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Case Report

Regression of Autoimmune Gastritis after Eradication of *Helicobacter pylori*

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Keywords
Autoimmune gastritis · Eradication · *Helicobacter pylori*

Abstract
We report a case of autoimmune gastritis (AIG) in which gastric mucosal atrophy improved with *Helicobacter pylori* eradication. Based on endoscopic findings (advanced gastric atrophy with vascular visibility and diffuse redness in remnant oxyntic mucosa), a woman in her 40s was suspected of having AIG coexisting with an active *H. pylori* infection. This was confirmed by a positive anti-parietal cell antibody (PCA, 1:160), an elevated serum gastrin level (638 pg/mL), and positive anti-*H. pylori* antibody (*Hp* Ab, 15.5 U/mL) and *H. pylori* stool antigen tests. Seven months after eradication, reduced vascular visibility and disappearance of diffuse redness on endoscopy and reduced PCA (1:40) and *Hp* Ab (5.1 U/mL) titers were observed, although histopathological findings (basal-predominant lymphocytic infiltration, destruction of parietal and chief cells, pseudopyloric metaplasia, and enterochromaffin-like cell hyperplasia) were consistent with AIG. Endoscopy 26 months after eradication showed further improvement in atrophic findings in the gastric corpus and histopathological recovery of parietal and chief cells in fundic glands. Serum gastrin levels returned to normal (64 pg/mL), and the PCA titer fell further (1:20).

Introduction

Autoimmune gastritis (AIG), a type of chronic atrophic gastritis, is characterized by immune-mediated inflammation that progressively destroys the parietal cells in fundic

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glands. *Helicobacter pylori* infection is one possible cause of AIG [1–4]; indeed, gastric atrophy improves after bacteria eradication in patients with *H. pylori*-positive AIG [5–7]. However, an experimental murine AIG model reported contrary findings, in which *H. pylori* infection suppressed development of AIG [8], and a recent case report suggested that AIG progressed after *H. pylori* eradication [9]. Here, we report a case of *H. pylori*-positive AIG in which regression of AIG after eradication therapy was detected on endoscopy, resulting in improved histopathological findings and serological markers.

Case Report

A woman in her 40s visited our hospital for further examination of microcytic anemia (red blood cell count, 3.93×10^6/μL; hemoglobin, 8.1 g/dL; mean corpuscular volume, 68.7 fL) and underwent esophagogastroduodenoscopy (EGD) in March 2019. Serum iron (11 μg/dL) and ferritin (7 ng/mL) levels were low, but vitamin B12 (431 pg/mL) was normal. The patient had never taken a proton-pump inhibitor. EGD showed extensive mucosal atrophy with marked vascular visibility in the entire area of the corpus except for the fornix, in which remnant oxyntic mucosa with diffuse redness and pseudopolyp-like lesions were observed (Fig. 1). The antrum was slightly atrophic. She was suspected of having AIG coexisting with an active *H. pylori* infection. This was confirmed by a strongly positive (1:160) anti-parietal cell antibody (PCA) test (indirect immunofluorescence method) and serum anti-*H. pylori* antibody (15.5 U/mL, enzyme immunoassay method) and *H. pylori* stool antigen (enzyme immunoassay method) tests; serum gastrin levels (radioimmunoassay method) were high (638 pg/mL) (Table 1). She received oral iron supplementation and eradication therapy for *H. pylori*.

In January 2020 (7 months after eradication therapy), another EGD showed reduced vascular visibility in the greater curvature of the middle to upper corpus (Fig. 2a), in addition to disappearance of diffuse redness in the fornix. PCA titers had decreased but remained positive (1:40) (Table 1). A biopsy specimen taken from the greater curvature of the middle corpus revealed basal-predominant dense lymphocytic infiltration of the lamina propria, resulting in obscured architecture of the fundic glands (Fig. 2b). Degeneration and pseudohypertrophy of parietal cells, a decrease in the number of chief cells, and foveolar hyperplasia were observed. Neither neutrophil infiltration nor intestinal metaplasia was observed. Degeneration of parietal cells and destruction of chief cells were illustrated by immunostaining for H^+/K^+-ATPase and pepsinogen I (PGI) (Fig. 2c, d). PGI-positive/MUC6-positive pseudopyloric metaplasia was observed (Fig. 2d, e). Linear hyperplasia of enterochromaffin-like cells was demonstrated by chromogranin A immunostaining (Fig. 2f). These serological and histopathological findings indicated that AIG persisted. Successful eradication was confirmed by a decrease in the serum anti-*H. pylori* antibody (5.1 U/mL) titer and the absence of *H. pylori* on immunohistochemical staining of a biopsy specimen.

