCab (+)		All		PCab (+)	
	r	*P* Value	r	*P* Value	r	*P* Value	r	*P* Value
Ferritin (ng/ml)	-0.30	0.01	-0.40	0.05	-0.26	0.16	-0.42	0.17
MCV (fL)	-0.07	0.53	0.18	0.40	-0.17	0.36	0.16	0.62
TIBC (mcg/dl)	0.19	0.10	0.29	0.17	0.40	0.03	0.33	0.30

PCab: parietal cell antibody, MCV: mean corpuscular volume, TIBC: total iron binding capacity.

additional autoimmune diseases [21], including autoimmune gastropathy [9]. In this paper, we show that a subset of patients with GD anemia have a concurrent autoimmune gastropathy as evidenced by the presence of PCabs and increased gastrin.

Autoimmune gastropathy, or Type A gastritis [17, 22, 23], is characterized by auto-antibodies directed against the acid producing gastric parietal cells [14]. These cells reside primarily in the corpus and fundus of the stomach and their destruction leads to achlorhydria [11, 12,

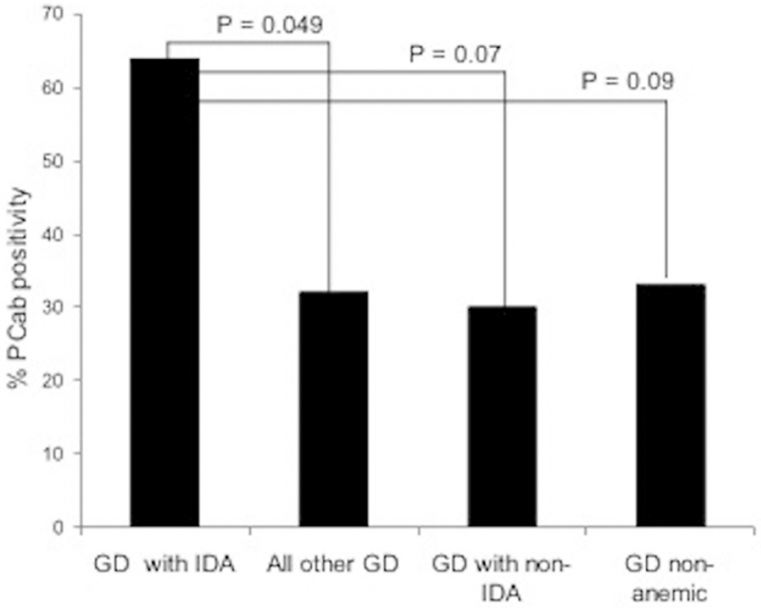

Figure 2. Parietal cell antibody positivity among Graves' disease subjects with iron deficiency anemia (IDA), non-iron deficiency anemia (non-IDA), and no anemia.

24]. In response to the high gastric pH, gastric antral cells secrete gastrin [24, 25]. Elevated serum gastrin levels and the presence of PCabs have been shown to be good markers of autoimmune gastropathy [1, 9, 26]. PCab+ correlates well with gastric acid secretion [27] and PCab titers have been shown to correlate with the severity of corpus atrophy and inversely correlate with parietal cell concentration [24, 25]. The gold standard for diagnosis of autoimmune gastropathy however, remains gastroscopy and gastric biopsy [28].

Our results concur with previous reports showing that both the prevalence of PCabs and serum gastrin levels are significantly higher in subjects with GD disease compared to controls [26, 29]. Furthermore, we found that the relationship between elevated serum gastrin levels and GD was strengthened when we focused on GD subjects manifesting PCabs and the association was further enhanced when we excluded subjects with *H. pylori* antibodies. Similar to others, we found that *H. pylori* abs in GD subjects were associated with only small, statistically significant but probably not clinically important elevations in gastrin levels when compared to controls [2, 30].

Elevated gastrin levels, as we have found, have been associated with hyperthyroidism by some [31] but not all authors [32] and are often shown to remain elevated despite correction of hyperthyroidism [33]. Our study cohort was comprised of subjects newly diagnosed with hyperthyroidism and GD. We found gastrin levels to be unchanged (P=0.91) after correction of the hyperthyroidism in a subset of patients in whom follow-up gastrin levels were analyzed after euthyroidism was achieved. Additionally, serum gastrin levels may be influenced by the β-adrenergic system [31] and therefore affected by the use of β-blockers. While subjects in our study were newly diagnosed with GD, some had been initiated on β-blocker therapy prior to presentation to our endocrine clinic. We therefore compared gastrin levels between subjects taking and those not taking β-blockers and found almost identical mean gastrin levels (P=0.95). Other authors have likewise observed no significant differences in mean serum gastrin levels of patients treated with and without β-blockers [33]. Of note, serum gastrin levels in our study were random and not fasting as would have been most ideal.

GD patients with hypergastrinemia and PCabs often have autoimmune gastritis. Centanni et al. found that 35% of AITD subjects had elevated gastrin levels and biopsy proven gastritis [9]. In a study by Tozzoli et al., 26.2% of adult GD subjects were found to have PCabs [19]. Segni et al. showed that 57% of children with GD have PCabs [26]. Conversely, Lahner found that 53% of patients with atrophic gastritis have an associated thyroid disorder [34]. A Gastro-thyroid connection has been discussed for a half century [35] and has been referred to as thyrogastric disease [36] and more recently defined as part of Autoimmune Polyglandular Syndrome (APS) type 3b [37]. A similar association with gastric autoimmunity has been described in patients with Type 1 diabetes mellitus [1, 38, 39]. A possible explanation for the coexistence of GD and type A gastritis may be an autoimmune cross-reaction of the two major antigenic targets of these diseases.

