Antibiotic-free management of *Helicobacter pylori* infection using liquid berberine, probiotics, and proton pump inhibitor: a case report

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ABSTRACT

Background: *Helicobacter pylori* infection is commonly treated with antibiotic-based regimens; however, antimicrobial resistance, treatment failure, and intolerance may limit therapeutic options. Antibiotic-sparing approaches remain investigational but may be considered in carefully selected patients who decline or cannot tolerate conventional therapy.

Case Presentation: We report a 38-year-old woman with recurrent, biopsy-confirmed *H. pylori* gastritis after failure of two previous antibiotic-based eradication regimens. Because of a family history of gastric cancer, bismuth-containing quadruple therapy was recommended, but the patient declined further antibiotic and bismuth-based treatment owing to concerns about adverse effects. After counseling and written informed consent, she received an off-label, antibiotic-free 14-day regimen consisting of pantoprazole 40 mg, *Lacticaseibacillus rhamnosus* LCR35, and liquid berberine, administered twice daily in sequence. Symptoms improved during treatment, and no serious adverse effects occurred. Follow-up stool antigen testing approximately 9 weeks after therapy was negative. Subsequent gastroscopy, approximately 12 weeks after treatment, showed discrete gastritis with biliary duodenogastric reflux, and rapid urease testing was negative.

Conclusion: This case suggests that an antibiotic-free combination of proton pump inhibitor, probiotic, and berberine was associated with negative follow-up *H. pylori* testing in a carefully selected patient who declined standard therapy. The approach should not replace guideline-recommended treatment, but it may warrant further investigation in controlled studies.

Keywords: *Helicobacter pylori*, *Lacticaseibacillus rhamnosus*, berberine, probiotic, antibiotic-free.

Type of Article: CASE REPORT **Specialty:** Gastroenterology

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Background

Helicobacter pylori (*H. pylori*) is a prevalent gastric pathogen linked to chronic gastritis, peptic ulcers, and gastric carcinoma [1,2]. Standard *H. pylori* eradication therapy relies on antibiotics (e.g., clarithromycin, amoxicillin, and metronidazole) combined with a proton pump inhibitor (PPI). However, the efficacy of these regimens is waning as antibiotic-resistant *H. pylori* strains become more common [3]. Although the global prevalence is declining (due to factors such as improved living conditions and socioeconomic changes), the success rates of legacy triple therapy have also decreased [4]. This has prompted recent guidelines to recommend more intensive treatments, such as extending therapy to 14-day bismuth-containing quadruple regimens [3]. Aggressive regimens carry a high side-effect burden (nausea, diarrhea, dysgeusia, black stool/tongue, etc.), leading to poor patient compliance [5]. Beyond the problem of side effects, antimicrobial resistance (AMR) is also becoming a major limitation. AMR was reported to be directly associated with ~1.14 million deaths in 2021; this AMR-related mortality is projected to be up to ~8.22 million deaths annually by 2050 [6]. The rise of AMR is omnipresent and may affect eradication rates in *H. pylori* [7]. Consequently, a growing subset of patients either cannot tolerate or refuse antibiotic-based *H. pylori* therapy. This clinical challenge highlights the need for alternative, efficacious, and safe protocols for the eradication of *H. pylori*.

Given these tolerability and AMR constraints, we implemented a non-antibiotic regimen comprising standard-dose PPI-based acid suppression, targeted probiotic therapy with *Lacticaseibacillus rhamnosus* (LCR35), and berberine. LCR35 has supportive clinical data as an adjunct in *H. pylori* management. It is approved in Austria for the treatment of

antibiotic-associated diarrhea [8]. Anecdotal reports further document that eradication may be achieved with probiotic monotherapy in a different context [9].

Berberine, a plant-derived isoquinoline alkaloid, has been reported to possess anti-*H. pylori* activity *in vitro* and in clinical settings. In controlled trials, adding berberine to standard regimens improved eradication rates, symptom relief, and ulcer healing while also reducing common side effects. A head-to-head comparison suggested non-inferiority to bismuth-containing quadruple therapy over 14 days [10]. Based on this evidence, berberine is increasingly discussed as an antibiotic-sparing adjunct in comprehensive management strategies for *H. pylori* [11]. Evidence to date primarily evaluates berberine as an adjunct to antibiotics; its role in antibiotic-free regimens remains investigational.

Case Presentation

Patient history

A 38-year-old Caucasian woman presented to an Austrian Study Center with recurring epigastric discomfort, bloating, and intermittent nausea. She was unmarried, had no children, and worked as a healthcare manager in a nursing home.