Follow-up EGDs and serological tests were conducted in December 2020 and August 2021. PCA titers had declined further (1:20 and 1:20, respectively), and serum gastrin levels returned to normal (68 pg/mL and 64 pg/mL, respectively) (Table 1). EGDs showed reduced gastric atrophy in the greater curvature of the middle to upper corpus (Fig. 3a). A follow-up biopsy from the greater curvature of the middle corpus was performed in August 2021, 26 months post eradication. Recovery of the architecture of the fundic glands and regression of lymphocytic infiltration were revealed (Fig. 3b). Parietal and chief cells had recovered, as demonstrated by immunostaining for H^+/K^+-ATPase and PGI (Fig. 3c, d). PGI-negative/MUC6-positive pyloric metaplasia was observed (Fig. 3d, e). Chromogranin A immunostaining

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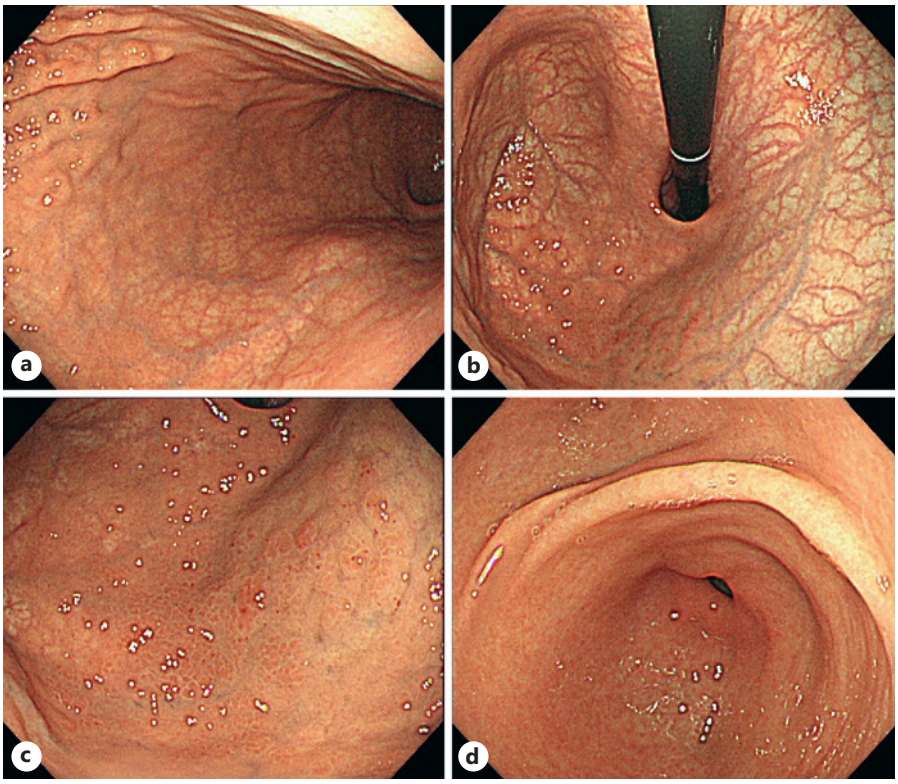

Fig. 1. Endoscopic findings in March 2019 show mucosal atrophy with vascular visibility in the greater and lesser curvature of the corpus (**a**, **b**), remnant oxyntic mucosa with diffuse redness and pseudopolyp-like lesions in the fornix (**c**), and mild atrophy in the antrum (**d**).

revealed reduced enterochromaffin-like cell hyperplasia (Fig. 3f). Neither intestinal metaplasia nor pancreatic acinar metaplasia was detected. These findings indicated that regression of gastric atrophy associated with AIG and partial recovery of fundic glands were ongoing after *H. pylori* eradication.

