Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.8741-21
Intern Med 62: 381-386, 2023
http://internmed.jp

【 CASE REPORT 】

Two Cases of Acute Gastric Mucosal Lesions Due to *Helicobacter pylori* Infection Confirmed to be Transient Infection

Mitsuhiko Suehiro[1], Ken Haruma[1], Tomoari Kamada[2], Takahito Oka[3], Katsunori Ishii[1], Ryo Katsumata[1], Tomohiro Tanikawa[1], Noriyo Urata[1], Takako Sasai[1], Minoru Fujita[4], Maki Ayaki[4], Noriaki Manabe[4], Hirofumi Kawamoto[1] and Yasumasa Monobe[5]

Abstract:
Two adult cases of acute gastric mucosal lesions (AGML) caused by *Helicobacter pylori* infection were confirmed by spontaneous eradication during the follow-up period. The clinical course of the initial infection by *H. pylori* in adults with AGML remains unclear, whether it is transient or progresses to a persistent infection. In these two reported cases, gastric biopsies at the time of the onset revealed the presence of *H. pylori*; however, serum *H. pylori* antibodies performed at the same time were negative. Retesting for *H. pylori* serum antibody, after six months in one and after two months in the other, was negative, confirming spontaneous eradication.

Key words: acute gastric mucosal lesions, *Helicobacter pylori*, initial infection, clinical course

(Intern Med 62: 381-386, 2023)
(DOI: 10.2169/internalmedicine.8741-21)

Introduction

Many reports of acute gastric mucosal lesions (AGML) diagnosed using endoscopy have been published (1-5), but with the establishment of disinfection methods for endoscopes and the decrease in the infection rate of *Helicobacter pylori* itself (6), the number of reported cases of AGML caused by *H. pylori* has been decreasing. However, despite the reduced frequency of occurrence of such cases, we still experience sporadic cases and need to know how to deal with them.

At present, AGML due to *H. pylori* infection is known to occur in many cases where the route of infection is unknown (7), and it is not clear how many cases of initial infection progress to persistent infections. To prove that AGML due to *H. pylori* infection is the first infection, the presence of *H. pylori* must be confirmed by a histological examination or culture using gastric biopsy tissue, a rapid urease test, urea breath test (UBT), or stool antigen test during the acute phase, and serum or urine antibodies to *H. pylori* must be negative.

We encountered two cases in which the presence of *H. pylori* was confirmed in gastric biopsy tissue at the onset of acute gastritis, and serum antibodies on the same day were negative, suggesting an initial infection with *H. pylori*. Furthermore, these two cases were spontaneously cleared of *H. pylori* in the subsequent course of the disease.

We herein report these cases because it is valuable to consider the diagnostic method to prove the initial infection with *H. pylori* and to consider the course of *H. pylori* infection in adults.

[1]Department of General Internal Medicine 2, General Medical Center, Kawasaki Medical School, Japan, [2]Department of Health Care Medicine, General Medical Center, Kawasaki Medical School, Japan, [3]Tamano Central Hospital, Japan, [4]Department of Endoscopy and Ultrasonography, General Medical Center, Kawasaki Medical School, Japan and [5]Department of Pathology, Kawasaki Medical School, Japan
Received: September 27, 2021; Accepted: April 27, 2022; Advance Publication by J-STAGE: June 7, 2022
Correspondence to Dr. Mitsuhiko Suehiro, m.suehiro@med.kawasaki-m.ac.jp

