J Gastroenterol 2005; 40:94–97
DOI 10.1007/s00535-004-1499-2

Journal of Gastroenterology

Case report

Helicobacter heilmannii infection in a child after successful eradication of *Helicobacter pylori*: case report and review of literature

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An 11-year-old boy with *Helicobacter pylori*-associated duodenal ulcer was successfully treated with a combination of lansoprazole, amoxicillin, and clarithromycin. Endoscopy and gastric biopsies were repeated 2 and 12 months later, showing ulcer healing and eradication of *H. pylori*. However, a 3-year follow-up study demonstrated *H. heilmannii* in the antral mucosa based on its characteristic morphology and positive urease test and negative culture. The patient had no contact with domestic animals such as cats and dogs. A 7-day course with lansoprazole, amoxicillin, and clarithromycin was performed again, resulting in successful eradication of the organism. Pediatric cases with *H. heilmannii* infection reported are reviewed.

Key words: child, eradication, gastritis, *Helicobacter heilmanniii*, *Helicobacter pylori*

Introduction

Helicobacter pylori infection is associated with the development of chronic gastritis, peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma. *H. pylori* is also an important causal factor for gastritis and peptic ulcer disease in children.[1,2] Recently, an increasing number of *Helicobacter* species other than *H. pylori*, including *H. heilmannii* (formerly *Gastrospirillum hominis*), *H. felis*, and *H. cinaedi*, have been identified in human stomach or feces.[3] Compared with *H. pylori*, *H. heilmannii* is longer (3.5–7.5 μm) with six to eight coils per cell and up to 12 sheathed flagella at each pole. It is thought that humans typically acquire *H. heilmannii* infection from domestic animals as a zoonosis.[3] Similar to *H. pylori*, *H. heilmannii* has been implicated in the pathogenesis of chronic gastritis, peptic ulcer disease, gastric cancer, and gastric MALT lymphoma in adults.[4–8] There are several reports in English of childhood *H. heilmannii* infection.[9–18] We report here a pediatric case in which *H. heilmannii* infection was identified after *H. pylori* was successfully eradicated for duodenal ulcer.

Received: February 12, 2004 / Accepted: April 26, 2004
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Case report

In April 2000, an 11-year-old boy was referred to the University Hospital because of persistent epigastric pain. His father had a history of duodenal ulcer. Upper gastrointestinal endoscopy showed ulceration in the duodenal bulb and ulcer scar at the gastric angle. The ^{13}C-urea breath test (UBT) was positive with Δ^{13}C value of 34.9‰ (cutoff value = 3.5‰).[19] The urease test, histology, stool antigen test, and culture were all positive for *H. pylori* infection (Table 1). He was treated with a 10-day course of triple therapy consisting of lansoprazole, amoxicillin, and clarithromycin and became symptom free. Upper gastrointestinal endoscopy was repeated 2 months after the therapy was completed, showing complete healing of the duodenal ulcer. Gastric histology showed chronic inflammation without neutrophil infiltration (Table 1). *H. pylori* testing as already mentioned confirmed eradication of the organism. The 1-year follow-up endoscopy demonstrated healed ulcer and *H. pylori* tests including ^{13}C-UBT (0.7‰) were all negative. Histology showed mild chronic gastritis.

On February 2003, the patient and his parents agreed to undergo 3-year follow-up endoscopy. At that time, he had no gastrointestinal symptoms. Active gastroduodenal ulcer was not found and the gastric mucosa was endocopically normal. ^{13}C-UBT was negative with Δ^{13}C value of 1.2% and the stool antigen test was also negative (Table 1). Culture of the biopsy specimen was nega-

Table 1. Results of histology and *Helicobacter pylori* tests of the patient

Date	Histological parameter (grade)[a]		Urease test[a]	^{13}C-UBT[b] (%)	Culture	Stool ELISA (HpSA)
	Inflammation	Activity				
July 2000	2/1	2/0	Positive/negative	34.9	Positive	Positive
Sept. 2000	2/1	0/0	Negative/negative	0.0	Negative	Negative
June 2001	1/1	0/0	Negative/negative	0.7	Negative	Negative
Feb. 2003	2/1	0/0	Positive/negative	1.2	Negative	Negative
Aug. 2003	1/0	0/0	Negative/negative	0.0	Negative	Negative

