Autoimmune Metaplastic Atrophic Gastritis in a Filipino Patient: A Case Report

Shareena Vanessa L. Montano, MD

Conrado B. De Castro, MD

Institute of Digestive and Liver Diseases, St. Luke's Medical Center-Quezon City, Philippines

Abstract

Background: Autoimmune metaplastic atrophic gastritis (AMAG) is a chronic, progressive inflammatory disease that affects roughly 0.1 percent of the general population and 2% of those over the age of 60. Pernicious anemia, atrophic gastritis, antibodies to parietal cell antigens and intrinsic factor, achlorhydria, and hypergastrinemia are all common findings in this disease. In addition, it is a major risk factor for stomach neoplasia.

Methods: We have a 44/F with no known comorbids who came in due to epigastric pain. One week prior to admission patient noted intermittent epigastric pain, burning and sharp in character, nonradiating lasting for 1 to 2 hours, aggravated by food intake. This was associated with episodes of regurgitation and occasional post-prandial vomiting and dizziness. On physical examination, she had pale palpebrae conjunctivae and abdominal examination revealed direct epigastric tenderness with no guarding or rigidity.

Results: Laboratories done showed megaloblastic anemia with low Vitamin B 12 levels and positive Fecal Immunochemical Test.Esophagogastroduodenoscopy revealed pale gastric mucosa and absentrugal folds.Colonoscopy showed normal terminal ileumand internal hemorrhoids grade 1. Multiple biopsies takenfrom the corpus revealed gastric fundic type mucosa with moderate chronic inflammation, mild intestinal metaplasia and severe atrophyand absentHelicobacter pyloriorganism. Histopathologic samples stained positive for immunohistochemical stains, chromogranin and synaptophysin. Further laboratories done also showed elevated serum gastrin. She was then discharged and started on lifelong parenteral Vitamin B12 supplementation.

Conclusion: AMAG is a rare disease entity. It should be suspected in patients with anemia and Vitamin B 12 deficiencey. Prompt recognition is important as it is a risk factor for gastric cancer and carcinoid tumors as well as preventing longterm complications of Vitamin B12 deficiency.

Keywords: Case report, Autoimmune metaplastic atrophic gastritis, AMAG, Vitamin B12, Endoscopy

Case Presentation

A 44-year old Filipino woman withoutany known comorbids came in due to intermittent epigastric pain of one week duration. The pain was nonradiating; burning and sharp in character. It was aggravated by food intake and would spontaneously resolve within two hours. Episodes were occasionally associated with regurgitation, post-prandial vomiting and dizziness.On physical examination, she had normal vital signs, afebrile with BMI of 23 kg/m2. Physical examination showed pale palpebral conjunctivae and direct tenderness on the epigastric area with no rigidity or guarding.

At the emergency ward she was given intravenous Pantoprazole 40mg and was hydrated with PNSS at a rate of 80cc/hr. Complete blood count showed macrocytic anemia (Hgb 8.1 d/dL,Hct 22.6%, MCH 43pgand MCV 121 fL). . Other laboratories requested showed normal ferritin (108.9 ng/mL), corrected reticulocyte count (1.8%), total serumiron (151 ug/dL), iron binding capacity (253pg/dL) and folate (16.90ng/mL). Peripheral blood smear revealed normochromic anemia with few macrocytes andhypersegmented neutrophils consistent with megaloblastic anemia.Patient also had markedly low Vitamin B12 (<83 pg/mL by CMIA assay; N: 187-883 pg/mL) and positive Fecal ImmunochemicalTest. She was assessed as a case of megaloblastic anemia secondary to Vitamin B12 deficiency andwas subsequently started on Mecobalamin 1000mcg IM daily.She was then referred to gastroenterology for the abdominal painEsophagogastroduodenoscopy and colonoscopy were performed aswork-up for consideration ofanemia and positive FIT.

Patient underwent esophagogastroduodenoscopy (Figure 1) using Fujifilm videoendoscope EGL 590zw SN 1G388K080 whichshowed pale gastric mucosa with absence of rugal folds at the corpus. There were patches of hyperemia without mucosal breaks at the antrum.The duodenal bulb down to the portion of the descending duodenum was unremarkable. On retroflexed view, the scope is loosely hugged by the cardia.

