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Single Case

A Case of Autoimmune Gastritis and Hepatitis with Enlarging Gastric Polyps after Reducing the Dose of Prednisolone

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Keywords
Autoimmune gastritis · Autoimmune hepatitis · Hyperplastic polyps · Gastrin

Abstract
Autoimmune gastritis is immune-mediated gastritis that destroys the oxyntic mucosa. Autoimmune hepatitis is an inflammatory liver disease caused by an autoimmune reaction. These diseases share similar pathogeneses as organ-specific autoimmune disorders; however, cases involving both diseases are quite rare and scarcely reported. Herein, we report a patient with concurrent autoimmune gastritis and hepatitis who developed enlargement of hyperplastic polyps and progression of gastric atrophy. The patient was a 79-year-old female referred to our hospital for the treatment of hyperplastic polyps detected on a follow-up upper gastrointestinal endoscopy. The patient's previous upper gastrointestinal endoscopy from 3 years prior revealed small hyperplastic polyps and no mucosal atrophy. However, the current upper gastrointestinal endoscopy revealed three 10-mm red polyps, severe mucosal atrophy in the corpus, and mild atrophy in the antral area. In addition, biopsy samples from the gastric body revealed decreased parietal cells and diffuse lymphocytic infiltration of the deep mucosa. Further, chromogranin A-positive endocrine cell micronests and enterochromaffin-like cell hyperplasia were detected. After confirming the diagnosis of autoimmune gastritis, endoscopic mucosal resection was performed for all the polyps, which were histopathologically diagnosed as hyperplastic polyps without malignancy. Therefore, clinicians should consider autoimmune gastritis for enlarged hyperplastic polyps and gastric atrophy progression.

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Introduction

Autoimmune gastritis (AIG) is chronic gastritis characterized by the autoimmune destruction and loss of parietal cells [1]. Its prevalence in Japan is reported to be 0.49% [2]. Furthermore, the characteristics of this disease include morphological and serological findings. The most typical endoscopic finding of AIG is severe corpus atrophy with no or mild atrophy in the antral area, which is known as corpus-dominant atrophy [3]. Other common findings include sticky adherent mucus, remnant oxyntic mucosa, a white globe appearance, and hyperplastic polyps. Considering the serological findings, the presence of serum antiparietal cell antibodies (PCAs) against the proton pump (H+/K + ATPase) or anti-intrinsic factor antibodies is essential for the diagnosis of AIG [1].

Gastric hyperplastic polyps, which might coexist with AIG, are common, red-colored polyps detected in patients of all ages and sexes. In some cases, these lesions can be difficult to distinguish from well-differentiated adenocarcinomas and can be macroscopically characterized by elongated, dilated, distorted, and branched pits of the mucosa, in addition to swelling and inflammation of the stroma [4]. Furthermore, gastric hyperplastic polyps should be carefully monitored or resected when necessary because they can potentially transform into malignant lesions.

Autoimmune hepatitis (AIH) is an organ-specific autoimmune disease of the hepatic parenchyma that can lead to liver failure and cirrhosis. The primary treatment is immunosuppression with prednisolone and azathioprine [5]. Like other autoimmune disorders, AIH is known to be comorbid with other autoimmune diseases, including chronic thyroiditis [6]. However, the comorbidity of AIH with AIG is very rare. In this regard, comorbid AIG and AIH were not detected in a nationwide Japanese study including 1,682 patients with AIH. Herein, we present a case of comorbid AIG and AIH in which hyperplastic polyps were enlarged, and gastric atrophy had progressed. This case report adheres to the CARE guidelines, and the checklist is attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000529151).

Case Presentation

A 79-year-old female was referred to our institution for further evaluation and treatment of multiple enlarged hyperplastic polyps in the gastric antrum. The patient had AIH for 7 years and was under treatment with prednisolone (5 mg daily) and esomeprazole (10 mg daily). The initial prednisolone dose, which was 40 mg/day at the diagnosis, was gradually tapered to 5 mg/day 4 years ago. The patient was a nonsmoker and a nondrinker and had no allergies. Previous upper gastrointestinal endoscopy (GIE), performed 3 years prior, revealed three small hyperplastic polyps and mild mucosal atrophy (Fig. 1a, b).

At the time of referral, all three polyps had enlarged to approximately 10 mm (Fig. 1c, d). In addition, severe mucosal atrophy in the corpus, mild atrophy in the antral area, and sticky adherent mucous were observed (Fig. 1e, f). Biopsy samples were taken from the gastric body, and pathological examination showed a decrease in parietal cells compared to normal mucosa and diffuse lymphocytic infiltration of the deep lamina propria with hematoxylin and eosin staining (Fig. 2a, b). Additionally, immunohistostaining revealed chromogranin A-positive endocrine cell micronest and enterochromaffin-like cell hyperplasia (Fig. 2c, d). A blood test revealed positive PCA and negative intrinsic factor antibodies. Pepsinogen 1 and 2 levels were 32.0 ng/mL and 14.2 ng/mL, respectively. The serum antibody test result for *Helicobacter pylori* was negative. The patient was diagnosed with AIG considering the results of the blood tests and endoscopic findings.

