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Case Report

Helicobacter pylori Reinfection Diagnosed by Endoscopic and Histologic Recurrence in a Patient with Gastric Mucosa-Associated Lymphoid Tissue Lymphoma

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Keywords
Gastric mucosa-associated lymphoid tissue lymphoma · Histologic recurrence · *Helicobacter pylori* reinfection · Nursing home

Abstract
Helicobacter pylori infection is a major cause of gastric mucosa-associated lymphoid tissue (MALT) lymphoma. Successful *H. pylori* eradication can induce a complete remission (CR); however, it takes a long time. In this case, the recurrence of gastric MALT lymphoma was observed by endoscopic and histologic findings during a 11-year follow-up and due to *H. pylori* reinfection twice. After the first successful eradication and achieving histologic CR, the patient was starting to work at a nursing home for older adults, where she frequently came in contact with their vomitus or feces. In the examinations 2 years later after the first successful eradication, endoscopic and histologic findings have demonstrated deterioration. Similar findings were continuously observed in the examinations 3 months later, and *H. pylori* reinfection was confirmed by the rapid urease test. After the second successful eradication, endoscopic and histologic CR of gastric MALT lymphoma was achieved. However, endoscopic and histologic findings have shown deterioration again 1 year later after the histologic CR and at 3.5 years later after the second successful eradication. *H. pylori* reinfection was confirmed by the repeated urea breath test, and the patient had received the third eradication treatment; and the patient had achieved successful eradication. In addition, proper hygiene practices were advised to avoid *H. pylori* reinfection. *H. pylori* reinfection is very rare in adults after successful eradication in

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developed countries. After successful eradication and proper hygiene practice, endoscopic and histologic CR has been maintained for 2 years up to the present.

Introduction

Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is induced by *Helicobacter pylori* infection [1–4]. MALT lymphoma is diagnosed by histologic and endoscopic findings [2–8]. Endoscopic findings are used for the diagnosis of gastric MALT lymphoma, which is subgrouped into superficial (gastritis), ulcer, and elevated types [9]. Pathologic diagnosis is required to confirm the final diagnosis of MALT lymphoma. *H. pylori* eradication treatment is recommended as a first-line standard therapy against *H. pylori*-positive gastric MALT lymphoma worldwide [5–8]. Large-scale retrospective and prospective clinical trials have already demonstrated a good long-term prognosis with *H. pylori* eradication alone [10–21], particularly in superficial-type gastric MALT lymphomas. Therefore, successful *H. pylori* eradication is necessary for the long-term remission of gastric MALT lymphoma. Although pathologic and endoscopic findings have gradually improved during the follow-up period despite successful eradication, *H. pylori* eradication treatment is ineffective in case of contentious deterioration of histologic findings. Furthermore, the recrudescence of *H. pylori* or *H. pylori* reinfection has induced deterioration. In general, the recrudescence of *H. pylori* due to incomplete eradication occurs within 1 year after successful eradication [22–25]. In this case, the recurrence of gastric MALT lymphoma was induced by *H. pylori* reinfection, which was suggested by endoscopic and histologic deterioration of gastric MALT lymphoma.

Case Report

A 53-year-old woman underwent an upper gastrointestinal (GI) endoscopy for gastric cancer surveillance as ordered by her family physician and was introduced to our hospital for further examination in January 2011. Her upper GI endoscopy revealed reddish, uneven regions in the gastric body, suggestive of a superficial or gastritis-type gastric MALT lymphoma. Gastric pathology showed numerous invasions of small lymphocytes and the presence of lymphoepithelial lesions, and MALT lymphoma was confirmed by a pathologist (Fig. 1a–c). The rapid urease test (RUT) was positive, and the urea breath test (UBT) was also positive ($\Delta^{13}C$ = 33.0%). A proton-pump inhibitor (lansoprazole 30 mg) and antibiotics, including amoxicillin (750 mg) and clarithromycin (400 mg), were administered twice daily for 1 week [7]. Six weeks after the treatment, the UBT was negative ($\Delta^{13}C$ = 0.0%) [7]. To confirm successful eradication, the UBT was repeated after 4 weeks, which was also negative ($\Delta^{13}C$ = 0.0%). Upper GI endoscopy was performed every 3–6 months following successful eradication. In September 2011, the endoscopic finding revealed a whitish, patchy, and scar-like gastric mucosa, which was suggestive of endoscopic remission; histologic diagnosis showed complete remission (CR) according to the Groupe d'Etude des Lymphomes de l'Adult (GELA) grading system (Fig. 1d–f) [26, 27]. Upper GI endoscopy was repeatedly performed every 6 months following CR. Since the histologic CR of gastric MALT was achieved, she began working at a nursing home for older adults in her hometown. In February 2013, the endoscopic finding showed a reddish and uneven gastric mucosa, which was suggestive of the recurrence of MALT lymphoma; pathologic diagnosis