Discussion

The first EGD in 2019 showed corpus-predominant advanced gastric atrophy and diffuse redness in the remnant oxyntic mucosa. Diagnosis of AIG was confirmed by the high PCA titer and hypergastrinemia. A diagnosis of active *H. pylori* infection was made based on positivity for serum anti-*H. pylori* antibodies and stool *H. pylori* antigen. Regression of AIG after eradication was indicated by improvement of gastric atrophy on follow-up EGDs and evidenced by histopathological recovery of the fundic glands, as well as reduced PCA titers and serum gastrin levels (Table 1).

A majority of AIG patients are infected with *H. pylori* before the development of gastric atrophy, and AIG progression is accompanied by a decrease or disappearance of *H. pylori* [10, 11]. However, the detection of AIG with ongoing gastric atrophy in a background of active *H. pylori* gastritis is difficult, as reported in a previous case report [12]. In our case, it is possible that AIG, initially masked by active *H. pylori* gastritis, progressed and only became noticeable at presentation, although there are insufficient data to confirm this.

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Table 1. Time course of laboratory findings

	Mar 2019	Jan 2020	Dec 2020	Aug 2021
PCA (1:X)	160	40	20	20
Gastrin, pg/mL	638		68	64
Hp Ab, U/mL	15.5	5.1		
Hp SA	(+)			
UBT, ‰	1.3			
Tg Ab, U/mL	<10.0			
TPO Ab, U/mL	12.5			

PCA, anti-parietal cell antibody (X < 10); *Hp* SA, *Helicobacter pylori* stool antigen test; *Hp* Ab, anti-*Helicobacter pylori* antibody (<10 U/mL); UBT, ^{13}C-urea breath test (<2.5‰); Tg Ab, anti-thyroglobulin antibody (<28.0 U/mL); TPO Ab, antithyroid peroxidase antibody (<16.0 U/mL).

Gastrin (42–200 pg/mL).

