

# Autoimmune Gastritis Treated With Mycophenolate Mofetil

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## ABSTRACT

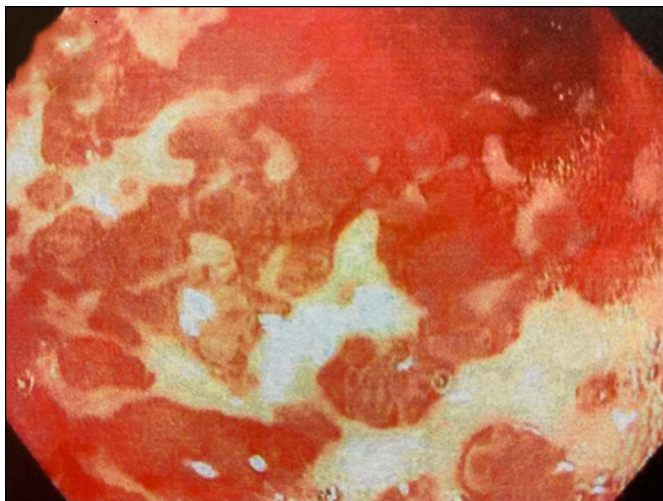
Autoimmune gastritis is an inflammatory condition of the gastric mucosa. We report a 64-year-old woman with chronic abdominal pain of 3-year duration. Endoscopic and histologic evaluation revealed autoimmune pangastritis. The gastritis was partially responsive to steroids but attempts to taper failed, and the patient had no relief from mercaptopurine, adalimumab, budesonide, or hydroxychloroquine. The patient was treated with mycophenolate mofetil which resulted in resolution of symptoms. Endoscopic and histologic examination after mycophenolate therapy showed near complete resolution of active inflammation. To the best of our knowledge, this is the first report of symptomatic autoimmune gastritis successfully treated with mycophenolate mofetil.

## INTRODUCTION

Classic autoimmune gastritis (AIG) is a gastric-body predominant inflammatory process mediated by antibodies which target the parietal cell H<sup>+</sup>,K<sup>+</sup>-ATPase.<sup>1</sup> Patients with body-predominant AIG present with symptoms including epigastric pain, weight loss, heartburn, and nausea.<sup>2</sup> The most serious long-term consequences are malignancy, vitamin deficiency (ie, vitamin B12), and pernicious anemia. There are few reports of patients with autoimmune pangastritis with diffuse involvement of the body and antrum.<sup>3,4</sup> In this report, we present a patient with severe abdominal pain and pangastritis who was treated with multiple immunosuppressants for symptomatic relief.

