Rare case of *Helicobacter pylori*-related gastric ulcer: Malignancy or pseudomorphism?

Ting-Ting Li, Feng Qiu, Zhi-Qiang Wang, Lu Sun, Jun Wan

**Abstract**

*Helicobacter pylori* (*H. pylori*) is a pathogen and the most frequent cause of gastric ulcers. There is also a close correlation between the prevalence of *H. pylori* infection and the incidence of gastric cancer. We present the case of a 38-year-old woman referred by her primary care physician for screening positron emission tomography-computed tomography (PET-CT), which showed a nodular strong accumulation point with standardized uptake value 5.6 in the gastric fundus. Gastroscopy was then performed, and a single arched ulcer, 12 mm in size, was found in the gastric fundus. Histopathological examination of the lesion revealed chronic mucosal inflammation with acute inflammation and a very small amount of *H. pylori* infection. The mitotic phase was 4/10 high power field, with some heterotypes and an obvious nucleolus. Follow-up gastroscopy 2 mo later showed the gastric ulcer in stage S2. The mucosal swelling had markedly improved. The patient remained asymptomatic, and a follow-up PET-CT was performed 6 mo later. The nodular strong accumulation point had disappeared. Follow-up gastroscopy showed no evidence of malignant cancer. *H. pylori*-associated severe inflammation can lead to neoplastic changes in histiocytes. This underscores the importance of eradicating *H. pylori*, especially in those with mucosal lesions, and ensuring proper follow-up to prevent or even reverse early gastric cancer.

**Key words:** *Helicobacter pylori*; Gastric ulcer; Gastric cancer; Positron emission tomography-computed tomography; Gastroscopy

**INTRODUCTION**

*Helicobacter pylori* (*H. pylori*) is a Gram-negative microaerophilic bacterium that colonizes the stomach of approximately two-thirds of the human population and is involved in the pathogenesis of various gastroenterological diseases including gastric ulcer and gastric cancer. *H. pylori*'s interaction with the host has an impact on the severity of these diseases and their clinical outcome.

The mechanisms of *H. pylori*-related colonization are not fully understood. However, different types of *H. pyl-
lori virulence factors, especially cytotoxin-associated gene A (CagA), vacuolating cytotoxin A (VacA), outer inflammation protein A and so on are reported to be correlated with H. pylori-related diseases. One of the major bacterial virulence factors, the VacA, seems to be involved in the physiologic mechanism. The VacA protein encoded by the polymorphic H. pylori VacA gene, is produced and secreted by all bacterium strains and induces the formation of intracellular vacuoles in epithelial cell lines in vitro. Environmental and demographic data also interfere with the pathophysiology of H. pylori-associated gastric diseases[3].

CASE REPORT

We present a case of a 38-year-old woman with a history of thyroid cancer who was referred by her primary care physician for a screening positron emission tomography-computed tomography (PET-CT). She was essentially asymptomatic and did not report any abdominal pain, dysphagia, nausea, or vomiting. Findings of a physical examination were unremarkable.

PET-CT showed a nodular strong accumulation point with standardized uptake value (SUV) 5.6 in the gastric fundus (Figure 1A). Gastroscopy was then performed, and demonstrated a single arched ulcer, measuring 12 mm in size, in the gastric fundus (Figure 2A and B). Histopathological examination revealed that the lesion had chronic mucosal inflammation with acute inflammation and H. pylori infection. There was an obvious mitotic phase with widespread lymphoma immunohistochemical staining was positive for CD4 (T cell), CD3 (T cell), CD20, Ki-67 (+25%), CD79a (+++), PAX-5, CD45RO and negative for CD56, TIA-1, TIF-1, Bel-6, CD10, CD30, CD34, CD117, CK, MUM-1, MPO (Figure 3A).

The patient was given H. pylori eradication therapy, based on proton pump inhibitor-clarithromycin-amoxicillin-mucosal protective agent treatment, the so-called quadruple 14 d therapy. One month later, gastroscopy was performed and showed a single arched ulcer, measuring 10 mm in size in the gastric fundus (Figure 2C). Histopathological examination revealed that the lesion had chronic mucosal inflammation with acute inflammation and a small amount of H. pylori infection (Figure 3B). The mitotic phase was 4/10 high power field with some heterotypes and an obvious nucleolus. Immunohistochemical staining showed tissue cell-like cells positive for S-100, vimentin, CD68, Ki-67 (30%) and negative for CD1a, CD21, Bcl-2, CD3, CD20, CD30, CD45RO, CD117 and PAX-5 (Figure 3C). For further examination, immunohistochemical staining was repeated by the Beijing Cancer Hospital and showed that staining for CD1a was positive for focal lesions (Figure 3D). The shape and immunophenotype indicated Langerhans histiocytosis. Because of the active growth of cancer cells, the patient was referred for medical oncology evaluation for this unusual pathologic finding with malignant potential.