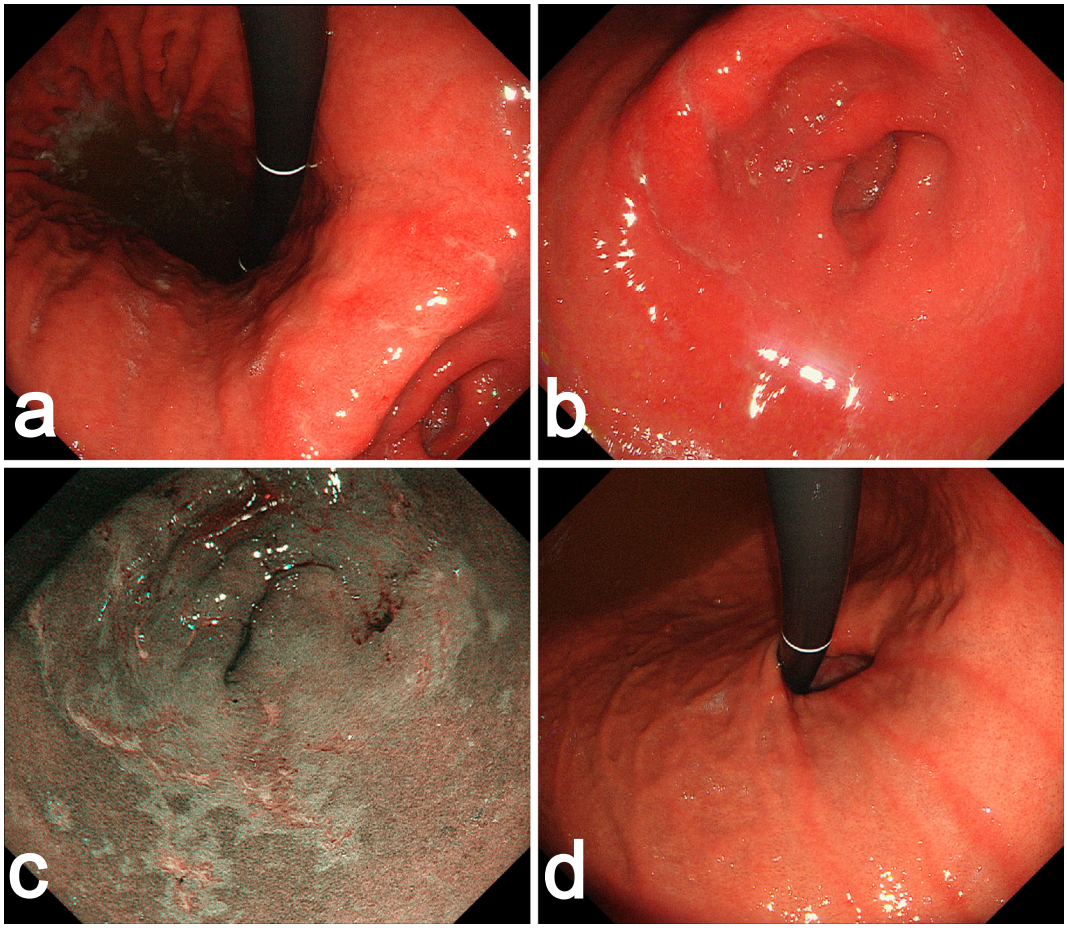

Figure 1. Endoscopic findings of Case 1. (a, b) Edematous mucosa extending from the gastric angle to the antrum. Surface erosion with white moss and partly covered with creamy mucus. (c) Erosion clearly visible on narrow-band imaging (NBI). (d) Absence of atrophy in the gastric body, suggestive of an initial infection with *H. pylori*.

Case Report

Case 1

A 38-year-old man presented with periodic chest pain, epigastric pain, and watery diarrhea for the past day. The patient visited our hospital for intensification. He had no history of drinking or smoking and no history of taking non-steroidal anti-inflammatory drugs (NSAIDs).

A physical examination revealed tenderness of the epigastric region. Blood chemistry tests were normal. Serum *H. pylori* antibody IgG was <3 U/mL, negative. Computed tomography (CT) of the abdomen showed edematous mucosa from the gastric angle to the antrum, confirming the diagnosis of acute gastritis, and the patient was given Omeprazole.

Endoscopy was performed the following day, revealing edematous mucosa from the gastric angle to the antrum, with shallow erosions in some areas, as well as narrowing of the pylorus (Fig. 1a, b). The erosions were clearly visible by narrow-band imaging (NBI) (Fig. 1c). The mucosa of the gastric body showed a red streak but no mucosal atrophy (Fig. 1d). Gastric biopsy specimens from the antrum showed marked inflammatory cell infiltration with disruption of mucosal superficial glandular ducts and increased capillaries (Fig. 2a), and staining with *H. pylori* monoclonal antibody showed a small population of *H. pylori* (Fig. 2b). Six months later, repeat endoscopy was performed, but there were no abnormalities in the gastric mucosa, and a histological examination of a gastric biopsy specimen and serum *H. pylori* antibody findings were negative (<3 U/mL).

