A Case Study of Remnant Gastric Ulcer: Eradication of *Helicobacter pylori* Not Only Improved the Ulcer But Also Decreased p53 Protein Expression

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Abstract

In this paper, we report the experience of a 66 year old man with remnant gastric ulcer 1 year after distal gastrectomy for early gastric cancer. First, *H.* _pylori_ antibiotic therapy was applied but failed. Next, antibiotics therapy was applied to eradicate *Helicobacter pylori*. After the treatment, not only was *Helicobacter pylori* eradicated and the stage of ulcer improved, but also the oncosuppressor p53 protein expressed in gastric mucosa had decreased to undetectable levels. Chronic bile reflux is believed to increase the risk of ulcerative lesions in remnant stomach, but this case suggests that *Helicobacter pylori*-infection may also contribute to the etiology of remnant gastric ulcer.

Key words  Remnant gastric ulcer, *H. pylori*, p53, Eradication

Introduction

Patients who have undergone distal gastrectomy for gastric ulcer or cancer are at risk of developing gastric ulcer and/or cancer in the remnant stomach.1,2 Chronic bile reflux is believed to increase the risk of lesions in the remnant stomach.3 Although *Helicobacter pylori* (*H. pylori*) is considered one of the major etiological agents for gastric cancer,4 this is not necessarily true for remnant gastric lesions.5,6

We experienced a case where a remnant gastric ulcer which occurred after a partial gastrectomy for early gastric cancer responded well to eradication of *H. pylori*. In addition, p53 protein expressed in mucosal cells around the ulcer disappeared after eradication of *H. pylori*.

Onset and Course of the Case (Fig. 1)

A 66 year old man visited our hospital because of epigastralgia without specific histories in his past or in his family. The patient was diagnosed as having an early stage of gastric cancer and a pylorus side partial gastrectomy was performed, followed by Billroth I reconstruction on February 3, 2000. The lesion was 19×13 mm in size and classified as Type 0-IIc. The histology was
well-differentiated adenocarcinoma and considered as fStage IA (T1N0H0P0M0) or Stage IA (T1N0M0) in TNM staging. Expression of p53 protein was negative in the paraffin embedded specimen (Fig. 2).

During follow-up at the outpatient clinic, the epigastralgia reemerged around January 2001. Upper endoscopic examination revealed a remnant gastric ulcer (H1 stage) in the residual stomach on February 5, 2001 (Fig. 3A). After starting therapy with H₂ receptor antagonists, his epigastralgia was partially improved. However, he visited our hospital again because of worsened epigastralgia. Existence of his remnant gastric ulcer was confirmed under endoscopic examination on December 3, 2001 (Fig. 3B). He was diagnosed with a positive H. pylori-infection by rapid urease test, ¹³C-urea breath test and pathological findings. In addition, p53 protein was highly expressed in mucosal cells by immunohistostaining (Fig. 3C). To measure
secretion of gastric acid, pH in the remnant stomach was monitored for 24 hours (Fig. 4). However, intragastric pH remained above 4.0 for 24 hours without administration of H₂ antagonist.

The patient had per-oral administration of lansoprazole, amoxicillin and clarithromycin for 1 week from January 22, 2002. After one month, the signs of epigastralgia improved. On May 13, 2002, the remnant...
gastric ulcer was improved to the S2 stage under endoscopic examination (Fig. 5A) and *H. pylori* infection was confirmed to be negative by rapid urease test, $^{13}$C-urea breath test and pathological findings. Moreover, p53 protein was changed to negative in the mucosal cells of the stomach in the biopsy specimen (Fig. 5B). The lesion of remnant stomach has remained stable to date: March 2005.

**Discussion**

The remnant gastric ulcer studied in this case improved with eradication of *H. pylori*. In explaining the risk of ulcer or cancer occurring in the remnant stomach after partial gastrectomy, the theory of chronic bile reflux is widely held, whereas the theory of infection with *H. pylori* is considered secondary, or not accepted. Evidence that Billroth II reconstruction was worse than Roux-Y reconstruction and Billroth I in preventing remnant gastritis because it enhanced duodenogastric reflux may support the theory of chronic bile reflux. However, recently duodenogastric reflux was demonstrated to facilitate the survival of *H. pylori* in the remnant gastric lesion after a distal gastrectomy. Moreover, proton pump inhibitor-based therapy was effective for *H. pylori* eradication from the remnant stomach; on the other hand, eradication of *H. pylori* with antibiotics resulted in a significant decrease in inflammatory cell infiltration of the mucosal layer of the remnant stomach. These suggest that both chronic bile reflex and *H. pylori*-infection may synergically induce lesions in the remnant stomach.

Although p53 was not expressed in the lesion of gastric cancer, it emerged in mucosal cells around the remnant gastric ulcer in this case. Of interest, expression of p53 decreased to below detectable levels after eradication of *H. pylori*. A previous study found that the accelerated cell turnover in the gastric epithelial cell induced by *H. pylori* infection was associated with p53 overexpression. It is considered that expression of p53 in the gastric mucosa may result from DNA damage induced by *H. pylori* infection. After eradication of *H. pylori*, the accumulation of p53 decreased and the reduction of inflammation was detected in the stomach mucosa.
These results suggest that *H. pylori* is considered one of the major etiological agents for gastric lesions. In contrast, it was reported that *H. pylori* infection might not play an important role in the pathogenesis of recurrent ulcers after partial gastrectomy. However, the case presented in this report demonstrated that eradication of *H. pylori* had occurred simultaneously with decreased expression of p53 as well as morphological improvement of the ulcerative lesion.

This case suggests that *Helicobacter pylori*-infection may contribute to the etiology of remnant gastric ulcer, although chronic bile reflux is believed to increase the risk of lesions in the remnant stomach. Further investigation is necessary to clarify the effects of *H. pylori*-eradication on preventing remnant gastric ulcer and/or cancer.

**References**