The patient had a prior diagnosis of *H. pylori* infection confirmed by esophagogastroduodenoscopy (EGD) and histology on July 19, 2018, approximately 6 years before the current intervention. The patient initially received clarithromycin-based triple therapy consisting of a PPI, amoxicillin, and clarithromycin, which represented a standard first-line eradication regimen in Austria at the time. Treatment failure was confirmed 6 weeks after completion of therapy by stool polymerase chain reaction (PCR) testing. Three months later, follow-up gastroscopy was performed, during which targeted biopsies were obtained for culture and susceptibility testing. Based on these findings, a second eradication attempt was undertaken using bismuth-containing quadruple therapy consisting of a PPI, bismuth salt, tetracycline, and metronidazole, in accordance with Austrian guideline recommendations. Follow-up testing again indicated persistent *H. pylori* infection. Detailed susceptibility results, antibiotic dosing, treatment duration, adherence, adverse effects, and the specific confirmatory tests used following the second treatment course were not available from the archived medical record. Histological examination revealed mild chronic and mildly active *H. pylori* gastritis with low-grade colonization in both antrum and corpus, without evidence of intestinal metaplasia or glandular atrophy.

There was a notable family history of *H. pylori*-associated gastric cancer in her paternal uncle and aunt. Given this history and her recurrent infection, a single-capsule bismuth-containing quadruple regimen (bismuth, metronidazole, tetracycline, and PPI) was recommended. The patient strongly rejected this option due to fear of bismuth-related side effects.

The patient was carefully informed about the need for *H. pylori* eradication and the recommendation for another antibiotic regimen. She remained adamant about avoiding bismuth and antibiotics due to prior adverse experiences. After we discussed an alternative off-label approach (with emphasis that it was not yet corroborated by trials), she gave written informed consent to proceed with an antibiotic-free therapy. This individualized, off-label treatment approach was selected after failure of two prior guideline-based eradication regimens and explicit patient refusal of further antibiotic or bismuth-containing therapy. The case was managed in accordance with ethical standards for individualized therapeutic decisions, with close clinical monitoring throughout.

Examination and assessment

On physical exam, the patient was alert, had normal vital signs, and a healthy body mass index of 22. Physical examination was unremarkable except for mild epigastric tenderness on deep palpation. She had no gastrointestinal bleeding, weight loss, or signs of anemia. Her baseline laboratory tests showed no abnormalities.

Non-antibiotic regimen treatment

Before initiation of the antibiotic-free regimen, active *H. pylori* infection was reconfirmed by a positive stool antigen test performed on September 12, 2024. In the context of the patient's previous documented eradication failures and persistent gastrointestinal symptoms, this finding supported the decision to proceed with the individualized off-label treatment approach after informed consent had been obtained. The therapy was initiated on September 19, 2024. The regimen consisted of three components taken twice daily (morning and evening):

- **Pantoprazole** - standard dose (40 mg)
- **LCR35 -** one sachet (1.5 g; minimum 1×10^9 CFU)
- **Liquid berberine** - 15 ml (100 mg berberine)

The liquid berberine preparation used in this case was BerBerSan® Berberstin (BerBerSan GmbH, Schladming, Austria). Each 15-ml dose contained 100 mg berberine hydrochloride derived from *Berberis aristata* root extract, delivered in a cold-pressed aqueous extract base of *Berberis vulgaris*, with ascorbic acid (vitamin C) and potassium sorbate (E202). The product is classified as a food supplement under Directive 2002/46/EC and the Austrian Food Safety and Consumer Protection Act. Independent accredited laboratory testing is performed to verify compliance with applicable European Union compositional and safety requirements for food supplements.

Each component was administered at 30-minute intervals in the following sequence: 1) the PPI was given first to elevate intragastric pH; 2) LCR35 followed once the pH was higher to support probiotic survival and mucosal contact; and 3) berberine was administered last to minimize its

Table 1. *Clinical timeline of H. pylori diagnosis, treatment, and follow-up (2018-2024).*

