Cap-polyposis-like Gastropathy with Hypoproteinemia Treated with *H. pylori* Eradication

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**Abstract**

We herein report the case of a 43-year-old man with distinct gastropathy and hypoproteinemia treated with *H. pylori* eradication therapy. Most reported cases of protein-losing gastropathy are divided into Ménétrier’s disease (MD) and diffuse varioliform gastritis (DVG). Our patient presented with leg edema due to marked hypoalbuminemia, which we ascribed to distinct gastropathy with novel endoscopic findings resembling cap polyposis in the colon, apparently different from both MD and DVG. *H. pylori* eradication therapy promptly induced the normalization of laboratory data and mucosal healing. Our case together with two previously published similar cases may contribute to establishing an association between cap-polyposis-like-gastropathy with hypoproteinemia and *H. pylori*.

**Key words:** *H. pylori*, gastritis, hypoproteinemia

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**Introduction**

Protein-losing gastropathy is a rare syndrome, with most patients classified as having Ménétrier’s disease (MD) or diffuse varioliform gastritis (DVG), depending on the endoscopic appearance and histological findings. Although the pathogenesis of protein-losing gastropathy is unknown and the optimal treatment has not been established, the symptoms of the condition are sometimes life-threatening and require gastrectomy, especially in patients with MD. Both of these diseases have been successfully treated with *H. pylori* eradication, thus suggesting that their pathogenesis may be associated with *H. pylori* infection (1). We herein report a case of gastropathy with hypoproteinemia and novel endoscopic findings in which *H. pylori* eradication therapy promptly induced normalization of laboratory data and mucosal healing.

**Case Report**

A 43-year-old Japanese man visited our hospital with a complaint of bilateral leg edema persisting for one month in November 2011. Although he experienced watery diarrhea around the onset of edema, it resolved within a few days. He did not suffer from abdominal pain, fatigue, appetite loss or weight loss. The patient had been well until one month before the consultation except that he had been medicated for gout for three years. He was a daily drinker, consuming 40 grams of alcohol per day, and an ex-smoker. He had no special family history. Marked hypoalbuminemia, assumed to be the cause of the edema, was diagnosed at another institute. The patient was determined to have a normal liver function and negative urine protein results, which raised the possibility of protein-losing gastroenteropathy.

On a physical examination, no specific abnormalities were found other than slight pitting edema on both lower legs. The laboratory data were notable for a total serum protein level of 4.4 g/dL, an albumin level of 2.8 g/dL and an IgG level of 398 mg/dL. Abdominal ultrasonography, colonoscopy, radiological enteroclysis, technetium-99m albumin imaging and other laboratory tests, including a blood count and immunological and biochemical assessments, showed no abnormalities. Upper gastrointestinal endoscopy revealed

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Figure 1. (A-C) Endoscopic views of the stomach before treatment showing multiple polypoid lesions covered by an exudative cap. (D-F) Endoscopic views 11 weeks after the initiation of H. pylori eradication therapy showing the disappearance of the polypoid lesions and erythematous edema.

multiple distinct polypoid lesions covered by a “cap” of white exudate, occurring on the apices of the folds primarily in the gastric body (Fig. 1A-C). The lesions were surrounded by slightly atrophic mucosa with erythematous edema. Histologically, the biopsy specimens of the lesions showed elongated tortuous crypts with a mixed inflammatory infiltrate comprised mostly of neutrophils in the lamina propria covered by inflammatory granulation tissue (Fig. 2A-C). Smooth muscle hyperplasia without fibrosis was detected in the lamina propria, confirmed by smooth muscle actin (SMA) staining (Fig. 2D). H. pylori was found in these specimens (Fig. 2E).

The patient underwent H. pylori eradication therapy with 20 mg/day of rabeprazole, 1,500 mg/day of amoxicillin and 800 mg/day of clarithromycin daily for seven days. His symptoms and hypoalbuminemia markedly improved five weeks after the initiation of therapy, when the laboratory data were confirmed to have normalized to a total serum protein level of 6.5 g/dL, an albumin level of 4.1 g/dL and an IgG level of 1,044 mg/dL. The eradication therapy was successful, as confirmed by a urea breath test performed eight weeks later. Gastroscopy performed 11 weeks after the initiation of therapy revealed the disappearance of the reddish mucosal edema and multiple polypoid lesions, healing with white scar formation (Fig. 1D-F). Gastric mucosal atrophy was detected involving the lower body (Fig. 1E).

The patient’s serum protein level has been normal for one year despite his unchanged drinking habit.

Discussion

We herein described the case of a patient with hypoproteinemia and distinct gastric mucosal lesions. The patient had neither systemic disease nor a past surgical history implicating malabsorption syndrome. His transient diarrhea of uncertain origin was not severe enough to impair absorption and cause hypoproteinemia. No other apparent causes of protein loss or inadequate synthesis were detected. We ascribed his hypoproteinemia to protein loss from the gastric mucosa although technetium-99m albumin imaging did not prove the existence of leakage.

While most previous cases of protein-losing gastropathy have been endoscopically classified as MD or DVG, the endoscopic findings in our case were distinct from those of MD and DVG. The gastropathy observed in this patient was likely associated with H. pylori infection, since H. pylori eradication therapy promptly induced the normalization of laboratory data and mucosal healing. We speculate that the H. pylori infection in this case was chronic, not acute, based on the finding of gastric mucosal atrophy.