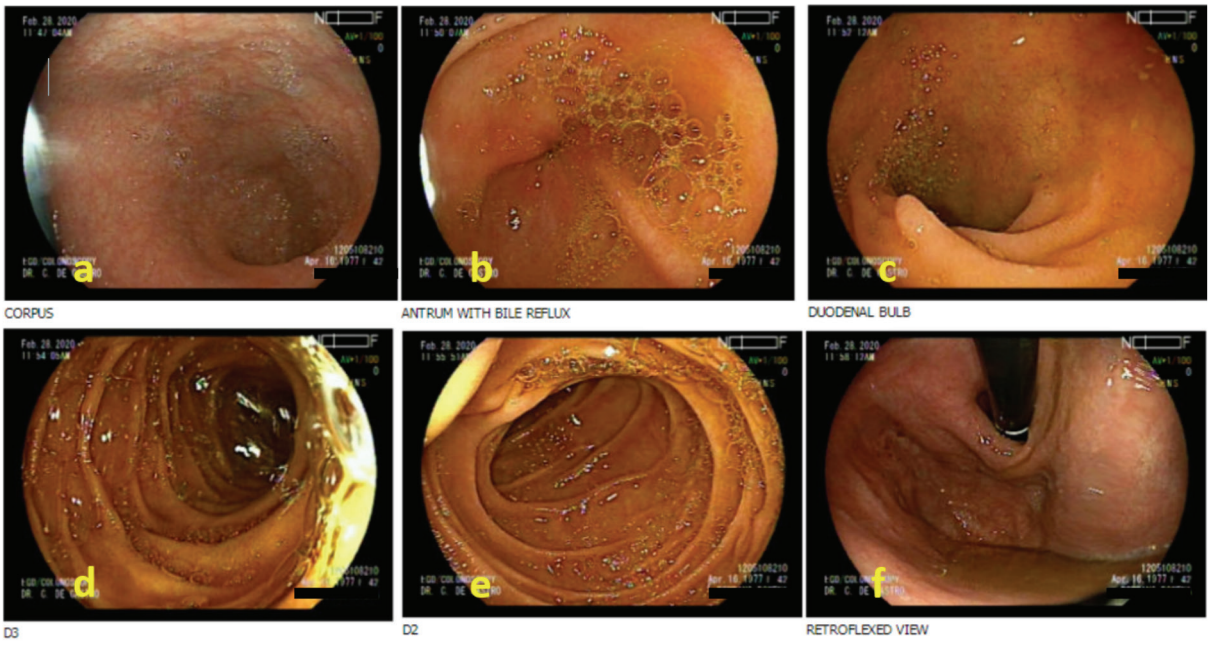

Figure 1. Esophagogastroduodenoscopy on white light. (a) Gastric corpus with pale mucosa and no appreciable rugal folds (b) Pylorus and antrum with patches of hyperemia without mucosal breaks (c,d,e) Normal duodenal bulb, descending portion of the duodenum and unremarkable ampulla (f) Retroflexed view with the cardia loosely hugging the scope.

Blue LaserImaging (BLI) (Figure 2) showed prominent vascularity, foveolar type micromucosal pattern andloss of normal regular collecting venules at the corpuswhich are findingsconsistent with autoimmune gastritis. There was regular antral pattern. Multiple biopsiesusingBoston Scientific Single-use Radial Jaw fromthe corpus, antrum and incisura angulariswere taken and sent for histopathologyfollowing the Sydney biopsy protocol.

