—Case Reports—

Helicobacter pylori Infection with a Duodenal Ulcer in a 6-year-old Boy

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Abstract

A 6-year-old boy was hospitalized because of dark feces and facial pallor of 1 week's duration. Other gastrointestinal symptoms, including vomiting and abdominal pain, were absent, but he felt dizziness when standing and fatigue on effort. Hematologic studies revealed iron-deficiency anemia, and endoscopy showed gastric erosions and a duodenal ulcer. All test results for *Helicobacter pylori* infection, including *H. pylori* antigen in stool, anti-*H. pylori* IgG immunoassay in serum, and the ^{13}C-urea breath test, were positive. Because an *H. pylori*-associated gastric ulcer had been diagnosed with endoscopy in the patient's father 3 years earlier, father-son transmission was suspected. The patient was treated with triple-agent eradication therapy (proton pump inhibitor [lansoprazol], amoxicillin, and clarithromycin) for 2 weeks. One month after therapy was completed, eradication of *H. pylori* was confirmed by negative results on the stool antigen test. Peptic ulcer disease can occur in young children, as in this case. The stool antigen test kit is a useful and reliable method that can be used even in preschool children to diagnose *H. pylori* infection.
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Key words: *Helicobacter pylori*, duodenal ulcer, dark feces, intrafamilial transmission, child

Introduction

Helicobacter pylori (*H. pylori*) is the primary pathogen involved in the development of chronic gastritis, peptic ulcer disease, and gastric malignances. In addition, several recent studies have investigated the relationship between *H. pylori* and extragastroduodenal disorders, such as chronic thrombocytopenic purpura[1], intractable iron-deficiency anemia[2], chronic otitis media[3], and short stature[4].

The prevalence of *H. pylori* among asymptomatic Japanese children has been reported to be 7% in children aged 1 to 4 years, 15% in those aged 5 to 9 years, and 20% in those aged 10 to 15 years[5]. Approximately 50% of adults worldwide are infected with *H. pylori*. However, *H. pylori*-associated peptic ulcer disease develops in only a small percentage of infected children.

In Japanese children, the prevalence of *H. pylori* in duodenal ulcers was reported to be 83%, suggesting

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Table 1 Laboratory data on admission

Test	Result
White blood cells	6,960 /μl
Red blood cells	269×10^4 /μl
Hemoglobin	6.3 g/dl
Hematocrit	22.6 %
Platelets	29.5×10^4 /μl
Iron	12 μg/dl
Unsaturated iron binding capacity	307 μg/dl
Total iron binding capacity	319 μg/dl
Ferritin	<5 ng/ml
Blood sugar	107 mg/dl
C reactive protein	<0.3 mg/dl
Aspartate aminotransferase	29 IU/l
Alanine aminotransferase	6 IU/l
Lactate dehydrogenase	221 IU/l
Na	139 mEq/l
K	4.0 mEq/l
Cl	103 mEq/l
Blood urea nitrogen	9.4 mg/dl
Creatinine	0.32 mg/dl
Total protein	6.1 g/dl
Albumin	3.7 g/dl
Total cholesterol	140 mg/dl
H. pylori IgG antibody in serum	191 U/ml (normal, <10)
H. pylori antigen in stool	(+)
^{13}C-urea breath test	7.4 per mil (normal, <2.5)
Immunologic fecal occult-blood test	(-)

that *H. pylori* infection is the principal causative factor for duodenal ulcers in children[6]. However, there are few reports about *H. pylori*-associated duodenal ulcers in children.

The *H. pylori* stool antigen (HpSA) test has recently been approved for the diagnosis of *H. pylori* infection and for monitoring the results of eradication therapy, although the ^{13}C-urea breath test (UBT) has usually been considered a reliable, noninvasive test.

We report a case of *H. pylori*-associated duodenal ulcer, causing anemia and melena but not abdominal symptoms, diagnosed with HpSA testing in a 6-year-old boy.