MD is a rare hypertrophic gastropathy characterized by giant rugal folds in the gastric body, protein loss and clinical symptoms, such as nausea, vomiting, abdominal pain and peripheral edema, sometimes requiring gastrectomy. The histological features include foveolar hyperplasia, glandular tortuosity and dilatation, lamina propria smooth muscle hyperplasia and a marked reduction in the number of parietal cells. Although the etiology of MD has yet to be elucidated and its optimal treatment has not been established, several
successful treatments have recently been reported, including \textit{H. pylori} eradication (1).

DVG is an erosive gastritis, occurring even more infrequently than MD, characterized by enlarged rugal folds and erosive mucosal bulging predominantly in the gastric body (2). This disorder must be separated from antral varioliform gastritis, a nonspecific lesion with a high frequency (2). Most cases of DVG correspond histologically to lymphocytic gastritis (2). While DVG does not necessarily cause hypoproteinemia, several patients with DVG have been reported to also have protein-losing gastropathy, which has been cured with \textit{H. pylori} eradication (1). It is remarkable that both MD and DVG have been successfully treated with \textit{H. pylori} eradication (1), thus strongly suggesting that the pathogenesis of these diseases may be associated with \textit{H. pylori} infection.

The endoscopic findings in our patient were markedly different from those of MD. Although the presence of multiple erosive lesions on large folds observed in this case are compatible with the findings of DVG, we were reluctant to diagnose this case as DVG for two reasons. First, the patient showed a histological discrepancy from lymphocytic gastritis, considered a histological counterpart of DVG (2). Second, we observed a morphological difference from DVG, in that enlarged gastric folds were absent and there was white exudative tissue on top of the erosive lesions, reminiscent of cap polyposis in the colon.

Cap polyposis is a rare colonic disease characterized by multiple polypoid lesions covered by inflammatory granulation tissue, mostly discovered in the sigmoid colon and/or rectum (4). Patients frequently have mucoid and bloody diarrhea, abdominal pain, tenesmus, hypoproteinemia and edema. Although the etiology of this condition is controversial, it is interesting that cases of colonic cap polyposis have also been successfully managed with \textit{H. pylori} eradication, the serum protein level being normalized in some patients (5).

Two cases of cap-polyposis-like lesions in the stomach have been previously reported: one case from Korea occurring in the stomach alone (6) and the other from Japan with lesions occurring in both the colon and stomach (7). Both patients developed hypoproteinemia and were cured after undergoing \textit{H. pylori} eradication.

Our patient has some features in common with the two earlier patients, which suggests a new endoscopic classification of protein-losing gastropathy. Endoscopically, multiple polypoid lesions are prominent covered by an exudative cap located primarily in the gastric body, tending to occur on the apices of the folds. Histologically, this condition presents with foveolar hyperplasia and inflammatory cells comprised mostly of neutrophils. Clinically, hypoproteinemia develops. Affected patients are infected with \textit{H. pylori}, and eradication therapy induces the disappearance of the gastric lesions and the amelioration of hypoproteinemia.

Patients presenting with cap-polyposis-like lesions accompanied by hypoproteinemia should be examined for \textit{H. pylori} and treated with eradication therapy, if positive for infection. This may prevent the need for invasive treatment.

The mechanisms of protein loss in patients with \textit{H. pylori}-associated gastropathy remains unknown. \textit{H. pylori} has been reported to not only induce epithelial cell proliferation, resulting in hypertrophic gastritis, but also disrupt the \textit{in vitro} epithelial barrier function. \textit{H. pylori} increases paracellular permeability by dysregulating tight junctions via several mechanisms, including the direct effects of CagA on tight junctions (8) or host cell signaling pathways, such as

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**Figure 2.** (A-C) Hematoxylin and Eosin staining of biopsy tissue of a polypoid lesion showing elongated tortuous crypts with a mixed inflammatory infiltrate comprised mostly of neutrophils in the lamina propria. (D) Smooth muscle actin staining showing intramucosal smooth muscle hyperplasia. (E) Giemsa staining revealing the presence of \textit{H. pylori}.
the phosphorylation of myosin light chain and the regulation of the tight-junctional proteins claudin-4 and claudin-5 (9). In fact, leakage of biotinylated albumin in vitro has been observed across monolayers infected with *H. pylori* (8). *H. pylori*-associated alterations in epithelial barrier properties may be responsible for protein leakage.

Moreover, it remains to be elucidated why only a small minority of *H. pylori*-infected patients develop this kind of protein-losing gastropathy. We speculate, however, that virulence factors derived from *H. pylori* may be involved based on a recent report that the *H. pylori* strain isolated from a patient with MD was different from other strains with respect to the MseI-RFLP pattern of the ureC gene and cytokine production, including that of hepatocyte growth factor and TNF-alfa (10). Although host factors and environmental factors may also be involved, this has not yet been demonstrated.

In conclusion, we herein reported a case of cap-polyposis-like gastropathy with hypoproteinemia and multiple polyoid lesions covered by an exudative cap, apparently different from the findings of MD and DVG. The patient was successfully treated with *H. pylori* eradication. Our findings may contribute to establishing the association between cap-polyposis-like-gastropathy with hypoproteinemia and *H. pylori* infection.

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

References


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