Proposal for safe eradication therapy of Helicobacter pylori in patients with porphyria

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Running Head: Eradication therapy of Helicobacter pylori in patients with porphyria

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Key Clinical Message: Eradication therapy of Helicobacter pylori may be safe if hemin has been intravenously administered in advance, even in patients with a history of recurrent acute attacks.

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Introduction

Helicobacter pylori infection increases the risk of gastric cancer and should be treated in young patients.[1]However, some drugs used to treat *H. pylori* inhibit cytochrome P450 3A4 and appear to induce porphyria, an illness that is often diagnosed in young adults. Porphyria is a potentially life-threatening condition that causes severe abdominal pain, nausea, constipation, confusion, and seizures.[2] Not all *H. pylori*therapies are contraindicated,[2] but the risk of*H. pylori* therapy–induced porphyria attacks is not well-understood. No statistical data have been reported regarding the safe use of these drugs. Thus, caution should be used when administering specific drugs because of their porphyria attack–inducing effects.[3]

Case history

We herein report a case of successful treatment of *H. pylori* in a female patient with porphyria. The patient, who was in her 20s, suffered from alcohol-induced whole body pain, constipation, hypertension, tachycardia, reversible cerebral vasoconstriction syndrome, posterior reversible encephalopathy syndrome, and epileptic seizures triggered. Elevated porphyrin precursors in the urine led to the diagnosis of acute intermittent porphyria. Hemin administration (the details of which we had previously reported)[4] promptly improved her symptoms. Thereafter, she experienced recurrent menstrual-related porphyria attacks that presented as constipation, abdominal pain, and leg pain. Constipation and elevated urinary porphyrin precursor levels regularly coincided with the period after ovulation; thus, we considered constipation as a symptom of mild porphyria. We hypothesize that the patient's constipation resulted from vasospasm-induced ischemia caused by nitric oxide synthase deficiency.[4] Once a month, on the day before or after she was expected to ovulate, the patient was intravenously administered 0.4 mg/kg of hemin (Figure. 1). This drug, which remains in the body for approximately three weeks, was safely administered without increasing the patient's ferritin levels. For four years after the start of hemin treatment, the patient maintained a stable course without severe attacks.

One day, she complained of upper abdominal pain unrelated to porphyria and was evaluated by upper gastrointestinal endoscopy. Chronic inflammation was observed in her gastric mucosa, and a rapid urease test was positive; thus, she was diagnosed with *H. pylori* –related chronic gastritis. The patient's medication regimen was modified such that hemin was administered at the onset of constipation; and clarithromycin, vonoprazan, and amoxicillin were administered for 1 week after the onset of menstruation (Figure. 1). This protocol eliminated*H. pylori* without triggering porphyria symptoms such as constipation.

Discussion

Clarithromycin is a first-line drug for *H. pylori* eradication. It is reportedly a cytochrome P450 3A4 inhibitor, but that is not in and of itself a contraindication for porphyria.[5,6] There have been no reports on the safety of metronidazole monotherapy or combination therapy for *H. pylori* in patients with porphyria; and although amoxicillin and vonoprazan are believed not to induce porphyria attacks, the evidence remains insufficient. We had previously described how porphyria attacks can be triggered by the accumulation of porphyrin precursors or the lack of heme,[4] indicating that porphyria attacks may be prevented by supplying the appropriate amount of hemin. Here, we present a protocol that can suppress medication-induced porphyria, even in patients with a history of recurrent acute attacks. More specifically, we believe this report may serve as a future reference for eradicating*H. pylori* in patients with porphyria.

CONFLICT OF INTEREST

None

AUTHOR CONTRIBUTIONS

Tadayuki Takata: Writing - Original draft, Data curation, Investigation. Yohei Kokudo: Investigation. Asahiro Morishita: Data curation and Investigation. Kodai Kume: Investigation. Tatsuo Yachida: Investigation. Masaki Kamada: Investigation. Hideki Kobara: Investigation. Kazushi Deguchi: Investigation. Tetsuo Touge: Supervision. Hisashi Masugata: Supervision. Tsutomu Masaki: Supervision. Requests for reprints should be addressed to the corresponding author. All authors had access to the data and a role in writing the manuscript.

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Figure legend

Figure. 1 Treatment flow chart. Hemin was intermittently administered according to the menstrual cycle.