Case Report

A 6-year-old boy complained of dizziness on standing and mild fatigue on effort and noticed dark feces 1 week before hospitalization. He had a healthy appetite and good activity. Gastrointestinal symptoms, including abdominal pain, discomfort, and vomiting, were absent. Three years earlier, an *H. pylori*-associated gastric ulcer had been diagnosed with endoscopy in the boy's father, coinciding with many years' history of gastric pain. Eradication therapy was started for several cycles in the father and was effective; no symptoms occurred thereafter.

The boy was 116.5 cm tall and weighed 20.8 kg. Body temperature was 37.0℃. Physical examination on admission revealed no marked abnormalities except for facial pallor.

Laboratory studies (**Table 1**) showed a red blood cell count of 269×10^4 /μl, a hemoglobin level of 6.3 g/dl, an iron level of 12 μg/dl, a total iron binding capacity of 319 μg/dl, an unsaturated iron binding capacity of 307 μg/dl, and a ferritin level <5 ng/ml. These data suggested iron-deficiency anemia. Because of the father's history, tests to determine the presence of *H. pylori* infection were done. Results of the HpSA test were positive, the UBT was 7.4 per mil (normal, <2.5 per mil), and enzyme-linked

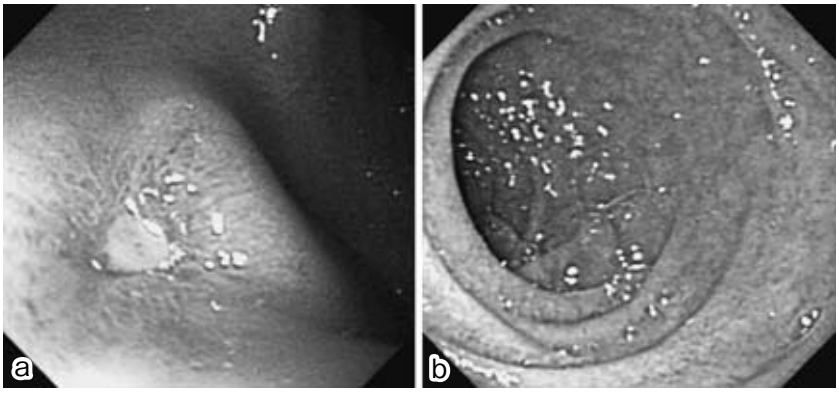

Fig. 1 Upper gastrointestinal endoscopic findings: (a) Healing stage of ulcer (H1 stage of Sakita-Miwa staging) was observed at the duodenal bulb. (b) Hemorrhagic erosions were observed around the antrum.

immunosorbent assay for *H. pylori* IgG antibody in serum (E-plate; Eiken Chemical Co., Tokyo) was 191 U/m*l* (normal, <10 U/m*l*). On the basis of these findings, *H. pylori* infection was diagnosed. Because of the possibility of upper gastrointestinal bleeding from a peptic ulcer, upper gastrointestinal endoscopy was performed; gastric erosions and an ulcer of the duodenal bulb were observed (**Fig. 1**).

Triple-agent eradication therapy was administered for 2 weeks with the proton pump inhibitor (PPI) lansoprazol (1.5 mg/kg/day), amoxicillin (50 mg/kg/day), and clarithromycin (20 mg/kg/day). An iron supplement was also administered.

The patient was discharged with a hemoglobin level of 8.3 g/d*l* on the ninth hospital day. The iron supplement and the PPI were continued for 2 months after discharge. One month after drug therapy was completed, eradication of *H. pylori* was confirmed by negative results on the HpSA test. Six months later, the level of *H. pylori* IgG antibody in serum had decreased to 44 U/m*l*, and the hemoglobin level had increased to 12.2 g/d*l*.

Discussion

In many patients with *H. pylori* infection chronic gastritis develops a few months to 1 year after first exposure[7]. Furthermore, peptic ulcer disease or gastric malignancies will develop in 10% to 15% of persons infected with *H. pylori*[8]. In peptic ulcer disease, duodenal ulcers occur one and half times to twice as frequently as gastric ulcers[9].