Case 2

A 34-year-old man was admitted to the emergency room with epigastric pain and nausea that had persisted for 2 days. The patient had no medical history and no history of smoking. He had a history of alcohol consumption (350 mL of beer per day) but no history of taking NSAIDs.

A physical examination revealed tenderness of the epigastric region. No abnormalities were observed on blood chemistry tests. Serum *H. pylori* antibody IgG was <3 U/mL, negative. CT of the abdomen revealed mucosal edema in the gastric antrum region, and acute gastritis was diagnosed (Fig. 3a, b).

Vonoprazan was administered immediately, and endoscopy was performed one week later, revealing that the mu-

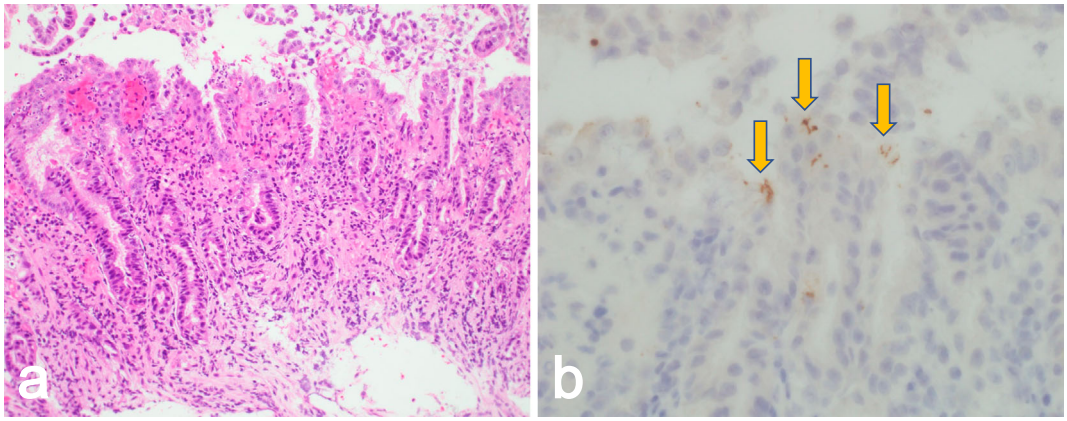

Figure 2. **Gastric biopsy tissue from the antrum of Case 1. (a) Histological findings from the antrum showed marked inflammatory cell infiltration with disruption of mucosal superficial glandular ducts and increased capillaries. (b) Staining with *H. pylori* monoclonal antibody showed a small number of *H. pylori* (arrow).**

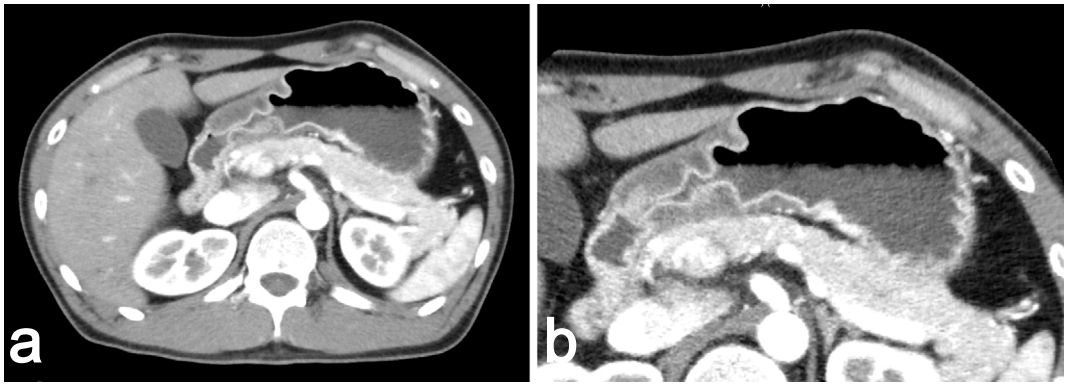

Figure 3. **CT images of the abdomen of Case 2 at the initial examination. Gastric antrum shows circumferential peaked thickening, mainly in the submucosa (a, b).**

cosa of the antrum was generally erythematous, with a healing ulcer spotted at the lesser curvature (Fig. 4a, b). The mucosa of the gastric body was slightly erythematous but without gastric mucosal atrophy (Fig. 4c). Biopsy tissue from the gastric fundus showed a regenerated epithelium and inflammation marked with the presence of neutrophils in the mucosa (Fig. 5a), which may have represented the convalescent phase of acute gastritis. Giemsa staining showed bacilli in the superficial layer of the gland ducts (Fig. 5b). Retesting of *H. pylori* serum IgG antibodies 2 months later was negative (<3 U/mL).