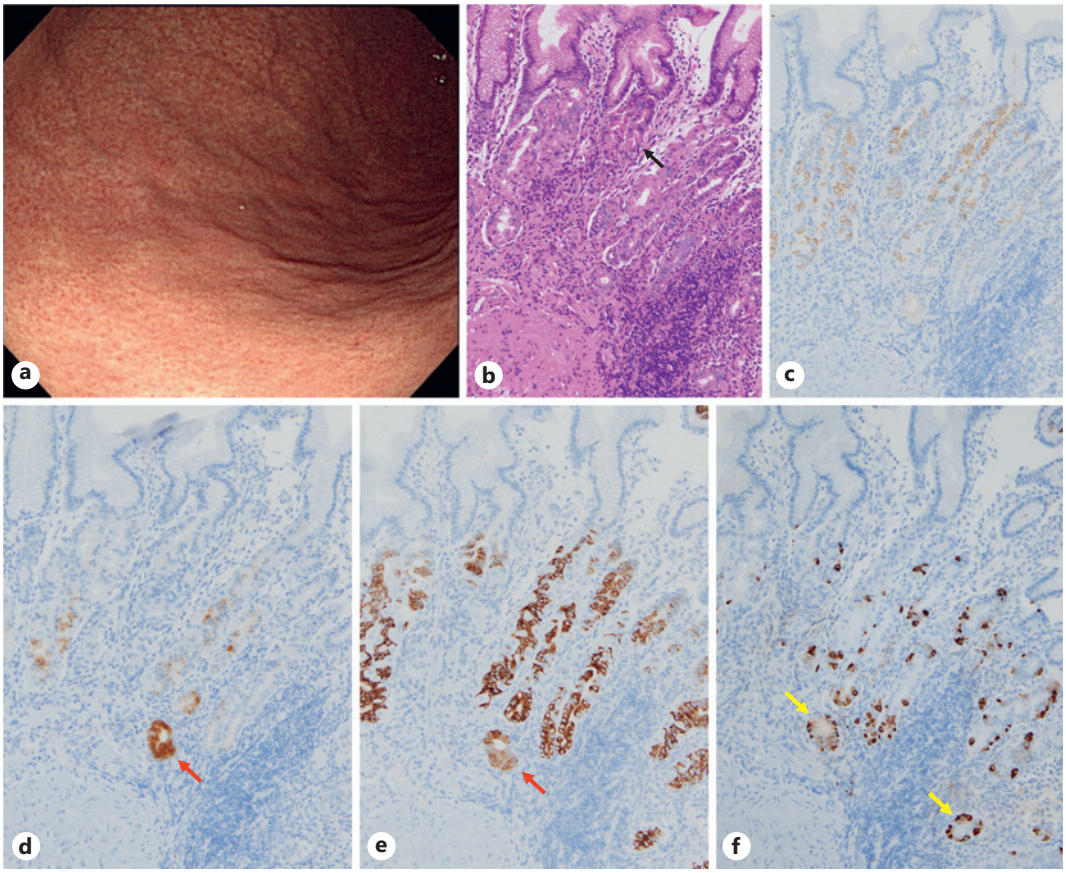

Fig. 2. Endoscopic and histopathological findings in January 2020. **a** Endoscopic findings in the greater curvature of the middle corpus show reduced vascular visibility. **b** Hematoxylin and eosin (H&E) staining (×200) shows basal-predominant dense lymphocytic infiltration, foveolar hyperplasia, remaining fundic glands with decreased numbers of parietal and chief cells, and parietal cell pseudohypertrophy (black arrow). Immunostaining for H^+/K^+-ATPase (**c**), PGI (**d**), and MUC6 (**e**) (×200) shows degeneration of remaining parietal cells (**c**), destruction of chief cells (**d**), and PGI-positive/MUC6-positive pseudopyloric metaplasia (red arrow) (**d**, **e**). **f** Chromogranin A immunostaining (×200) shows linear hyperplasia of ECL cells (yellow arrows). ECL, enterochromaffin-like.