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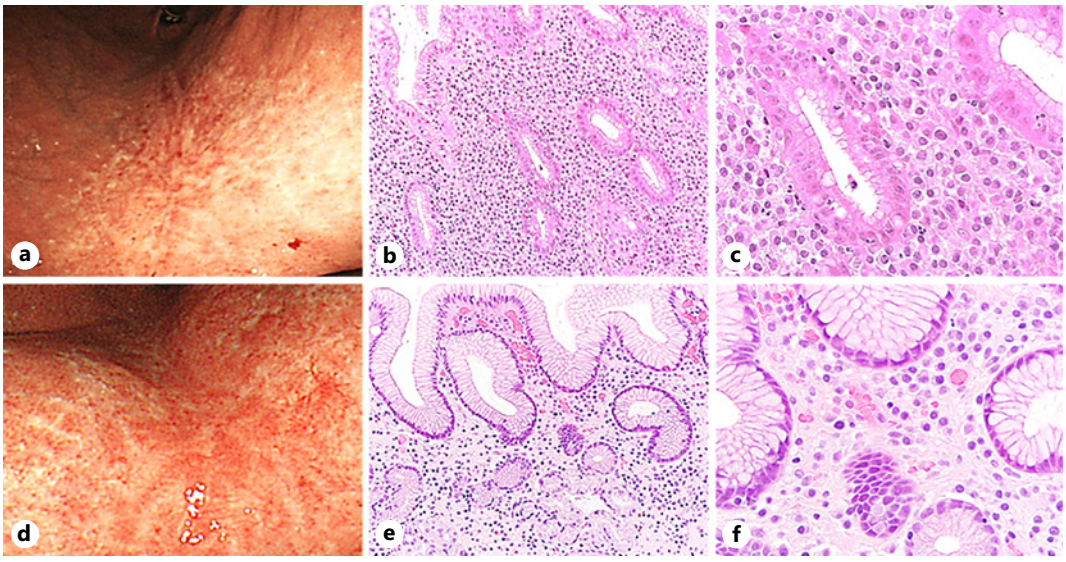

Fig. 1. Endoscopic and histologic findings before (January 2011, first diagnosis) and after (September 2011, histologic complete remission [CR]) the first eradication treatment. **a–c** Before eradication. **d–f** After successful eradication. **a**, **d** Endoscopy. **b**, **e** Histology, ×200. **c**, **f** Histology, ×50.

revealed responding residual disease (rRD) according to the GELA system (Fig. 2a, b). In May 2013, the endoscopic finding and histologic diagnosis was similar to the previous findings, and the recurrence of MALT lymphoma was confirmed. The RUT demonstrated a positive result. The patient had not taken any drugs that may lead to a false-positive RUT result. Because the first eradication was successful (repeat UBTs were negative), *H. pylori* reinfection was strongly suggested, which was diagnosed 2 years following successful eradication. Owing to her frequent contact with the vomitus or feces of the older adults, she was speculated to have harbored the infection from the nursing home. A proton-pump inhibitor (esomeprazole 20 mg) and antibiotics, including amoxicillin (750 mg) and metronidazole (250 mg), were administered twice daily for 1 week [7]. Six weeks after the treatment, the UBT was negative ($\Delta^{13}C = 0.7\%$). To confirm successful eradication, the UBT was repeated 16 weeks after, which also revealed a negative result ($\Delta^{13}C = 0.2\%$). Upper GI endoscopy was performed every 3–6 months. In January 2016, an endoscopic examination demonstrated a whitish, patchy, flat, and scar-like gastric mucosa (endoscopic remission), and the histologic diagnosis showed CR according to the GELA system (Fig. 2c, d). However, in January 2017, the endoscopic finding showed a reddish and uneven gastric mucosa, which was suggestive of the re-recurrence of gastric MALT lymphoma, and the histologic diagnosis showed responding residual disease according to the GELA system (Fig. 3a, b). The UBT was positive ($\Delta^{13}C = 22.0\%$), and the third eradication treatment was performed. A proton-pump inhibitor (esomeprazole 20 mg) and antibiotics, including amoxicillin (750 mg) and metronidazole (250 mg), were administered twice daily for 1 week, and proper hygiene practices were advised to avoid *H. pylori* reinfection. Eight weeks after the third treatment, the UBT was negative ($\Delta^{13}C = 0.7\%$). In April 2022, the endoscopic finding revealed a whitish and scar-like gastric mucosa (endoscopic remission), and the histologic diagnosis showed CR according to the GELA system (Fig. 3c, d). Results of endoscopic findings, histologic diagnosis, and *H. pylori* infection tests are briefly summarized in Table 1.