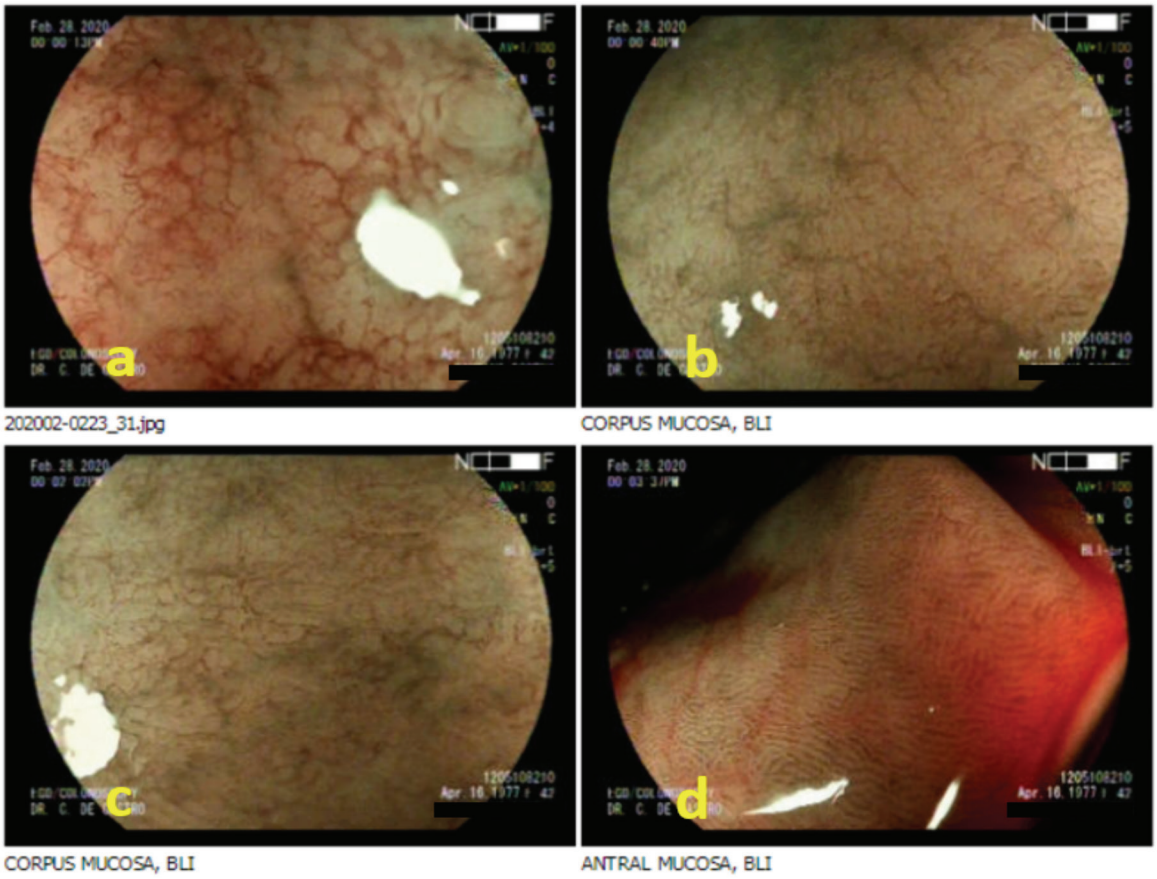

Figure 2. Gastric mucosa on Blue Laser Imaging. (a) Prominent vascularity at the corpus (b,c)Loss of regular collecting venules at the corpus with foveola type micromucosal pattern d. Normal antral pattern

Due to the suspicion of atrophic gastritis on esophagogastroduodenoscopy, fasting serum gastrin using enzyme labeled immunometric assayand intrinsic factor determinations were done. Serum gastrin(494 pg/mL; N: 13-115 pg/mL) was elevated and intrinsic factorwas within normal limits (18.7 U/mL; N: <=6 Positive).