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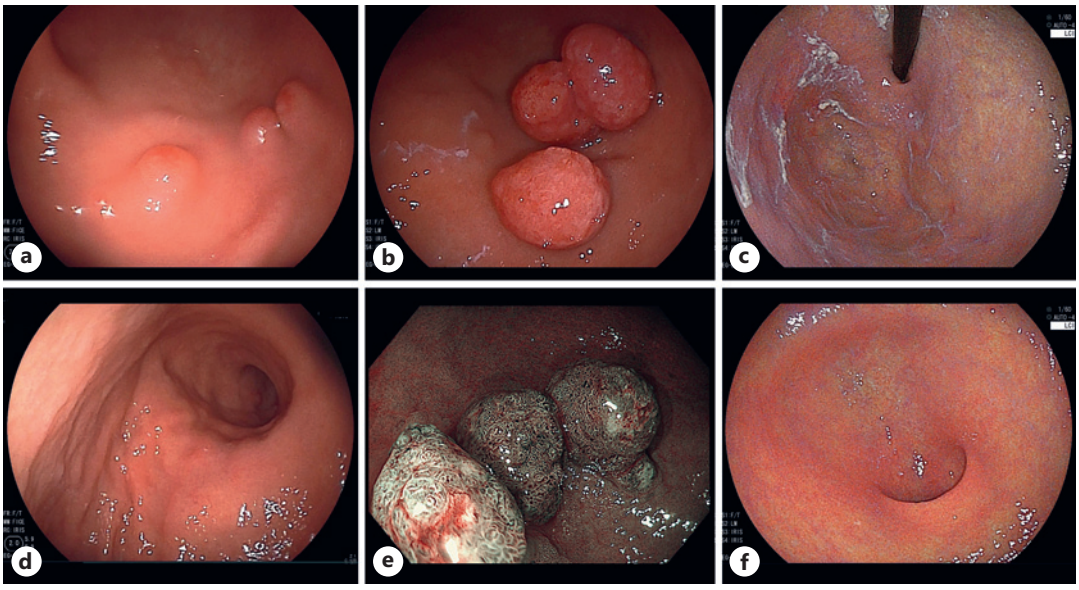

Fig. 1. Endoscopic findings. Three small hyperplastic polyps (**a**) and no mucosal atrophy (**b**) 3 years before the referral. **c**, **d** Hyperplastic polyps at the greater curvature of the angulus at the referral. **e**, **f** Background mucosa showed corpus-dominant gastric atrophy and sticky adherent mucous at the referral.

Endoscopic mucosal resection was performed for all polyps. The sizes of the polyps were 13 mm × 10 mm × 10 mm, 15 mm × 10 mm × 10 mm, and 16 mm × 13 mm × 10 mm (Fig. 3a). Histopathological examination showed elongated, branched, dilated foveolar epithelia in all three polyps. Additionally, edema and cell infiltration were found in the stroma, and no malignant lesions or adenomas were detected in any of the samples (Fig. 3b–d). The patient was discharged uneventfully 2 days after treatment. Follow-up using upper GIE was planned 6 months after the treatment.

Discussion

To the best of our knowledge, this is the first case report of enlargement of hyperplastic polyps and progression of gastric atrophy in a patient with comorbid AIG and AIH. Moreover, this is the second case report presenting a patient with comorbid AIG and AIH. Positive serum PCA and GIE findings, such as corpus-dominant gastric atrophy and hyperplastic polyps, suggested AIG in this case. Histopathological findings of the corpus, including a decrease in parietal cells, diffuse lymphocytic infiltration of the deep lamina propria, and the presence of endocrine cell micronest, were also consistent with the histological features of AIG. In addition to these morphological findings, serological findings enabled us to confirm the diagnosis of AIG in this patient.

AIG is known to have a wide range of presentations, including intragastric signs and manifestations outside the stomach. Common complications of AIG include gastric cancer, gastric neuroendocrine tumor (NET), hyperplastic polyps, autoimmune thyroiditis, rheumatoid arthritis, type 1 diabetes mellitus, iron-deficiency anemia, and pernicious anemia.

