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LETTER TO THE EDITOR

Dramatic and prompt efficacy of *Helicobacter pylori* eradication in the treatment of severe refractory iron deficiency anemia in adults

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Dear Editor,

Iron deficiency anemia (IDA) is one of the most common nutritional diseases worldwide. The basic treatment for IDA is oral iron medication; however, some patients with IDA are occasionally refractory to this type of therapy [1]. Recently, the role of *Helicobacter pylori* in the etiology of IDA has become a focus of considerable interest [2, 3]. Although the association of *H. pylori* with IDA has been examined extensively, most studies have focused on mild IDA in school-aged children and young people [4–6]. Here, we report two adult cases of severe IDA refractory to oral iron therapy in which the anemia was dramatically and promptly improved by *H. pylori* eradication (Fig. 1).

Case 1 A 73-year-old male was referred to our hospital because of severe anemia. He had been receiving oral iron (100 mg/day) therapy for more than 6 months, but his anemia had not improved significantly. Laboratory examinations revealed severe IDA (red blood cell count 269×10^{10}/l, hemoglobin 4.7 g/dl, hematocrit 17.5 %, mean corpuscular volume 65.1 fl, mean corpuscular hemoglobin concentration 17.5 pg, serum iron 8 μg/dl, serum ferritin 4.7 ng/ml, unsaturated iron binding capacity 487 μg/dl). Endoscopic examination of the upper and lower gastrointestinal (GI) tract revealed mild atrophic gastritis with *H. pylori* infection, but no bleeding was detected in any part of the GI tract. A stool occult blood test gave a negative result. CT examination also revealed no abnormalities. Because oral iron therapy had failed in this patient, iron was administered intravenously, and this resulted in a gradual increase in the hemoglobin level. *H. pylori* eradication was performed using a standard regimen of amoxicillin, clarithromycin, and lansoprazole. Eradication was successful, and iron was then administered orally (100 mg/day). In contrast to the lack of response to oral iron therapy before *H. pylori* eradication, the patient's hemoglobin level promptly increased to normal. Since discontinuation of iron therapy, IDA has not recurred for more than 3 years.

Case 2 A 36-year-old male was referred to our hospital because of severe IDA that was refractory to oral iron therapy. Laboratory examinations revealed the following values: red blood cell count 235×10^{10}/l, hemoglobin 4.6 g/dl, hematocrit 17.0 %, mean corpuscular volume 72.3 fl, mean corpuscular hemoglobin concentration 19.6 pg, serum iron 10 μg/dl, serum ferritin 5.3 ng/ml, and unsaturated iron binding capacity 453 μg/dl. Endoscopic examination of the whole GI tract and CT scan revealed no abnormalities. Since *H. pylori* infection was detected, *H. pylori* eradication was performed. Similarly to the clinical course in case 1, IDA was promptly improved by oral iron administration. This patient also has shown no recurrence of IDA for more than 2 years after withdrawal of iron therapy.

Although an association between *H. pylori* infection and IDA has been established, it is still unknown how *H. pylori* mediates the pathogenesis of IDA. However, a number of possible mechanisms have been proposed, including impairment of gastric acidity by *H. pylori* infection [7]. Recently, it has been reported that *H. pylori* directly perturbs iron trafficking in epithelial cells [8, 9]. That is, CagA of *H. pylori* is able to alter the internalization, intracellular transport, and polarity of the transferrin/transferrin receptor iron uptake system [9]. The prompt improvement of iron adsorption observed after *H. pylori* eradication in the present two cases strongly