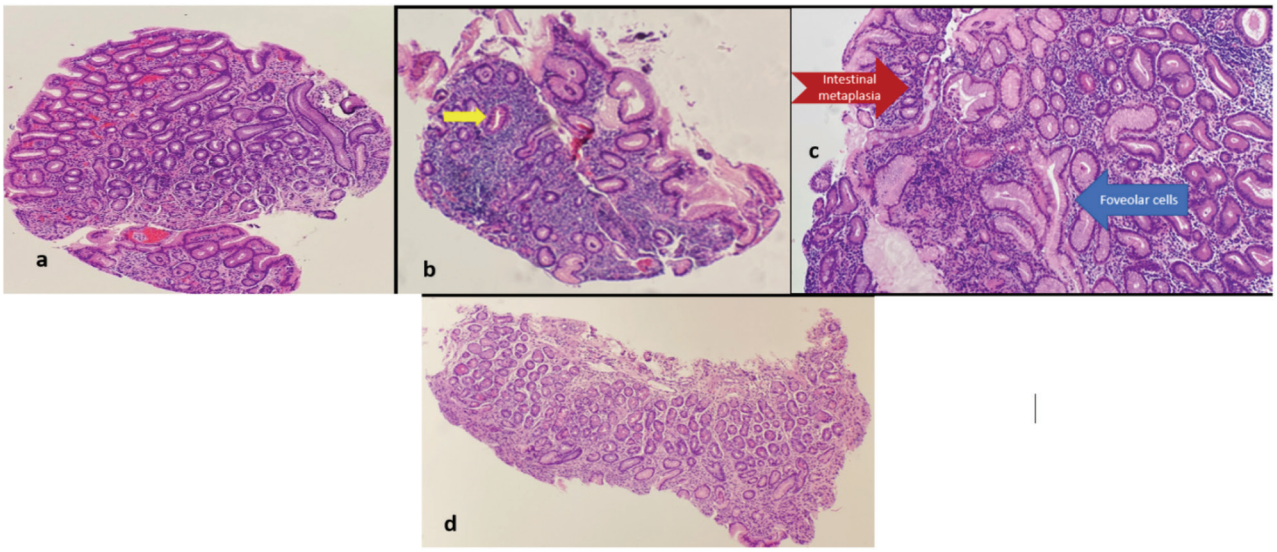

Figure 3. Microsections of gastric mucosa on H&E stain.(a) Gastric antral mucosa on LPO showed loosely packed mucinous glandular component with lightly eosinophilic to clear cytoplasm. There is a near even distribution in the volume of space occupied by gastric pit and glandular mucosa with few neutrophils and and plasma cells (b) Gastric corpus mucosa on LPO disclose a gastric fundic type mucosa with moderate chronic inflammation (as presented by presence of plasma cells), mild intestinal metaplasia (yellow arrow) (c) Gastric corpus mucosa on HPO showing presence of goblet cells (red arrow) consistent with intestinal metaplasia with severe atrophy characterized disorganized glands and gland drop out by architectural pattern. (d) Microsection of gastric incisura mucosa on LPO

Microsections of gastric antral-type mucosa (Figure 3a) showed mild chronic inflammation with no active inflammation, intestinal metaplasia, atrophy or dysplasia. No H. pylori organism was also seen.Furthermore, microsections of gastric corpus (Figure 3b,c)showed gastric fundic type mucosa with moderate chronic inflammation, mild intestinal metaplasia and severe atrophy. No H. pylori organism was seen. Lastly, microsections of the incisura (Figure 3d) showed gastric antral type mucosa with evenly spaced glands and mild chronic inflammation.