Date	Event	Result/Outcome
19 Jul 2018	Initial EGD with biopsies and histology	*H. pylori*-positive gastritis confirmed
Aug 2018†	Clarithromycin-based triple therapy (PPI, amoxicillin, clarithromycin)	Treatment completed
Sep 2018†	Stool PCR test	Positive; eradication failure confirmed
Dec 2018†	Follow-up gastroscopy with culture and susceptibility testing	Persistent infection documented
Dec 2018†	Bismuth-containing quadruple therapy (PPI, bismuth, tetracycline, metronidazole)	Treatment completed
Feb 2019†	Follow-up testing	Persistent *H. pylori* infection documented
12 Sep 2024	Stool antigen test prior to intervention	Positive; active *H. pylori* infection reconfirmed
19 Sep 2024	Start antibiotic-free regimen (pantoprazole, LCR35, liquid berberine)	Treatment initiated
02 Oct 2024	End antibiotic-free regimen	Treatment completed
04 Dec 2024	Stool antigen test	Negative
23 Dec 2024	Colonoscopy	Bland perianal skin tags; otherwise, normal findings
24 Dec 2024	Follow-up gastroscopy	Discrete gastritis with biliary duodenogastric reflux; no ulcerative, tumorous, or polypoid lesions
24 Dec 2024	Rapid urease test (RUT) performed on gastric biopsy material	Negative

†Exact dates unavailable from archived medical records.

potential impact on the live probiotic. The patient received detailed written instructions to encourage adherence.

The planned treatment period was 14 days (September 19-October 2, 2024), per recommended standard eradication protocols [12]. Throughout therapy, the patient had remote check-ins every 3 days via telephone to report adherence and adverse events. No serious adverse effects occurred. She only noted a mild, self-limited headache on days 4 and 5 and a transient bitter taste after taking the liquid berberine [13].

Clinically, the patient's symptoms improved steadily throughout the treatment course. She noted a reduction in bloating and epigastric pain within the first week. By day 10, she was asymptomatic, with no stomach discomfort. She required no rescue medications (no antacids, antibiotics, non-steroidal anti-inflammatory drugs, or additional probiotics) during the 14-day treatment.

The treating physician specifically assessed whether any concurrent changes in diet, physical activity, supplementation, or medication use had occurred during the treatment and follow-up period. The patient reported no changes in dietary habits, lifestyle factors, medication use, or additional supplement intake (Table 1).

Outcome and follow-up

Approximately 9 weeks after completing therapy, following a PPI washout period that exceeded the recommended minimum of 14 days, the patient underwent the first post-treatment assessment with a *H. pylori* stool antigen test on December 04, 2024, which was negative. Approximately 3 months after therapy, follow-up gastroscopy was performed on December 24, 2024, at Privatklinik Villach. The examination demonstrated discrete gastritis with biliary duodenogastric reflux, without ulcerative, tumorous, or polypoid lesions. The esophageal mucosa was unremarkable. The duodenal bulb showed isolated small gastric mucosal heterotopia islands, and the postbulbar duodenum was unremarkable.

A rapid urease test performed on gastric biopsy material during follow-up gastroscopy was negative. Formal histological examination, including special staining for *H. pylori*, was not performed at this visit.

In addition, a colonoscopy performed on December 23, 2024, demonstrated bland perianal skin tags, with otherwise normal findings up to the cecum.

Discussion

This case describes negative follow-up *H. pylori* testing after an antibiotic-free regimen in a patient who declined further guideline-recommended therapy.

Patient selection and safety

The increasing prevalence of antibiotic resistance poses practical constraints in the management of *H. pylori*. A strong family history of gastric malignancy heightened baseline risk, and two prior guideline-based antibiotic regimens had failed. The patient also firmly refused bismuth-containing quadruple therapy. In this context, after detailed counseling and written informed consent, we implemented an antibiotic-free regimen supported by emerging, albeit limited, evidence [9].

Current guidelines caution that patients with complicated or high-risk presentations (e.g., bleeding ulcers, mucosa-associated lymphoma, or other high-risk features)

should receive prompt antibiotic therapy, without delay or substitute alternatives [12]. Our patient did not meet red-flag criteria; thus, a carefully monitored, off-label alternative was ethically justifiable. The findings in this case are hypothesis-generating and support the need for controlled studies of antibiotic-sparing strategies in carefully selected patients. Conventional *H. pylori* regimens commonly cause adverse events, which can deter patients from completing therapy and, consequently, exacerbate the AMR crisis [5,12]. No serious adverse events were observed in this patient.

Mechanistic considerations

The applied strategy may leverage *H. pylori's* complementary vulnerabilities.

Probiotic antagonism may occur locally. Clinically, adjunctive probiotics have been associated with modestly higher eradication rates and meaningful reductions in gastrointestinal adverse effects during *H. pylori* therapy [8,14].