Although the precise mechanism of transmission of *H. pylori*infection is unclear, person-to-person transmission between close contacts and family members is strongly suspected. The route of transmission may involve the fecal-oral, gastric-oral (in vomitus), or oral-oral routes[10]. In the present case, the possibility of father-son transmission could not be ruled out because the father had had gastric ulcer disease with *H. pylori* 3 years earlier. Shimizu et al.[11] have studied the transmission route of *H. pylori* in two families using DNA analysis. They found direct evidence of father-son transmission in one family and of father-elder son and mother-younger son transmission in another family.

The chief complaints of our patient were dizziness on standing, mild fatigue, and dark feces; he had no abdominal symptoms. Several recent pediatric studies have evaluated the relationship between *H. pylori* infection and recurrent abdominal pain or dyspepsia in children[12–14]. With only a few exceptions, there does not appear to be an association between *H. pylori* infection and an increased prevalence of recurrent abdominal pain in children[14]. There is a real need, however, for randomized controlled clinical trials to evaluate the role of *H. pylori* in the pathogenesis of recurrent abdominal pain.

The prevalence of *H. pylori* antibodies in the blood of infected children aged 2 to 6 years is 44.4%[15]. A lower prevalence is related to a shorter duration of exposure to *H. pylori*. In the present case, the high antibody titer indicated long exposure to *H. pylori*.

The sensitivity and specificity of the UBT and the

H. pylori IgG antibody test are variable in children, and children younger than 12 years are more likely to have false-negative results. Commercial HpSA test kits have recently become popular and have been covered by insurance in Japan since 2003. The HpSA test is performed with an enzyme-linked immunosorbent assay and either monoclonal or polyclonal antibodies. This test has been adopted in the guidelines for the diagnosis and treatment of *H. pylori* infection[16]. Kato et al.[17] have also reported a high specificity and sensitivity of the HpSA test in children who cannot perform the UBT, suggesting that HpSA testing is a reliable method in preschool children, including infants.

There has been much discussion about the optimal number of agents and the duration of treatment to eradicate *H. pylori* in children. Many clinical studies have shown that triple-agent therapy with a PPI, amoxicillin, and clarithromycin has a higher eradication rate than does dual-agent therapy with a PPI and clarithromycin[18–20].

Regarding the duration of therapy, a retrospective multicenter study has achieved eradication rates of 73.4% and 91.3% with 1 and 2 weeks of therapy, respectively[21]. On the basis of this study, we administered a triple-agent therapy for 2 weeks' duration in our patient. On the other hand, the rates of clarithromycin resistance have recently increased. Kato et al. have reported that primary resistance to clarithromycin is shown by 29% to 37% of *H. pylori* isolates in Japanese children[22]. In these cases, triple-agent therapy with metronidazole instead of clarithromycin achieved a higher eradication rate[21]. In the present case, eradication was successful with clarithromycin. In addition, the PPI was continued for 8 weeks after the triple-agent therapy had finished, because the healing of the duodenal ulcer cannot be monitored with repeated upper gastrointestinal endoscopy in a child.

In conclusion, we have reported a case of *H. pylori*-induced duodenal ulcer likely caused by father-son transmission in a 6-year-old boy. Peptic ulcer disease can occur in young children, as in this case. The HpSA test is a useful and reliable method that can be used even in preschool children to diagnose *H. pylori* infection.