Thyroid peroxidase and the gastric H^+/K^+ ATPase have been shown to share an 11-residue epitope [40]. Likewise, of similar interest is the recent description of potential links between *H. pylori* infection and the pathogenesis of autoimmune gastropathy as well as the pathogenesis of autoimmune thyroid disease [41]. In fact, it has been proposed that *H. pylori* infection via antigenic mimicry (leading to the production of PCabs) may trigger gastric autoimmunity [18, 42] and a progressive clinical course characterized initially by IDA and subsequently pernicious anemia (PA) [11, 16, 43]. *H. pylori* infection, via a similar mechanism, has been implicated in the pathogenesis of thyroid autoimmunity [41].

In this study, we show that patients with GD and serology consistent with autoimmune gastropathy were more likely to have iron deficiency, evidenced by low serum ferritin, low MCV, and elevated TIBC. Iron absorption is highly dependent on normal gastric acid secretion to solubilize and reduce dietary iron, and iron absorption is therefore impaired by the achlorhydria associated with autoimmune atrophic gastritis [5]. Anemia was observed by Centanni et al. in 82% of patients with AITD and gastritis vs. 22% of patients without gastritis [9]. IDA is diagnosed in up to 52% of patients with autoimmune gastritis [7, 43]. Conversely, atrophic gastritis is diagnosed in 20-30% of patients with IDA and no gastrointestinal symptoms [2, 3]. In our study, GD patients with a clinical diagnosis of IDA were twice as likely to have PCabs compared to all other GD subjects, including those with 'GD anemia' (non-iron deficiency anemia).

In this study, GD subjects with iron deficiency anemia showed a significant trend for higher prevalence of PCabs when compared directly to those with 'GD anemia' (64% vs. 30%, P= 0.07) and those with normal hemoglobin levels (64% vs. 33%, P=0.09). Of the 26 subjects diagnosed with 'GD anemia', 7 presented for follow-up hemoglobin levels after correction of hyperthyroidism with 100% (7/7) showing normalization of hemoglobin levels. On the contrary, of the 11 GD patients diagnosed with iron deficient anemia, 4 presented for follow-up hemoglobin levels after achieving euthyroidism with 0% (0/4) showing normalization of hemoglobin (P=0.003, 0/4 vs. 7/7).

When we examined individual markers of IDA such as serum ferritin and MCV in all GD subjects as well as all anemic GD subjects, we found statistically significant inverse associations or significant inverse trends between PCab positivity and ferritin and MCV values. Additionally, mean TIBC levels trended to be higher in PCab+ subjects. Mean serum gastrin levels were also found to have a strong negative correlation to serum ferritin levels in all GD subjects.

The association of PCabs with the specific markers of IDA appeared to be stronger than the association of gastrin levels with these markers. This may possibly be due to the high rate of concurrent *H. pylori* infection which initially leads to atrophy of the gastric antral mucosa and the gastrin producing G cells [15]. Additionally, the number of subjects in our study with anemia and particularly IDA was small, which likely affected our ability to show stronger correlations. We did not exclude celiac disease as a contributing cause of IDA in our study population. Celiac disease represents the cause of unexplained IDA in only a very small (~5%) percentage of patients [2] however the percentage may be higher when studying subjects with autoimmune disease such as our patient population.

The association of PA with autoimmune thyroid disease [35] as well as autoimmune gastropathy is well known [14]. However, none of the subjects in our cohort presented with macrocytosis and B12 levels were within normal limits (200-900 pg/ml) for all but 2 GD subjects. Other authors have reported prevalence rates for PA in GD as high as 2.3% [8]. However, PA is thought to develop after a median of 20-40 years of chronic atrophic gastritis [16, 17, 44]. The subjects in our cohort were relatively young and newly diagnosed with GD. Furthermore, recent reports suggest that the anemia associated with atrophic gastritis may initially present as IDA (particularly in young menstruating women whose iron stores are challenged) and progress to PA over time [2, 3, 5, 9, 43]. This may explain why our cohort of predominantly younger and female subjects exhibited IDA and not PA. These subjects may however, be at risk of developing PA in the future.

Autoimmune gastritis represents a significant cause of unexplained IDA [3] and often goes

undiagnosed [1-3]. Studies have shown that only half of patients with autoimmune gastritis have gastrointestinal symptoms [7]. The risks associated with undiagnosed autoimmune atrophic gastritis need to be considered. Chronic IDA is associated with palpitations, pallor, fatigue, poor exercise tolerance, decreased work performance, and can influence learning ability, cellular immunity and increase the frequency of premature and low birth weight deliveries [1, 4]. Additionally, IDA secondary to gastropathy has been associated with refractoriness to iron supplementation and chronic atrophic gastritis has been associated with malabsorption of levothyroxine [15, 45, 46] which can be mitigated with clinical interventions addressing the achlorhydria [47, 48]. Furthermore, atrophic gastritis has been associated with gastric cancer [6, 49], gastric carcinoid [14, 49-51] and malt lymphoma [2]. For these reasons, endoscopic follow-up in patients with autoimmune gastritis is recommended every 3-5 years [52]. Recent evidence suggests that autoimmune atrophic gastritis may be predicted non-invasively using PCabs, anemia, and/or high gastrin levels [53, 54].

In conclusion, a subset of patients presenting with GD may suffer from iron deficiency anemia due to concurrent autoimmune atrophic gastropathy. Consideration should be given to early diagnosis and treatment of these conditions to avoid associated future risks.

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Disclosure of conflict of interest

None.

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