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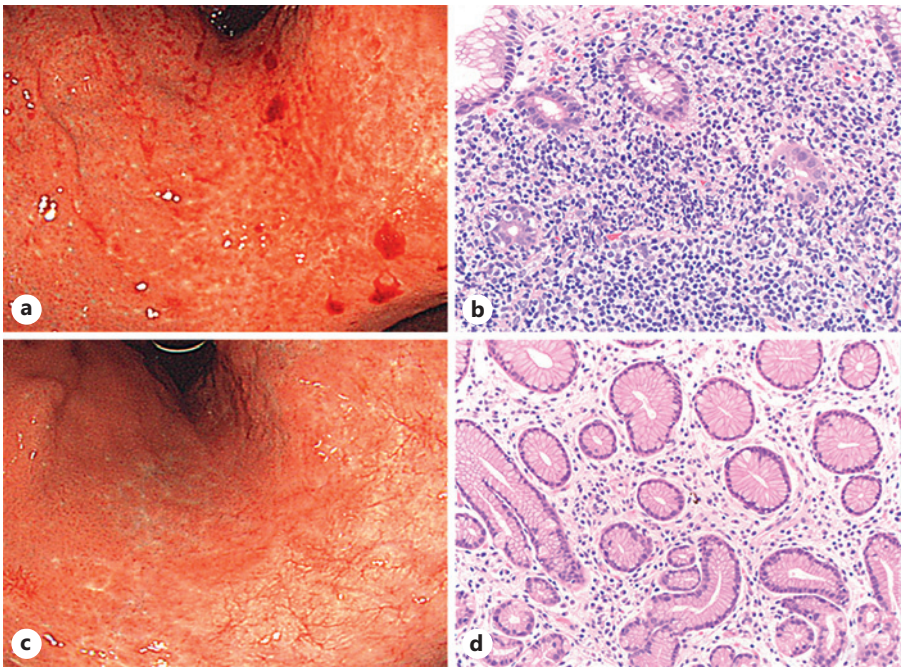

Fig. 2. Endoscopic and histologic findings before (February 2013, histologic responding residual disease [rRD]) and after (January 2016, histologic CR) the second eradication treatment of *H. pylori* reinfection. **a**, **b** Before eradication. **c**, **d** After successful eradication. **a**, **c** Endoscopy. **b**, **d** Histology, ×100.

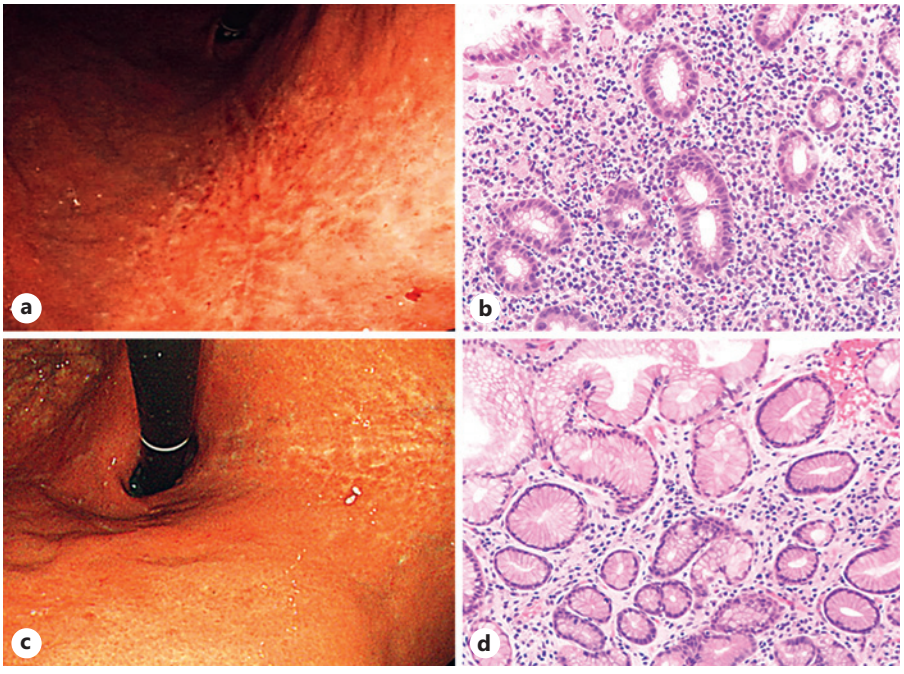

Fig. 3. Endoscopic and histologic findings before (January 2017, histologic rRD) and after (April 2022, histologic CR) the third eradication treatment of *H. pylori* reinfection. **a**, **b** Before eradication. **c**, **d** After successful eradication. **a**, **c** Endoscopy. **b**, **d** Histology, ×100. rRD, responding residual disease.