References

1. Sato R, Murakami K, Watanabe K, et al.: Effect of *Helicobacter pylori* eradication on platelet recovery in patients with chronic idiopathic thrombocytopenic purpura. Arch Intern Med 2004; 164: 1904–1907.
2. Konno M, Muraoka S, Takahashi M, Imai T: Iron-deficiency anemia associated with *Helicobacter pylori* gastritis. J Pediatr Gastr Nutr 2000; 31: 52–56.
3. Agirdir BV, Bozova S, Derin AT, Turhan M: Chronic otitis media with effusion and *Helicobacter pylori*. Int J Pediatr Otorhi 2005; 23.
4. Perri F, Pastore M, Leandro F, et al.: *Helicobacter pylori* infection and growth delay in older children. Arch Dis Child 1997; 77: 46–49.
5. Kato S, Okamoto H, Nishino Y, et al.: *Helicobacter pylori* and TT virus prevalence in Japanese children. J Gastroenterol 2003; 38: 1126–1130.
6. Kato S, Nishino Y, Ozawa K, et al.: The prevalence of *Helicobacter pylori* in Japanese children with gastritis or peptic ulcer disease. J Gastroenterol 2004; 39: 734–738.
7. Ganga-Zandzou PS, Michaud L, Vincent P, et al.: Natural outcome of *Helicobacter pylori* infection in asymptomatic children: A two-year follow-up study. Pediatrics 1999; 104: 216–221.
8. Del Giudice G, Michetti P: Inflammation, immunity and vaccines for *Helicobacter pylori*. Helicobacter 2004; 9 (suppl): 23–28.
9. Nervi G, Liatopoulou S, Cavallaro LG, et al.: Dose *Helicobacter pylori* infection eradication modify peptic ulcer prevalence? A 10 years' endoscopical survey. World J Gastroenterol 2006; 12: 2398–2401.
10. Drumm B, Perez-Perez GI, Blaser MJ, Sherman PM: Intrafamilial clustering of *Helicobacter pylori* infection. New Eng J Med 1990; 322: 359–363.
11. Shimizu T, Oguchi S, Yamashiro Y, et al.: *Helicobacter pylori* transmission between a boy with duodenal ulcer and his father. Pediatr Infect Dis J 1999; 18: 655–656.
12. Macarthur C, Sunders N, Feldman W: *Helicobacter pylori*, gastroduodenal disease, and recurrent abdominal pain in children. JAMA 1995; 273: 729–734.
13. McCallion WA, Bailie AG, Ardill JE, Bamford KB, Potts SR, Boston VE: *Helicobacter pylori*, hypergastrinaemia, and recurrent abdominal pain in children. J Pediatr Surg 1995; 30: 427–429.
14. O'Donohoe JM, Sullivan PB, Scott R, Rogers T, Brueton MJ, Barltrop D: Recurrent abdominal pain and *Helicobacter pylori* in a community-based sample of London children. Acta Paediatr 1996; 86: 671–673.
15. Rocha OAM, Aguiar RG, de Magalhães QDM, et al.: Evaluation of enzyme-linked immunosorbent assay for the diagnosis of *Helicobactor pylori* infection in children from different age groups with and without duodenal ulcer. J Pediatr Gastroenterol Nutr 1999; 28: 157–161.
16. Asaka M: Guidelines in the management of *H. pylori* infection in Japan. Nippon Rinsho 2005; 63 (suppl):

12–16.
17. Kato S, Ozawa K, Okuda M, et al.: Accuracy of the stool antigen test for the diagnosis of childhood Japanese *Helicobacter pylori* infection: a multicenter Japanese study. Am J Gastroenterol 2003; 98: 296–300.
18. Dohil R, Israel DM, Hassall E: Effective 2-week therapy for *Helicobacter pylori* disease in children. Am J Gastroenterol 1997; 92: 244–247.
19. Kato S, Ritsuno H, Ohnuma K, Iinuma K, Sugiyama T, Asaka M: Safety and efficacy of 1-week triple therapy for eradicating *Helicobacter pylori* in children. Helicobacter 1998; 3: 278–282.
20. Shashihar H, Peter J, Lin C, Rabah R, Thomas R, Tolia V: A prospective trial of lansoprazole triple therapy for pediatric *Helicobacter pylori* infection. J Pediatr Gastroenterol Nutr 2000; 30: 276–282.
21. Kato S, Konno M, Maisawa S, et al.: Results of triple eradication therapy in Japanese children: a retrospective multicenter study. J Gastroenterol 2004; 39: 838–843.
22. Kato S, Fujimura S, Udagawa H, et al.: Antibiotic resistance of *Helicobacter pylori* strains in Japanese children. J Clin Microbiol 2002; 40: 649–653.

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