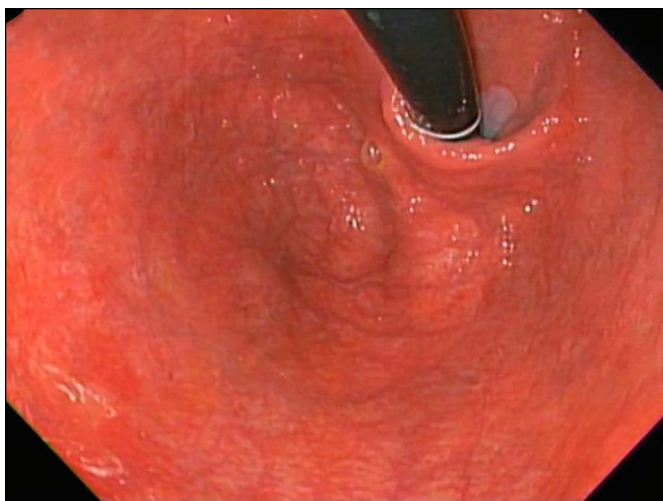
## CASE REPORT

A 64-year-old white woman presented to our clinic for a second opinion on her unremitting epigastric postprandial abdominal pain, and nausea of 3-year duration associated with 35-pound weight loss. She had a history of hypertension (treated with olmesartan), hypothyroidism, and lichen planus. Her previous workup showed microcytic anemia and low normal vitamin B12 levels. Abdominal computed tomography was normal. Endoscopy at an outside institution showed deeply ulcerated gastric mucosa (Figure 1). The duodenum, terminal ileum, and colon were endoscopically and histologically unremarkable. Gastric biopsies showed *Helicobacter pylori* gastritis which was treated with quadruple therapy including a maximal dose of proton pump inhibitor. Her abdominal pain continued and endoscopy a month later showed persistent gastric ulcerations. Biopsies of the gastric antrum and body showed continued severe inflammation; however, *H. pylori* was eradicated. Peripheral blood studies including gastrin, anti-intrinsic factor antibodies, and antiparietal cell antibodies were unremarkable. A clinical diagnosis of Crohn's disease was considered because of the previous endoscopic findings. Additional workup including video capsule endoscopy, 24-hour pH-impedance monitoring, esophageal manometry, computed tomography mesenteric angiogram, and gastric emptying studies was all unrevealing. She continued to have severe and unremitting abdominal pain. She continued maximal proton pump inhibitor and was started on prednisone (40 mg daily for 2 weeks, 10 mg taper per week until 5 mg daily) with moderate improvement in clinical symptoms and endoscopic findings. While on 5-mg prednisone, endoscopy showed partial improvement in gastric ulcerations (Figure 2).



**Figure 1.** Initial endoscopy shows severe inflammation with deep ulceration throughout the stomach.

With tapering doses of prednisone, she had recurrence of epigastric abdominal pain and weight loss associated with early satiety, nausea, and hair loss. Clinical suspicion of Crohn's continued based on the lack of improvement in gastrointestinal symptoms and persistent gastric ulcerations. A rheumatologic evaluation at an outside institution revealed elevated C-reactive protein (55 mg/L), antinuclear (1:320), anti-Smith (>8 U), and antichromatin antibodies (>2 U) which were concerning for systemic lupus erythematosus as well as gastric Crohn's disease. In an attempt at steroid sparing therapy, she was sequentially treated at outside institutions with mercaptopurine (6 months), adalimumab (5 months), budesonide (4 months), and hydroxychloroquine (6 months) without improvement in symptoms, serological markers, endoscopy, or histology. She remained on varying doses of prednisone which partially improved her abdominal pain.



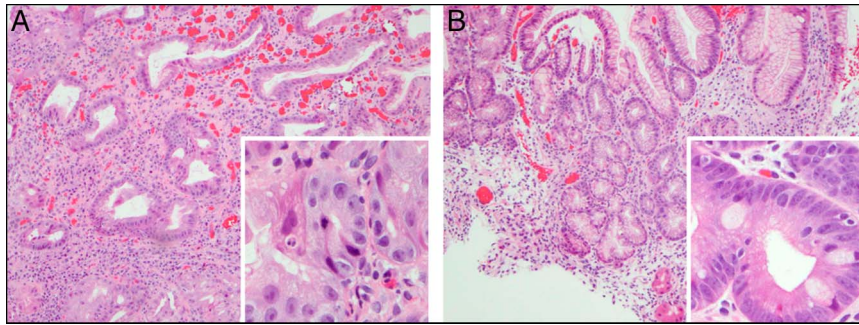
**Figure 2.** Treatment with steroids (prednisone, 5 mg per day) showed some improved, but continued inflammation (gastric body).

Two years after her initial presentation, she was referred to our institution on prednisone 20 mg daily with continued abdominal pain, weight loss, and nausea. Outside biopsies from previous endoscopies were reviewed, and olmesartan-associated gastritis or autoimmune pangastritis was added as additional considerations. Olmesartan was discontinued; however, endoscopy 3 months later showed continued severe inflammation in the stomach with superficial ulcers in the antrum. The histology was still suggestive of autoimmune pangastritis (Figure 3 A). Her prednisone dose was tapered and then discontinued. A subsequent evaluation showed some endoscopic improvement but continued ulceration. Her abdominal pain improved, but she then developed arthralgia and muscle weakness. She was referred to a rheumatologist at our institution and was found to have persistently elevated serum antinuclear antibody, anti-Smith, and anticentromere antibodies. The primary diagnosis was now considered autoimmune pangastritis secondary to atypical systemic lupus erythematosus. At this point, she had been off prednisone for 4 months. Since hydroxychloroquine had been previously ineffective, she was started on mycophenolate mofetil (MMF) at 250 mg twice a day and was escalated to 750 mg twice a day over a month. She had resolution of abdominal pain and arthralgias. Histology after MMF treatment showed resolution of active inflammation, but continued chronic inflammation with extensive metaplasia (Figure 3B). Thirty-two months after MMF initiation, endoscopy showed complete resolution of mucosal ulcerations (Figure 4). Biopsies showed no active inflammation, but inactive chronic gastritis with atrophy and intestinal metaplasia were noted (Figure 5). The patient is currently on MMF 500 mg twice a day and has remained asymptomatic with only minimal endoscopic or histologic inflammation.