AIH is known to be associated with other autoimmune disorders such as chronic thyroiditis, Sjögren syndrome, primary biliary cholangitis, and rheumatoid arthritis [6]. The prevalence of AIH in the standardized Japanese population is 0.024% [7]. Although both AIH

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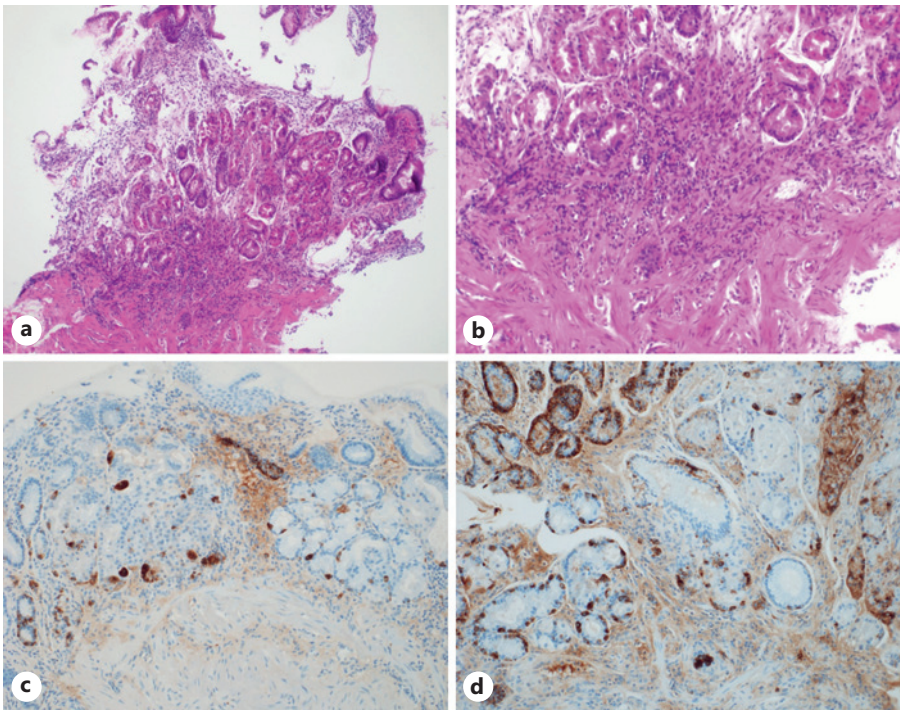

Fig. 2. Histopathological findings of biopsy samples from greater curvature of the corpus. Hematoxylin and eosin staining showed decreased parietal cells and diffuse lymphocytic infiltration of the deep lamina propria (**a**: ×20, **b**: ×100). Immunohistochemistry revealed chromogranin A-positive ECM and enterochromaffin-like cell (ECL) hyperplasia (**c**: ×40, **d**: ×100).

and AIG share similar pathogeneses as organ-specific autoimmune diseases, patients with comorbid AIH and AIG are rare because both AIG and AIH have low prevalence. Actually, only one previous case of comorbid AIG with AIH has been reported in the English literature [8]. The reason for this rarity is still unknown. Therefore, further evaluations, including the accumulation of cases, clinical observation with a large population, and basic research to detect mechanisms on a molecular basis, are needed to understand the relationship between AIH and AIG.

In this case, several factors were assumed due to the apparent enlargement of the hyperplastic polyps. The development and progression of hyperplastic polyps in the stomach are strongly associated with the repair of mucosal damage caused by chronic gastritis [9]. In addition, hypergastrinemia and duodenal reflux also play crucial roles. Furthermore, the progression of AIG with histologically proven lymphocyte infiltration suggested that active inflammation contributed to the enlargement of hyperplastic polyps in this case. However, another study reported that the size of the hyperplastic polyps decreased as AIG progressed [10]. In our case, the pathogenesis of hyperplastic polyp enlargement could not be linked to gastritis. Furthermore, long-term therapy with proton pump inhibitors (PPIs) induced serum hypergastrinemia. In this regard, gastrin induces proliferative effects on the gastric mucosa, enhancing the effects of growth factors, such as epidermal growth factor and tumor growth factor-α families, thereby promoting the proliferation of crypt epithelial cells [11]. Therefore, PPI-induced and AIG-related hypergastrinemia may have caused the formation and enlargement of the hyperplastic polyps. Considering the patient's use of a PPI and the existence of AIG, polyp enlargement in this patient did not seem to be rare. However, this finding can suggest suspicion of AIG as an underlying disease.