LCR35 is one such strain with supportive data and an established safety/usage profile in Austria [8,9].

Third, berberine provides a non-antibiotic antimicrobial input. Experimental work reports direct anti-*H. pylori* activity and inhibitory effects on urease, conceptually overlapping with bismuth's anti-urease and membrane-disruptive actions [15]. Clinically, randomized studies and a meta-analysis indicate that adding berberine to standard therapy increases eradication rates and ulcer healing while also reducing common side effects [10].

Broader implications

Further investigation of antibiotic-sparing approaches may be warranted in carefully selected clinical scenarios where standard therapy is declined or not feasible.

Limitations and future directions

This is a single case presentation, and one successful outcome does not guarantee similar success in all patients. The inherent limitations include a lack of control and the possibility that some unmeasured factor contributed to eradication. Thus, caution is necessary before generalizing this approach. Moving forward, prospective clinical trials of non-antibiotic regimens should be conducted. As with any uncontrolled single-patient observation, the possibility of unmeasured confounding factors cannot be completely excluded despite the patient's report that no relevant dietary, lifestyle, medication, or supplement changes occurred during the observation period.

An additional limitation is the incomplete availability of historical treatment records from the patient's prior eradication attempts. Although the treatment strategies could be identified as clarithromycin-based triple therapy followed by bismuth-containing quadruple therapy, detailed information regarding antibiotic dosing, treatment duration, adherence, adverse effects, microbiological susceptibility results, and the specific confirmatory tests used to follow each treatment course was not available for retrospective verification.

Another limitation is the absence of histological confirmation during follow-up endoscopy. Although a negative stool antigen test at approximately 9 weeks and a negative rapid urease test at approximately 12 weeks after therapy provided concordant findings consistent with eradication, gastric biopsies were not submitted for histological examination or special staining. Consequently, complete histological confirmation of *H. pylori* clearance was not available.

Conclusion

This case describes a patient with previously documented treatment-refractory *H. pylori* infection who declined further guideline-recommended antibiotic and bismuth-containing therapy. An off-label 14-day regimen consisting of pantoprazole, *L. rhamnosus* LCR35, and liquid berberine was followed by symptom improvement and negative follow-up stool antigen and rapid urease testing. Because this report describes a single patient without a control group, causality cannot be established, and the findings should be considered hypothesis-generating only. This approach should not replace current guideline-recommended antibiotic-based eradication regimens. Further controlled studies are required to evaluate the safety, efficacy, and reproducibility of antibiotic-sparing strategies in carefully selected patients.

All procedures performed in this case were in accordance with the ethical standards of the responsible national and institutional committees and with the 1964 Helsinki Declaration and its later amendments. The patient provided written informed consent for the described treatment and for publication of this case presentation.

What is new?

Standard *H. pylori* treatment relies on antibiotics, but AMR and treatment intolerance may limit success. Probiotics and berberine have mainly been studied as adjuncts to antibiotic therapy. This case describes recurrent *H. pylori* infection managed with an antibiotic-free regimen consisting of pantoprazole, *L. rhamnosus* LCR35, and liquid berberine, with symptom improvement and negative follow-up testing.

List of Abbreviations

AMR	Antimicrobial resistance
H. pylori	*Helicobacter pylori*
LCR35	*Lacticaseibacillus rhamnosus*
PPI	Proton pump inhibitor

Conflicts of interest

Nikon Moghadasian, Thomas Ambrus, and Mohammed H. Moghadasian have no competing interests to disclose. Agnieszka D. Magg, Babak Bahadori, and Bernhard Sikora have a commercial interest in the berberine product used. In compliance with the ICMJE uniform disclosure form, Agnieszka D. Magg, Babak Bahadori, and Bernhard Sikora report a commercial interest in

the berberine product used. All other authors declare no competing interests.

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Consent for publication

Consent was obtained from the patient for publication of this case presentation in accordance with ethical standards and the Helsinki Declaration.

Other relationships

All authors declare no other relationships or activities that could have influenced the submitted work.

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Summary of case

1	Patient (gender, age)	38-year-old woman
2	Final diagnosis	Recurrent *H. pylori* gastritis
3	Symptoms	Epigastric discomfort, bloating, intermittent nausea
4	Medications	Pantoprazole 40 mg; *L. rhamnosus* LCR35; liquid berberine
5	Clinical procedure	EGD, stool antigen testing, rapid urease testing, and colonoscopy
6	Specialty	Gastroenterology