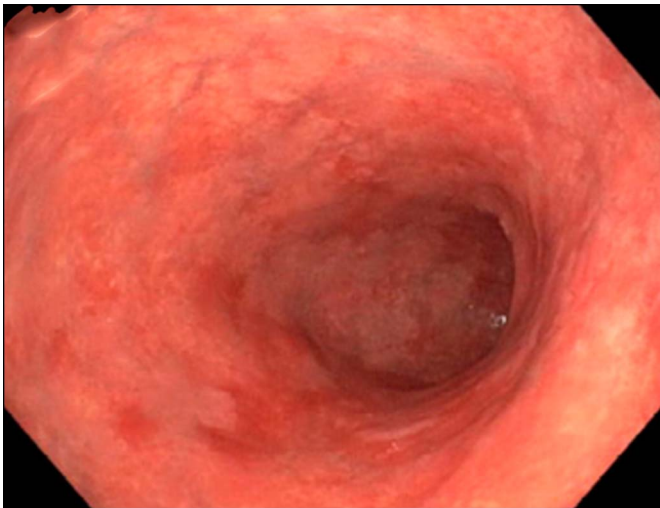
## DISCUSSION

AIG is a precancerous condition characterized by autoimmune destruction of gastric parietal cells.<sup>1</sup> The incidence of AIG is estimated to be approximately 4% of gastroenterology clinic patients with elderly women being disproportionately affected.<sup>2</sup> The diagnosis can be clinically challenging because gastrointestinal symptoms are nonspecific and hematologic manifestation based on B12/iron deficiency present late in the disease process.<sup>5</sup> An average delay of 14 months between symptoms onset and disease identification has been reported.<sup>6</sup> A high degree of suspicion, early measurement of intrinsic factor and parietal cell antibodies, and adequate endoscopic sampling of gastric mucosa can expedite diagnosis and help prevent disease consequences.<sup>1,5,7</sup>

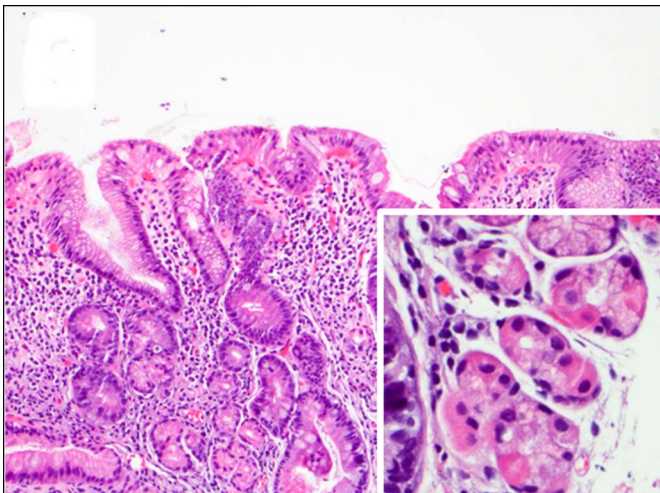
Lupus is a complex disorder with a wide range of gastrointestinal manifestations.<sup>8</sup> Another aspect of this patient's history was her treatment of hypertension with olmesartan, an angiotensin II receptor antagonist. Previous reports have described olmesartan associated with severe enteropathy as well as gastritis.<sup>9-11</sup> Olmesartan-associated gastritis was an initial consideration for this patient, but discontinuation of olmesartan did not resolve her gastritis.