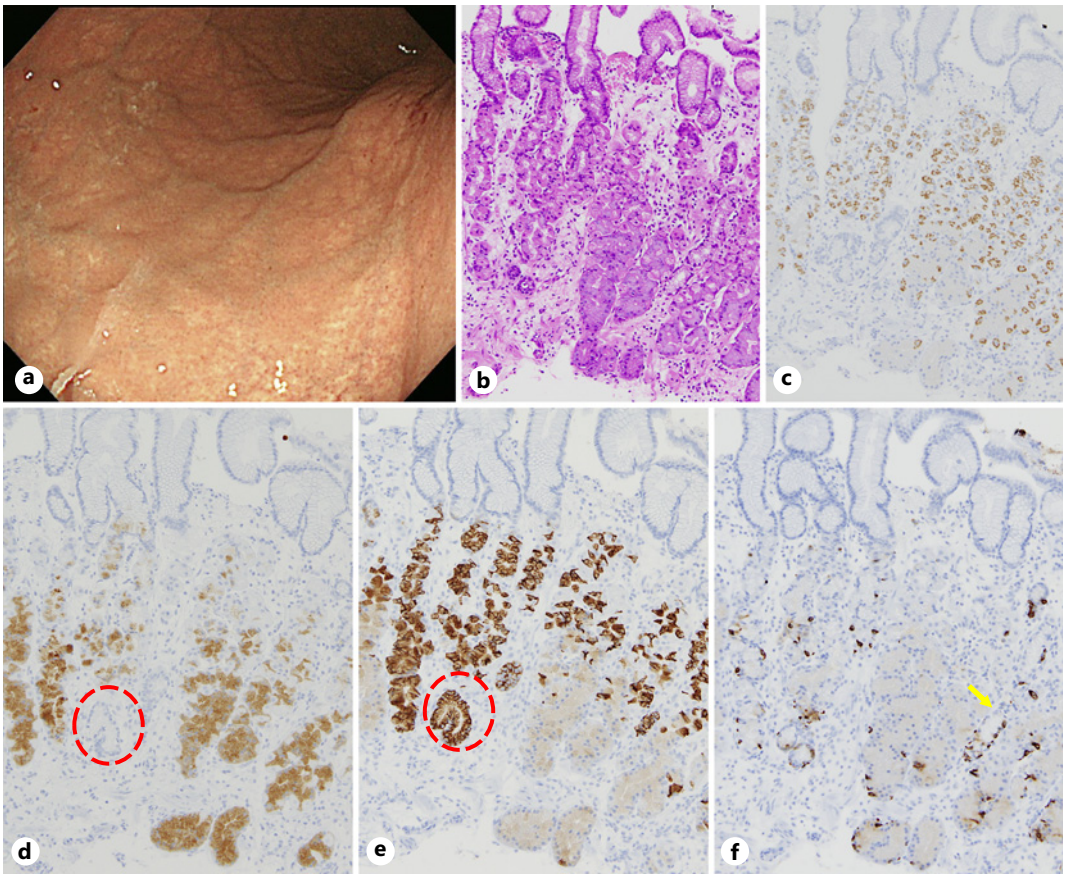

Fig. 3. Endoscopic and histopathological findings in August 2021. **a** Endoscopic findings in the greater curvature of the middle corpus show improved gastric atrophy. **b** H&E staining (×200) shows regression of lymphocytic infiltration and recovery of fundic glands. Immunostaining for H^+/K^+-ATPase (**c**) and PGI (**d**) (×200) shows recovery of parietal and chief cells. **d**, **e** Immunostaining for MUC6 (×200) shows PGI-negative/MUC6-positive pyloric metaplasia (red circle). **f** Chromogranin A immunostaining (×200) shows linear hyperplasia of ECL cells (yellow arrow). ECL, enterochromaffin-like.

Conflicting results have been presented regarding the effects of *H. pylori* eradication on *H. pylori*-positive AIG. One study reported that eradication led to healing of active gastritis in 80% of patients with non-atrophic *H. pylori*-positive AIG [5], whereas a previous case report showed rapid progression of gastric atrophy after eradication in a patient with *H. pylori*-positive AIG [9], supporting a hypothesis that *H. pylori* infection inhibits development of AIG (based on experimental data from a murine model) [8]. Another case report showed that early-stage AIG appeared after eradication of *H. pylori* in a patient with active *H. pylori* gastritis [12]. Other studies reported reversal of gastric atrophy after eradication in 20% of patients with *H. pylori*-positive AIG, while gastric atrophy was persistent at long-term follow-up in the remaining 80% [6, 7]. The presence of mild atrophy and moderate-severe inflammation and the absence of intestinal metaplasia are histopathological factors predictive of improvement of gastric atrophy [7]. Histopathological findings from the first biopsy in our case showed these predictive factors.

There are two types of pyloric gland-like metaplasia that occur to compensate for oxyntic mucosal damage in chronic atrophic gastritis, such as *H. pylori* gastritis and AIG [13, 14], namely, PGI-positive/MUC6-positive pseudopyloric and PGI-negative/MUC6-positive pyloric

metaplasia. Both types are characteristic features of AIG with advanced gastric atrophy. A few glands with pyloric gland-like metaplasia were observed in our case (Fig. 2, 3), suggesting regression of gastric atrophy after *H. pylori* eradication.

AIG is associated with an increased risk for two types of gastric neoplasm: adenocarcinoma and neuroendocrine tumor. Regarding gastric cancer in AIG, cancer risk is restricted to those with histologically high-risk stages of gastritis and is associated mainly with previous or current *H. pylori* infection [15, 16]. From the viewpoint of cancer prevention, it would be of great clinical importance to accurately identify AIG patients with active *H. pylori* infection before progression of gastric atrophy and to evaluate their histopathological findings after eradication. Patients with persistent gastric atrophy after eradication, along with intestinal metaplasia, should receive endoscopic surveillance.

In conclusion, endoscopic, serological, and histopathological findings demonstrated regression of gastric atrophy following eradication in a patient with AIG coexisting with active *H. pylori* infection. An accumulation of similar cases would help to clarify the exact link between active *H. pylori* infection and development of AIG. Follow-up of such cases would provide further information about the long-term effects of eradication on cancer risk in patients with AIG. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000528388).

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Statement of Ethics

The study complies with the provisions of the Declaration of Helsinki. Informed written consent was obtained from the patient prior to publication of the report and any accompanying images. The study protocol was reviewed, and the need for approval was waived by the Ethics Committee of the Uji-Tokushukai Medical Center.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

T.K. wrote the draft of this manuscript. Y.N. and T.K. acquired the data. R.K. analyzed the pathological findings. K.H. supervised the case report. All the authors have read and approved the final version of the manuscript.

Data Availability Statement

All data analyzed during the study are included in this article. Inquiries can be sent to the corresponding author.

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