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Table 1. Summary of endoscopic findings, histology, and *H. pylori* test in this case

Date	Endoscopic finding	Histology	*H. pylori* test
Jan 2011	Reddish, uneven mucosa	MALT lymphoma	UBT: 33.0%
Mar 2011			UBT: 0.0%
Apr 2011			UBT: 0.0%
Jun 2011	Reddish mucosa	rRD	
Sep 2011	Whitish, scar-like mucosa	CR	
Aug 2012	Whitish, scar-like mucosa	CR	
Feb 2013	Reddish, uneven mucosa	rRD	
May 2013	Reddish, uneven mucosa	rRD	RUT: positive
Jul 2013			UBT: 0.7%
Dec 2013	Reddish	pMRD	UBT: 0.2%
Jul 2015	Whitish, scar-like mucosa	pMRD	
Jan 2016	Whitish, scar-like mucosa	CR	
Jan 2017	Reddish, uneven mucosa	rRD	UBT: 22.0%
Apr 2017			UBT: 0.7%
Mar 2018	Reddish mucosa	rRD	
Mar 2019	Whitish, scar-like mucosa	pMRD	
Oct 2020	Whitish, scar-like mucosa	CR	
Apr 2022	Whitish, scar-like mucosa	CR	

rRD, responding residual disease; CR, complete remission; pMRD, probable minimal residual disease.

Discussion

H. pylori infection is a major cause of gastric MALT lymphoma, which is derived from marginal zone B lymphocytes in extranodal lymphoid tissues [1–4]. *H. pylori* eradication can induce CR, and the standard treatment is the eradication of *H. pylori*-positive gastric MALT lymphoma worldwide [5–8]. Several large-scale retrospective and prospective clinical trials have demonstrated a good long-term prognosis following successful eradication [9–21]. However, achieving histologic CR following successful eradication takes time. Therefore, repeated endoscopic and histologic examinations are required during the follow-up period. The recrudescence of *H. pylori* or *H. pylori* reinfection could have induced deterioration of MALT lymphoma. In general, the recrudescence of *H. pylori* due to incomplete eradication occurs within 1 year following successful eradication [23–25]. In this case, endoscopic and histologic findings were worse at 2 years after achieving pathologic CR, and *H. pylori* reinfection was confirmed by an RUT or UBT, which was probably due to contact with vomitus or feces of the older adults from the nursing home [22–25]. The recrudescence of *H. pylori* due to incomplete eradication was unlikely to occur because the first successful eradication had been confirmed by the UBT twice at 6 and 10 weeks after the treatment, and histologic CR had been maintained for 2 years. Additionally, *H. pylori*-negative gastric MALT lymphoma is also unlikely because endoscopic and histologic remission was induced three times after successful *H. pylori* eradication [28]. In developed countries, *H. pylori* reinfection is very rare among adults following successful *H. pylori* eradication [22–25]. However, bacteriologic comparison by DNA fingerprinting between two *H. pylori* strains is required to show direct scientific evidence of recrudescence or reinfection [23, 29], if the reinfection was due to a different strain. Unfortunately, it was impossible as the first *H. pylori* strain was

not preserved in this case. This is a limitation of our case report. Generally, medical staff working in endoscopic rooms or nursing homes for older adults may have a high risk of *H. pylori* reinfection through contaminated endoscopic equipment or vomitus during emesis even in adults [23–25]. In our case, the patient was continuously working in a nursing home after the first histologic CR, and she had *H. pylori* reinfection twice during 2–3 years following successful eradication. Therefore, proper hygiene practices were advised to avoid *H. pylori* reinfection in the nursing home for older adults. After the third successful eradication treatment, endoscopic and histologic CR has been maintained for 2 years up to the present.

In conclusion, this case report suggests that careful endoscopic and histologic observations could provide important clues to speculate rare *H. pylori* reinfection in adult patients with gastric MALT lymphoma in developed countries, and careful inquiry is important regarding the hygiene of environment with high risk of *H. pylori* infection in adults. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000528309).

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Statement of Ethics

This patient was tested and treated under National Health Care Insurance for medical practice. Ethics approval was not required for this case in accordance with the national guidelines. Written informed consent was obtained from the patient for publication of the details of the medical case and any accompanying images.

Conflict of Interest Statement

All the authors declare that there is no conflict of interest regarding the publication of this article.

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Author Contributions

Toshiro Sugiyama has contributed to planning and writing the manuscript. Toshiro Sugiyama, Sohachi Nanjyo, and Chieko Kato have contributed to care for the patient and

collection of the endoscopic pictures. Takahiko Nakajima has contributed to diagnosing the pathology. All the authors approved the publication on 24 April 2022 and approved the revised final manuscript on 24 October 2022.

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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