Follow-up gastroscopy 2 mo later showed that the gastric ulcer was in stage S2 (Figure 2D). The mucosal swelling was markedly reduced. Endoscopic ultrasonography showed that the local echo was normal and each layer was clearly divided (Figure 2E). Histopathological examination showed chronic mucosal inflammation with lymphoid tissue hyperplasia in the lamina propria (Figure 3E).

The patient remained asymptomatic, and a follow-up PET-CT was performed 6 mo later. The nodular strong accumulation point with SUV 5.6 in the gastric fundus...
Figure 2  Gastroscopy showed a single arched ulcer and changes after treatment. A, B: A single arched ulcer, measuring 12 mm in size, was found in the gastric fundus (July 1, 2011); C: A single arched ulcer, measuring 10 mm in size, was found in the gastric fundus (August 16, 2011); D: The gastric ulcer was in stage S2 (October 13, 2011); E: Endoscopic ultrasonography showed that the local echo was normal and each layer was clearly divided (October 13, 2011); F: The gastric ulcer was in stage S2 (April 25, 2012).

Figure 3  Histopathology changes after treatment. A: Histopathological examination revealed that the lesion had chronic mucosal inflammation with acute inflammation and a small amount of Helicobacter pylori (H. pylori) infection. The mitotic phase was obvious and lymphoma was widespread (hematoxylin and eosin (HE), ×400, July 2, 2011); B: Histopathological examination revealed chronic mucosal inflammation with acute inflammation and a only a small amount of H. pylori infection. The mitotic phase was 4/10 high power field (HE, ×400, August 17, 2011); C: Immunohistochemical staining showed tissue cell-like cells with S-100 (×400, August 17, 2011); D: Immunohistochemical staining was repeated by the Beijing Cancer Hospital and showed that staining for CD1a was positive for focal lesions (×400, August 25, 2011); E: Histopathological examination showed chronic mucosal inflammation with lymphoid tissue hyperplasia in the lamina propria (HE, ×10, October 14, 2011); F: Histopathological examination revealed that chronic mucosal inflammation with acute inflammation (HE, ×10, May 8, 2012).
had disappeared (Figure 1B). Follow-up gastroscopy at the same time showed that the gastric ulcer was in stage S2 (Figure 2F). Histopathological examination revealed that the lesion had chronic mucosal inflammation with acute inflammation (Figure 3F). Therefore, we found no evidence of malignant cancer.

**DISCUSSION**

*H. pylori* infection is a worldwide disease, with about half of the world’s population harboring this bacterium in their stomach. The infection is asymptomatic in most individuals. However, it is the leading cause of non-ulcer dyspepsia, peptic ulcers and gastric tumors.

*H. pylori* is able to survive in the gastric acidic environment because of its ability to synthesize urease, an enzyme which can neutralize the stomach acidic pH. It seems to play a role in the mechanisms which lead to gastric cancer by inducing methylation in different genes, interfering with apoptotic pathways and by causing inflammatory events leading to gastritis, then to atrophic gastritis and possibly to gastric cancer. It may affect the acid secretion of the parietal cells by causing mucosal inflammation. Gastric acid secretion depends on the localization and the degree of the inflammation. Acute infection with *H. pylori* results in hyperchlorhydria, whereas chronic infection can cause either hypo- or hyper-chlorhydria, depending on the distribution of the infection and the degree of corpus gastritis. *H. pylori* is a powerful carcinogen, since it is able to induce genetic changes, such as hypermethylation events, contributing to cell transformation.

*H. pylori* is well recognized as a class I carcinogen because long-term colonization by this organism can provoke chronic inflammation and atrophy, which can further lead to malignant transformation. Chronic inflammation plays important roles in the development of various cancers, particularly in digestive organs, including *H. pylori*-associated gastric cancer. During chronic inflammation, *H. pylori* can induce genetic and epigenetic changes, including point mutations, deletions, duplications, recombinations, and methylation of various tumor-related genes through various mechanisms, which act in concert to alter important pathways involved in normal cellular function, and hence accelerate inflammation-associated cancer development. Al fizah et al. reported that variant of *H. pylori* CagA proteins induce different magnitudes of morphological changes in gastric epithelial cells. In his study, the CagA protein was injected into gastric epithelial cells and showed that *H. pylori* induced morphological changes in GES-1 cells and significantly increased the proliferation of GES-1 cells. Because the transition from inflamed mucosa to atrophic change is a common route to carcinogenesis, the effect of *H. pylori* eradication on the incidence of this early precursor lesion is of interest. Since *H. pylori* infection is associated with gastric carcinoma, therapy is warranted for its eradication.

This was a rare case of a *H. pylori*-related gastric ulcer that resembled gastric cancer. PET-CT SUV was high, and gastroscopy showed a large ulcer with malignant-like histopathological features. However, after *H. pylori* eradication treatment, the lesion recovered quickly and follow-up examination showed no evidence of malignant cancer.

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