Discussion

We present two cases of acute gastritis due to primary infection with *H. pylori*. Since the authors had experienced three similar cases in the past (8), and two of them were transient infections, the present two cases were also observed without administering eradication treatment, and both cases were confirmed to be transient infections.

To our knowledge, based on a literature search in the databases of the *Central Journal of Medicine* and PubMed, there have been nine previous cases that were followed up without eradication therapy after the initial infection and had the status of the infection subsequently checked. Table shows the nine cases previously encountered and the two cases described in the present study (8-13). Of the 11 total cases, 2 were confirmed to be persistent infections, and 9 were transient infections, suggesting that majority were transient infections. In general, *H. pylori* was transmitted at an early age, and once infection was established, it likely progressed to a chronic persistent infection that developed over time into atrophy of the gastric mucosa (14). Since the eradication therapy can cause serious side effects in rare cases (15), it should be performed when persistent infection is confirmed.

The pathogenesis of acute *H. pylori* infection in adults, particularly whether it is transient or progresses to a persistent infection, is unclear. Two previous reports have suggested that once *H. pylori* enters the stomach, the infection persists (16, 17). To prove that an *H. pylori* infection is the first, it is necessary to prove that *H. pylori* is present and that there is no history of *H. pylori* infection. In the two cases reported in our study, there was no history of *H. pylori* infection, the serum *H. pylori* antibodies were negative, and gastric biopsy tissue revealed the presence of *H. pylori*.