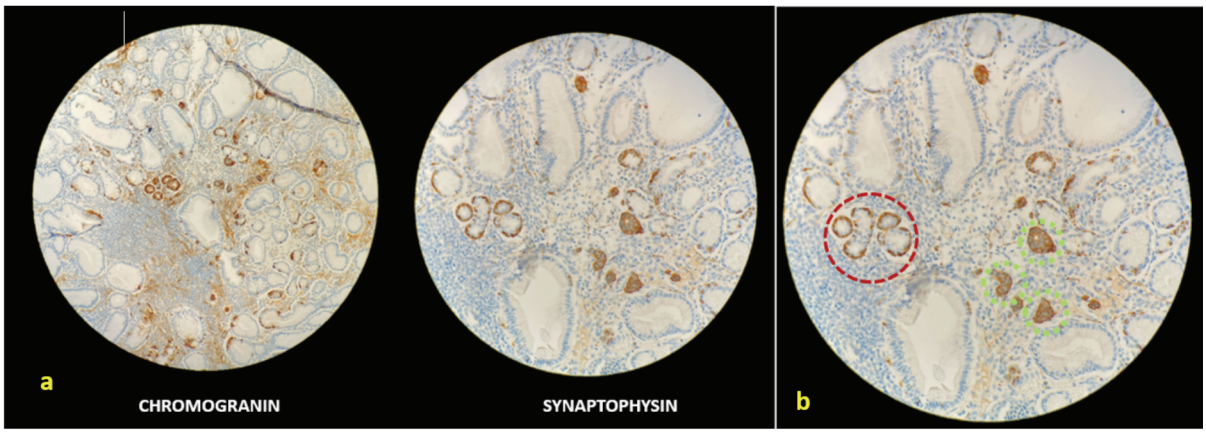

Figure 4. Immunohistochemical stains.(a) Positive for chromogranin and synaptophysin (b) On HPO, the cells encircled in red show linear hyperplasia which is defined as linear groups of 5 or more cells inside the glandular basement membrane. Meanwhile, those encircled in green exhibit micronodular hyperplasia, defined as clusters of 5 or more cells within epithelium measuring <150 um in diameter. Hence, these stains highlighted the presence of enterochromaffin-like cell hyperplasia in linear and micronodular patterns.

Immunohistochemical stains, chromogranin and synaptophysin were requested(Figure 4a)to check for neuroendocrine cell proliferation especially ECL-cell hyperplasia which stained positive, a findingconsistent with autoimmune gastritis. It also demonstrated linear and micronodular ECL cell hyperplasia (Figure 4b), a finding that helps differentiate autoimmune gastritis from H. pylori gastritis.

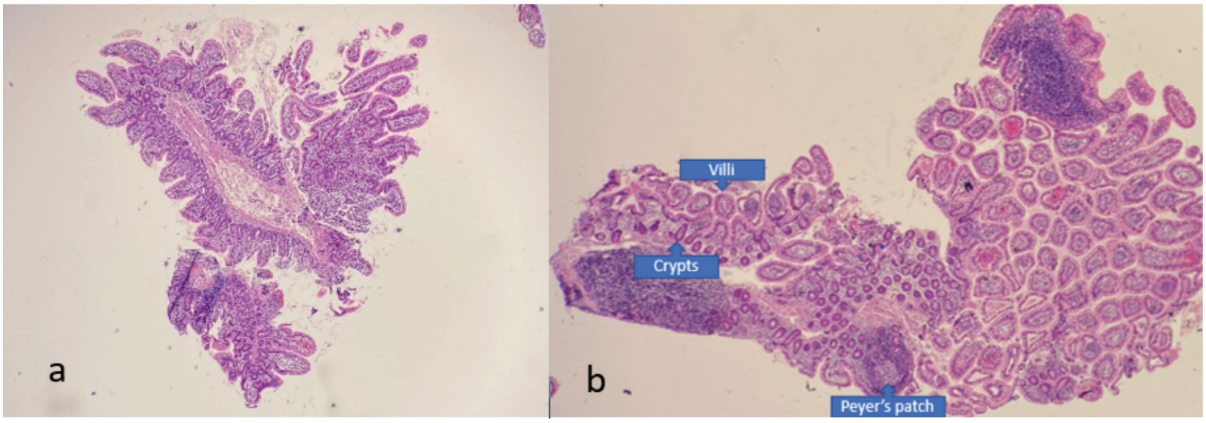

Figure 5. Duodenal and Ileal mucosa. (a) Normal duodenal mucosa on LPO (b) Ileal biopsy on LPO showed lymphoid aggregates, Peyer's patch, crypts and villi. The ileal mucosa did not show any diagnostic alteration as well as no active inflammation with no neutrophils present

Histopathology of the duodenal mucosa (Figure 5a) showed no diagnostic alteration, no active and chronic inflammation, villous blunting, increased intraepithelial lymph nodes or dysplasia.In addition, colonoscopy showed normal terminal ileum, normal colonic mucosa with no noted mucosal alterations, polyps or mass lesions but she was noted to have internal hemorrhoids grade 1. Biopsies from the ileal mucosa (Figure 5b) showed normal findings.

With the findings of Vitamin B 12 deficiency, megaloblastic anemia, atrophic gastritis and histopathology showing intestinal metaplasia, severe atrophy at the corpus also staining positive for synaptophysin and chromoganin as well as elevated serum gastrin, patient was managed as a case of AMAG) She was then started on Mecobalamin 1000mcg IM daily initially for seven days and was discharged improved. She was advised follow-up with Hematology and Gastroenterology services. However, patient was lost to follow-up as of time of writing.