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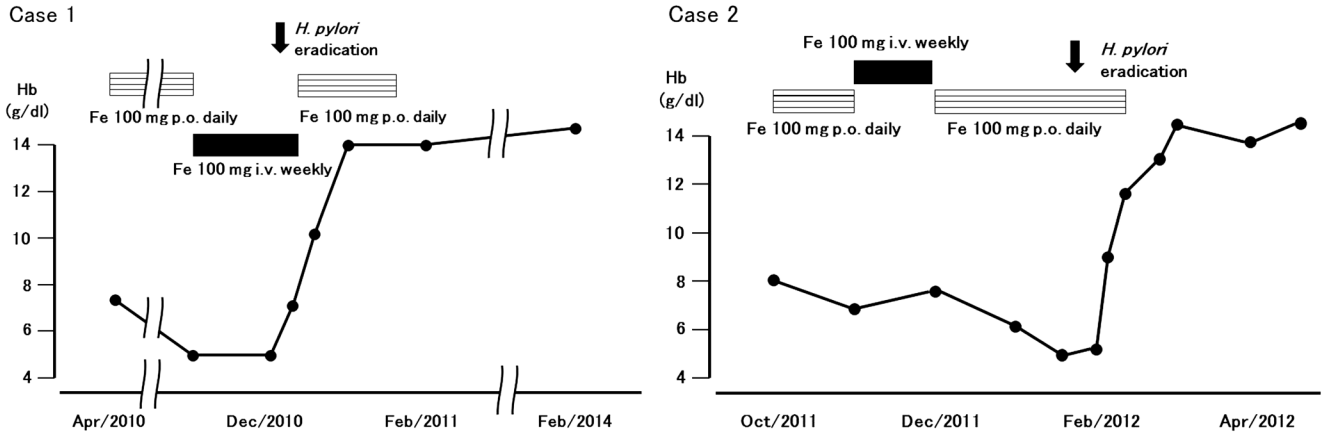

Fig. 1 Clinical courses of cases 1 and 2. Refractory IDA was promptly improved by oral iron administration after *H. pylori* eradication and did not recur after withdrawal of iron therapy in both cases

suggests a direct interaction between *H. pylori* and iron transport. As it has also been reported that IDA accelerates *H. pylori*-induced carcinogenesis [10], *H. pylori* eradication is highly recommended in patients with IDA.

Conflict of interest The authors declare that they have no conflicts of interest.

References

1. Hershko C, Camaschella C (2014) How I treat unexplained refractory iron deficiency anemia. Blood 123:326–333
2. Muhsen K, Cohen D (2008) *Helicobacter pylori* infection and iron stores: a systematic review and meta-analysis. Helicobacter 13: 323–340
3. Cardenas VM, Mulla ZD, Ortiz M, Graham DY (2006) Iron deficiency and *Helicobacter pylori* infection in the United States. Am J Epidemiol 163:127–134
4. Baggett HC, Parkinson AJ, Muth PT, Gold BD, Gessner BD (2006) Endemic iron deficiency associated with *Helicobacter pylori* infection among school-aged children in Alaska. Pediatrics 117:e396–404
5. Muhsen K, Barak M, Henig C, Alpert G, Ornoy A, Cohen D (2010) Is the association between *Helicobacter pylori* infection and anemia age dependent? Helicobacter 15:467–472
6. Azab SF, Esh AM (2013) Serum hepcidin levels in *Helicobacter pylori*-infected children with iron-deficiency anemia: a case–control study. Ann Hematol 92:1477–1483
7. Annibale B, Capurso G, Lahner E, Passi S, Ricci R, Maggio F, Delle Fave G (2003) Concomitant alterations in intragastric pH and ascorbic acid concentration in patients with *Helicobacter pylori* gastritis and associated iron deficiency anaemia. Gut 52:496–501
8. Lee JH, Choe YH, Choi YO (2009) The expression of iron-repressible outer membrane proteins in *Helicobacter pylori* and its association with iron deficiency anemia. Helicobacter 14:36–39
9. Tan S, Noto JM, Romero-Gallo J, Peek RM Jr, Amieva MR (2011) *Helicobacter pylori* perturbs iron trafficking in the epithelium to grow on the cell surface. PLoS Pathog 7:e1002050
10. Noto JM, Gaddy JA, Lee JY et al (2013) Iron deficiency accelerates *Helicobacter pylori*-induced carcinogenesis in rodents and humans. J Clin Invest 123:479–492