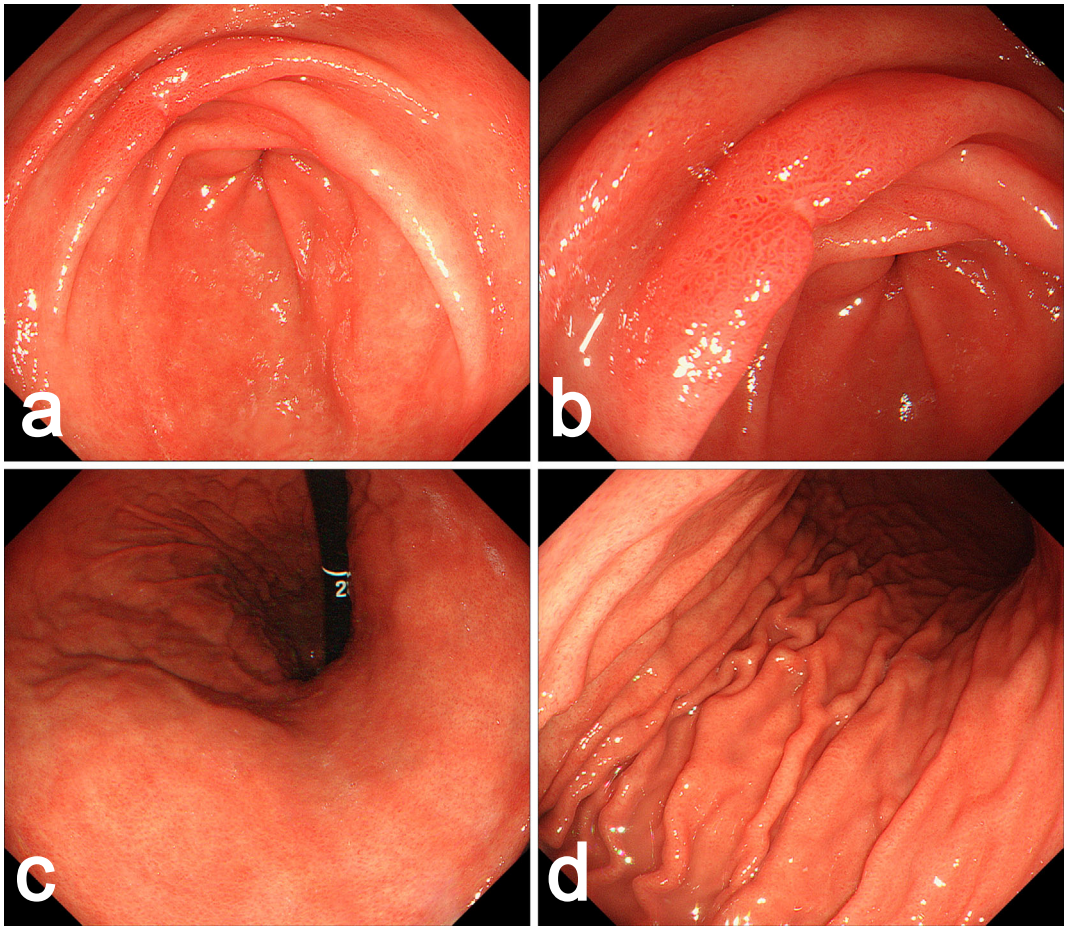

Figure 4. **Endoscopic images of Case 2. (a, b) Generalized erythematous mucosa of the antrum with a healing ulcer at the lesser curvature. (c, d) Slightly erythematous mucosa of the gastric body without gastric mucosal atrophy.**

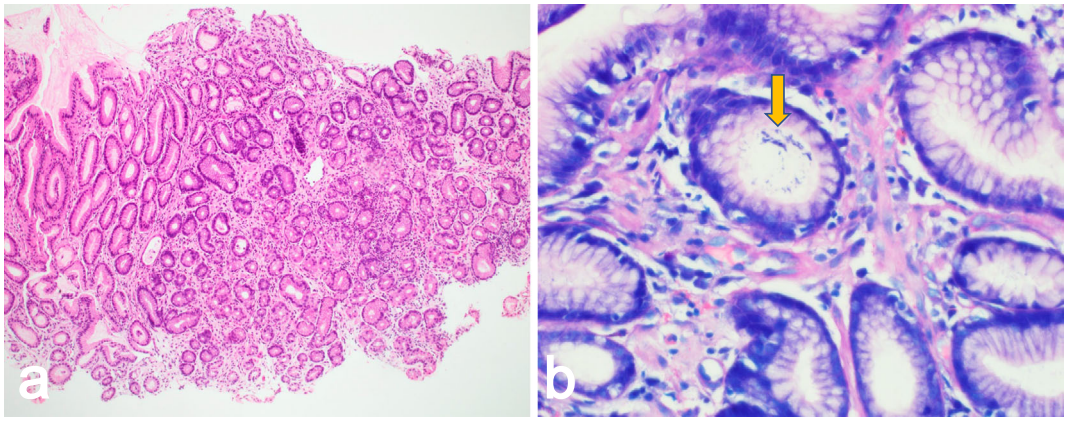

Figure 5. **Biopsy tissue from the body of the stomach. (a) Inflammation marked with presence of neutrophils is seen in the mucosa. (b) Giemsa staining shows bacilli in the superficial layer of the gland ducts (arrow).**

In addition, there was no atrophy in the gastric body mucosa, and the presence of regular arrangement of collecting venules (RAC) was confirmed, as reported by Yagi et al (10). In our patients, the histological diagnosis by a gastric biopsy showed spiral bacilli, which were considered to be *H. pylori*, and serum *H. pylori* antibodies at the time of onset of AGML had a cut-off value of ≤3; therefore, we considered the gastric mucosal background at the time of endoscopy to be primary *H. pylori* infection. In addition, the two patients were followed up without immediate eradication therapy and retested for *H. pylori* serum antibody (after six months in one and after two months in the other), showing negative findings, which confirmed spontaneous eradication. The infection in our patients was considered to have

Table. A Case Report in Japan of Initial *Helicobacter Pylori* Infection Diagnosed and Untreated, with Subsequent Follow-up to Confirm the Presence of *H. Pylori* Infection.