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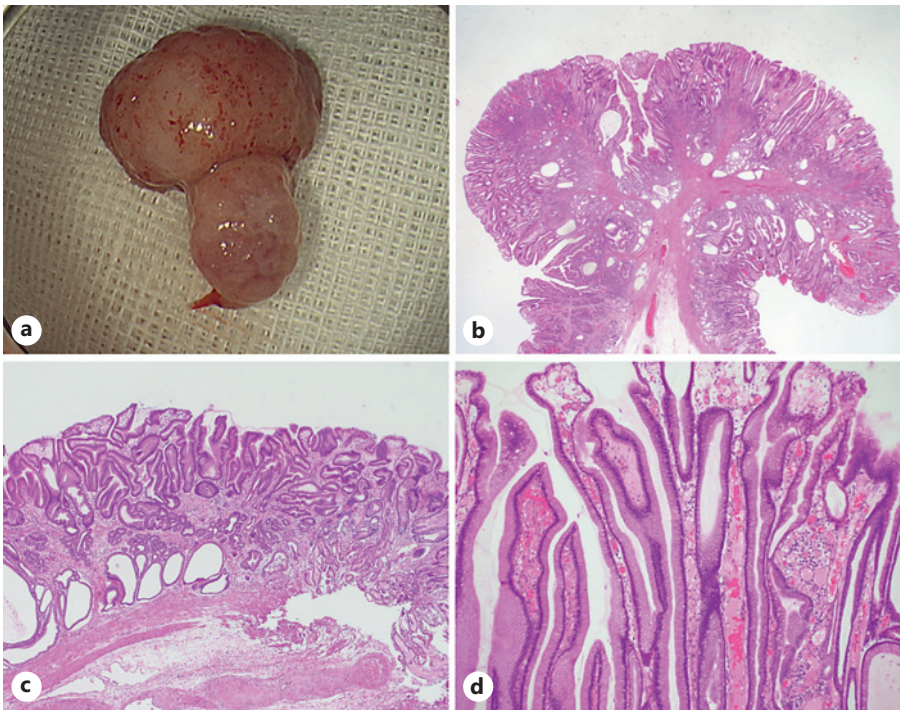

Fig. 3. Gross photograph and histopathological findings of a polyp. **a** Gross photograph. Hematoxylin and eosin staining showed elongated, branched, dilated foveolar epithelium and edematous inflamed stroma (**b**: ×20, **c**: ×40, **d**: ×100).

Notably, the progression of gastritis over 4 years, characterized by gastric atrophy and enlargement of hyperplastic polyps, was suggested in this case. A recent prospective clinical study showed that approximately half of the patients with potential AIG without histologic or endoscopic atrophy progressed into overt AIG, diagnosed by histologic and endoscopic oxyntic atrophy [12]. In particular, our case confirmed that patients with a comorbid autoimmune disorder and elevated serum gastrin levels were at risk of AIG progression. Thus, the patient's condition might progress over a natural clinical course. Another possible factor for the progression of AIG is the alteration in prednisolone administration. In a previous case report, prednisolone improved AIG [13]. However, in our case, the prednisolone dose was reduced to 5 mg/day 4 years before the patient was diagnosed with overt AIG. Previous data show that ≥15 mg of prednisolone daily is required to improve AIG [13]. Therefore, the dose reduction of prednisolone may have contributed to the progression of AIG. However, other studies have suggested that the prednisolone dose does not affect gastric atrophy [14]. Hence, further accumulation of cases and basic research are needed to elucidate this theme.

Early and precise diagnosis of AIG is challenging due to its rarity but unfamiliarity and the diagnostic trigger by which clinicians suspect AIG is an endoscopic finding [1]. Therefore, we can conclude that the enlargement of hyperplastic polyps and the progression of corpus-dominant gastric atrophy are also effective indicators of AIG. Furthermore, when diagnosed, AIG should be followed up for at least 3–5 years to monitor for severe complications such as gastric cancer, NETs, and pernicious anemia [15]. Thus, the diagnosis of AIG is beneficial for the early detection and treatment of gastric cancer and NETs, as well as other autoimmune diseases and pernicious anemia.

In conclusion, we reported a case of comorbid AIG and AIH that was treated with prednisolone. Reduction of prednisolone might affect the progression of AIG. In this regard,

when the enlargement of hyperplastic polyps and progression of gastric atrophy is detected, serum antibodies should be evaluated to diagnose AIG, and other manifestations of AIG should be screened.

Acknowledgment

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Statement of Ethics

All procedures were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The cases were reviewed and approved by the institutional Ethics Committee of Kawasaki Medical School. Approval number was 5812-00. Written informed consent was obtained from the patients to publish this case report and accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization and writing – review and editing: T.K. Data curation: R.K., T.K., Y.I., H.N., and K.H. Formal analysis, project administration, and visualization: R.K. and T.K. Investigation: R.K., T.K., and K.H. Methodology: R.K., T.K., M.S., and K.H. Resources: R.K., T.K., T.M., A.S., M.S., Y.M., Y.I., H.K., and H.N. Software: R.K. and Y.M. Supervision: T.K., T.M., H.K., and K.H. Validation: Y.I. and K.H. Writing – original draft: R.K. Approval of final manuscript: all authors.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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