Discussion

AMAG is an antibody mediated disorder targeted against parietal cell H, K-ATPase resulting to destruction of glands in the corpus. It is often linked with long-term hematologic implications such as pernicious anemia. Its prevalence increases with age and is higher in women. Acid production and intrinsic factor secretion arereduced when parietal cells are lost which leads to ineffective vitamin B12 absorption in the terminal ileum. This reduced vitamin B12 absorptionis the primary deficiency that leads to pernicious anemia. Moreover, because gastric acidity decreases, somatostatin inhibition of acid secretion is reduced, resulting to increased gastrin production from antral G cells. Hypergastrinemia leads to ECL cell growth and hyperplasia with concomittant increased risk of type I gastric carcinoids.[1`3]AMAG also increases risk of developing stomach adenocarcinoma to nearly seven-fold.[3]

Patients with AMAG may be asymptomatic, however they frequently have dyspepsia and postprandial distress which was noted in this case. Furthermore, patients with AMAG typically experience vague or nonspecific symptoms such as weariness, irritability, cognitive deterioration that are most likely attributable to anemia. [3]

Laboratory parameters seen in patients with AMAG include elevated serum gastrin, decreased PepsinogenI/II ratio, low serum Vitamin B12, megaloblastic anemia, anti-intrinsic factor antibody and antiparietal cell antibody. Biopsy, however, remains as the most reliable method to evaluate the presence of metaplastic atrophic gastritis.[3]Five biopsy samples should be taken, according to the updated Sydney System: two from the corpus, two from the antrum and one from the incisura angularis

to standardize reports of gastric biopsies.[5] Histopathology would demonstrate atrophy of the gastric mucosa with loss of glandular cells and their replacement by metaplastic epithelium. In this case, metaplasia, glandular atrophy, and inflammation were confined to the gastric body and fundustypical of AMAG. Furthermore, immunostaining for endocrine cells such as G cells and enterochromaffin-like cellswere done confirming pseudopyloric metaplasia. Lastly, in order to assess the severity of gastric atrophy, OLGA staging is used which is based on the assumption that gastric cancer risk is related to the degree of gastric glandularatrophy. It distinguishes four stages of severity by scoring atrophy histologically in both oxyntic andantral/ angular biopsy samples. Our patient has stage II atrophy,and stages III and IV are associated with a greater risk of developing gastric cancer.2Some laboratory examinations are not readily available in our setting such as anti intrinsic factor antibody and anti parietal cell antibody. However, we were able to confirm our diagnosis through a combination of history, endoscopic findings, histopathology and laboratory examinations.

The treatment is lifelong replacement therapy with injectable cobalamin at a dose of 1000 mcg daily or every other day for a week, then weekly for one to two months, and finally monthly for the rest of the patient's life. Within the first 5 days to 2 weeks of treatment, cobalamin therapy reverses all aberrant hematologic abnormalities, with serum cobalamin normalcy after two weeks. Macrocytosis usually goes away during the first month of treatment, although hemoglobin normalization takes longer.5Judicious review of current literature shows no specific management for the abdominal discomfort associated with AMAG.

Upper endoscopy should be performed to identify prevalent lesions (carcinoid tumors and gastric cancer) at the time of diagnosis and to stage the severity of autoimmune metaplastic atrophic gastritis. The presence of dysplasia or precancerous lesions warrants a follow-up within 1 year.3According the the 2019 ESGE Guidelines, endoscopic follow-up every three to five years in patients with AMAG.

Recommendation

Autoimmune metaplastic atrophic gastritis is a rare disease entity but carries an increased risk of developing gastric carcinoid and adenocarcinoma. It should be suspected in patients with megaloblastic anemia and low Vitamin B12.Other laboratory abnormalities that are associated with AMAG include hypergastrinemia, antibodies to parietal cells and intrinsic factor.Treatment is centered on lifetime parenteral Vitamin B12 supplementation. Esophagogastroduodenoscopy with mucosal biopsy following the updatied Sydney systemneeds to be done at time of diagnosis to confrim and stage the disease; and to detect potentially malignant lesions. Surveillance upper gastrointestinal endoscopy is recommended yearly for patients with dysplastic lesions; and 3-5 years if without dysplasia.

Conflict of Interest

The authors declare no conflict of interest.

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