Reference	Age	Sex	Time of decision	Final diagnosis method and results of *H. pylori* infection
(9)	24	M	16 months	RUT(-), Histology(-), UBT(-), serum antibody(-)
(10)	27	F	6 months	Histology(-), culture(-)
(11)	39	F	1 month	RUT(-), immunohistology(-), serum antibody(-)
(12)	41	M	2 years	RUT(-), UBT(-), serum antibody(-), stool antigen(-)
	23	F	174 days	Histology(+), immunohistology(+), culture(+), serum antibody(-), stool antigen(+)
(13)	60	F	4 months	RUT(-)
(14)	27	F	2 months	UBT(+), serum antibody(+)
	65	M	2 months	Histology(-), culture(-)
	62	M	42 days	Culture(-)
Our case	38	M	6 months	Histology(-), serum antibody(-)
	34	M	2 months	UBT(-), serum antibody(-)

RUT: rapid urease test, UBT: urea breath test

been eliminated spontaneously. In general, upon detection of infection with *H. pylori*, eradication therapy is initiated immediately. However, there are cases of patients in whom spontaneous eradication occurs, as presented here, so we believe that eradication therapy should be started only after persistent infection is confirmed.

The route of transmission of *H. pylori* infection in adults is often unknown (8), but it has been reported to be transmitted through dental procedures (14), endoscopy (1-5), drinking water (18), and contact with infected partners (19). Similarly, the route of infection was not clear in the two patients in our study, as they had no recent history of dental visits, endoscopic examinations, overseas travel, or drinking well water.

When AGML due to *H. pylori* infection is suspected, there are several methods of diagnosing the infection, including culture and speculum examination using gastric biopsy tissue, measurement of serum and urine antibodies, a rapid urease test, a urea breath test, and a stool antigen test. Itano et al. performed rapid urease tests in 36 cases of AGML that developed after endoscopy and reported that all of them were negative (20). Sakai et al. also reported that the rapid urease test and urea breath test in two cases may have produced false-negative results due to the low number of bacteria (21). In any case, negative serum antibodies are necessary to prove initial infection with *H. pylori*.

Culture using a gastric biopsy specimen requires a special medium for the culture of *H. pylori* that is not used regularly outside of certain facilities where this culture method is used to check for resistant bacteria. In addition, in AGML, proton pump inhibitors (PPIs) may have already been administered before endoscopy due to the presence of severe pain, so the rapid urease test may show a false positive in PPI-treated cases due to an increased intragastric pH. In our patients, a PPI or vonoprazan had already been administered at the time of endoscopy.

Regarding the pathological diagnosis using gastric biopsy tissue, Watanabe et al. pointed out that the distribution of *H. pylori* is high around the lesion and that biopsies collected at a distance from the lesion or 7 to 21 days after the onset of the disease, after the acute phase, are likely to show false negatives due to a decrease in or the elimination of the bacteria (22). Although we are hesitant to perform gastric biopsies when multiple ulcers with clots are seen, there have been no reports of complications, including bleeding on an examination, when gastric biopsies were performed in the acute phase, including in our two cases.

Acute gastritis is diagnosed by clinical symptoms and endoscopic findings and can also be caused by sources other than *H. pylori* infection, such as stress or drugs. Acute gastritis is associated with symptoms, such as severe pain in the pericardial area and hematemesis, so once diagnosed, patients need to be treated with strong gastric acid secretion inhibitors, PPIs, or vonoprazan. Regarding the timing of eradication of acute gastritis due to *H. pylori* infection, *H. pylori* infection initially occurs in childhood, and its persistent infection can lead to peptic ulcers and gastric cancer after decades of long-term follow-up (23). Therefore, there is no need for hasty eradication in cases of acute *H. pylori* infection.

We encountered two cases of AGML that appeared to have achieved spontaneous eradication after acute infection with *H. pylori*. In addition, we reviewed the literature on similar cases of spontaneous eradication after acute infection and recommended that eradication not be started immediately - only after persistent infection is confirmed - as the initial infection with *H. pylori* is often transient.

The authors state that they have no Conflict of Interest (COI).

References

1. Langenberg W, Rauws EA, Oudbier JH, Tytgat GN. Patient-to-patient transmission of *Campylobacter pylori* infection by fiberopic gastroduodenscopy and biopsy. J Infect Dis **161**: 507-511, 1990.

2. Katoh M, Saito D, Noda T, et al. *Helicobacter pylori* may be transmitted through gastrifiberscope even after manual Hyamine washing. Jpn J Cancer Res **84**: 117-119, 1993.

3. Miyaji H, Kohli Y, Azuma T, et al. Endoscopic cross-infection with *Helicobacter pylori*. Lancet **345**: 464, 1995.

4. Moriai T, Hirahara N. Clinical course of acute gastric mucosal lesions caused by acute infection with *Helicobacter pylori*. N Engl J Med **341**: 456-457, 1999.