**Figure 3.** (A) Gastric biopsies taken while the patient was being treated with steroids show active inflammation, glandular atrophy, and pyloric gland metaplasia; inset shows magnified pyloric gland and active inflammation. (B) Nine-month post-mycophenolate mofetil treatment, the active inflammation has resolved; however, there is continued chronic inflammation. The gastric body shows pyloric and intestinal metaplasia; inset shows intestinal glands with goblet cells.



**Figure 4.** Nine-month post-mycophenolate mofetil treatment, steroids had been tapered and patient was asymptomatic with no endoscopic evidence of ulceration or inflammation (gastric body).



**Figure 5.** The glandular atrophy is no longer complete; there is a re-emergence of occasional glands comprised of parietal and chief cells as shown in the inset.

Historically, management of AIG has centered around nutritional therapy including vitamin supplementation and gastric cancer screening. We are not aware of treatment strategies to alter the inflammatory disease course. MMF is an immunosuppressant that inhibits T- and B-cell proliferation, that in our patient resulted in complete symptomatic relief of pain and remission of disease activity by endoscopy and histology.<sup>12</sup> The patient has tolerated >32 months of MMF therapy with no adverse events. As far as we know, this is the first human report of immunosuppressive control of AIG. Further studies are needed to validate the efficacy and safety of MMF therapy in AIG.

## DISCLOSURES

**Author contributions:** All authors contributed equally to this manuscript. JY Park is the article guarantor.

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Informed consent was obtained for this case report.

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## REFERENCES

1. Park JY, Lam-Himlin D, Vemulapalli R. Review of autoimmune metaplastic atrophic gastritis. *Gastrointest Endosc* 2013;77:284–92.
2. Miceli E, Lenti MV, Padula D, et al. Common features of patients with autoimmune atrophic gastritis. *Clin Gastroenterol Hepatol* 2012;10:812–4.
3. Jevremovic D, Torbenson M, Murray JA, Burgart LJ, Abraham SC. Atrophic autoimmune pangastritis: A distinctive form of antral and fundic gastritis associated with systemic autoimmune disease. *Am J Surg Pathol* 2006;30:1412–9.
4. Pogoriler J, Kamin D, Goldsmith JD. Pediatric non-Helicobacter pylori atrophic gastritis: A case series. *Am J Surg Pathol* 2015;39:786–92.
5. Kulnigg-Dabsch S, Resch M, Oberhuber G, Klinglmueller F, Gasche A, Gasche C. Iron deficiency workup reveals high incidence of autoimmune gastritis with parietal cell antibody as reliable screening test. *Semin Hematol* 2018;55:256–61.

6. Lenti MV, Miceli E, Cococcia S, et al. Determinants of diagnostic delay in autoimmune atrophic gastritis. *Aliment Pharmacol Ther* 2019;50:167–75.
7. Mahmud N, Stashek K, Katona BW, et al. The incidence of neoplasia in patients with autoimmune metaplastic atrophic gastritis: A renewed call for surveillance. *Ann Gastroenterol* 2019;32:67–72.
8. Tian XP, Zhang X. Gastrointestinal involvement in systemic lupus erythematosus: Insight into pathogenesis, diagnosis and treatment. *World J Gastroenterol* 2010;16:2971–7.
9. Rubio-Tapia A, Herman ML, Ludvigsson JF, et al. Severe spruelike enteropathy associated with olmesartan. *Mayo Clin Proc* 2012;87:732–8.
10. Ma C, Park JY, Montgomery EA, et al. A comparative clinicopathologic study of collagenous gastritis in children and adults: The same disorder with associated immune-mediated diseases. *Am J Surg Pathol* 2015;39:802–12.
11. Shenbagaraj L, Swift G. Olmesartan-associated severe gastritis and enteropathy. *BMJ Case Rep* 2018;11:e226133.
12. Allison AC. Mechanisms of action of mycophenolate mofetil. *Lupus* 2005; 14(Suppl 1):s2-8.

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