5. Sugiyama T, Naka H, Yachi A, Asaka M. Direct evidence by DNA fingerprinting that endoscopic cross-infection of *Helicobacter pylori* is a cause of postendoscopic acute gastritis. J Clin Microbiol **38**: 2381-2382, 2000.

6. Kamada T, Haruma K, Ito M, et al. Time trends in *Helicobacter pylori* infection and atrophic gastritis over 40 years in Japan. Helicobacter **20**: 192-198, 2000.

7. Brown LM. *Helicobacter pylori*: epidemiology and routes of transmission. Epidemiol Rev **22**: 283-297, 2000.

8. Kamada T, Hata J, Manabe N, et al. Can dental treatment be the infection route of *H. pylori* transmission in adults? Three cases of acute gastric mucosal lesions after dental treatment. Dig Endosc **19**: 32-35, 2007.

9. Ohara S, Sekine H, Iijima K, et al. A case of acute gastric mucosal lesion caused by *Helicobacter pylori* infection with long-term follow-up. Helicobacter Res **4**: 87-91, 2000 (in Japanese).

10. Yagi K, Nakamura A, Sekine A. Two cases of AGML after initial *Helicobacter pylori* infection, which was diagnosed by normal endoscopic finding, regular arrangement of collecting venules (RAC). Gastroenterol Endosc **44**: 656-660, 2002 (in Japanese, Abstract in English).

11. Chatani N, Yada T, Ohkubo K, et al. A case of acute gastric mucosal lesions secondary to primary infection with *H. pylori*. Prog Dig Endosc **81**: 84-85, 2012 (in Japanese).

12. Fukuda Y, Shinozaki K, Sasaki T, et al. Acute gastric mucosal lesions caused by acute *Helicobacter pylori* infection - clinical outcomes of six cases and problems in the diagnosis of *H. pylori* infection. Nihon Shokakibyo Gakkai Zasshi **111**: 899-908, 2014 (in Japanese, Abstract in English).

13. Kawai N, Shibatohge M, Morita M, et al. A case of acute gastric mucosal lesion suspected to be caused by acute *Helicobacter pylori* infection. Takamatsu Sekijyuji Byoin Kiyou **5**: 52-55, 2017 (in Japanese).

14. Mittal SK, Mathew JL. *Helicobacter pylori* infection in children: a review. Trop Gastroenterol **24**: 106-115, 2003.

15. Tokunaga K, Kato H, Ohsaki K. Indications and problems of *Helicobacter pylori* eradication therapy in the elderly. Jpn J Helicobacter Res **21**: 21-29, 2019.

16. Marshall BJ, Armstrong JA, McGechie DB, Glancy R. Attempt to fulfil Koch's postulates for pyloric campylobacter. Med J Aust **142**: 436-439, 1985.

17. Morris AJ, Ali MR, Nicholson GI, Perez-Perez GI, Blaser MJ. Long-term follow-up of voluntary ingestion of *Helicobacter pylori*. Ann Intern Med **114**: 662-663, 1991.

18. Hulten K, Han SW, Enroth H, et al. *Helicobacter pylori* in the drinking water in Peru. Gastroenterology **110**: 1031-1035, 1996.

19. Schutze K, Hentshel E, Dragosics B, et al. *Helicobacter pylori* reinfection with identical organisms: transmission by the patients' spouses. Gut **36**: 831-833, 1995.

20. Itano S, Terada N, Hashimoto O, et al. Acute gastric mucosal lesion (AGML) following upper endoscopic examination. Gastroenterol Endosc **37**: 2176-2184, 1995 (in Japanese, Abstract in English).

21. Sakai Y, Yasuhiro T, Noda Y. Investigation of *Helicobacter pylori* (*H. pylori*) related to acute gastromucosal lesion (AGML) after an endoscopic examination. Gastroenterol Endosc **38**: 2583-2590, 1996 (in Japanese, Abstract in English).

22. Watanabe H, Narisawa R, Endo Y, et al. Endoscopic view of AGML cases - pathology of acute gastric lesions: definition, causes and changes over time. Endoscopic Digestiva **6**: 804-809, 1994 (in Japanese, Abstract in English).

23. Sipponen P, Maarros HI. Chronic gastritis. Scand J Gastroenterol **50**: 657-667, 2015.