[a] Gastric antrum/corpus. The grade is based on the Updated Sydney System
[b] ^{13}C-urea breath test; cutoff value, 3.5‰
HpSA, Premier Platinum HpSA

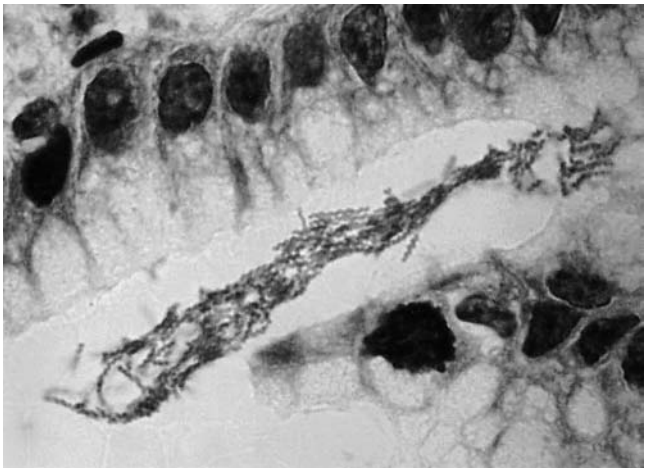

Fig. 1. Micrograph shows *Helicobacter heilmannii* in a gastric pit in the antral mucosa. Abundant long, tightly spiraled microorganisms are observed. Giemsa stain. ×1000

tive for *H. pylori*. However, urease test was positive for the antral specimen whereas it was negative for the corpus specimen. *H. heilmannii* with its characteristic morphology was found in the antral mucosa (Fig. 1). According to the Updated Sydney System,[20] inflammation of the antrum increased up to grade 2 but that of the corpus was unchanged. No neutrophil infiltration was found. The patient and his family did not have contact with domestic animals, including cats and dogs. Because the parents desired eradication therapy, he was treated again with a 7-day course with lansoprazole (20 mg, b.i.d.), amoxicillin (750 mg, b.i.d.), and clarithromycin (400 mg, b.i.d.). Upper gastrointestinal endoscopy and biopsy were performed 6 months later. ^{13}C-UBT, urease test, culture, and the stool antigen test showed negative results. *H. heilmannii* was not histologically detected. The degrees of inflammation in the antrum and corpus decreased to grades 1 and 0, respectively (see Table 1).

Discussion

The present case showed acquisition of *H. heilmannii* infection after successful eradication of *H. pylori*. Cases with simultaneous infection with *H. pylori* and *H. heilmannii* have been reported, although rare.[21] In our case, detailed histological examination of the first and subsequent biopsy specimens did not show *H. heilmannii*-like organisms. Compared with *H. pylori* infection, *H. heilmannii* infection is less prevalent with the rate of 0.3%–0.4% of children[11,14,16] and <0.5% of adults undergoing endoscopy.[3] Because cats, dogs, and pigs are reservoirs of *H. heilmannii*, it is thought that close contact with these domestic animals is the major risk factor for acquisition of the infection.[3,22] In one study of a child with *H. heilmannii* infection,[12] the pet dogs were endoscopied, demonstrating the organism in the stomach. In addition, *ureAB* gene sequencing strongly supports the cat-to-human transmission of *H. heilmannii*.[17] In most pediatric cases with *H. heilmannii* infection, dogs and/or cats were reported as domestic animals (Table 2). However, three infected cases including ours did not have known contact with such domestic animals.[10,18] Because we used an endoscope disinfected with 0.3% peracetic acid and sterilized disposable biopsy forceps, it is not likely that *H. heilmannii* was transmitted via the endoscopic procedure. The exact transmission route of *H. heilmannii* remains to be established.

As described in Table 2, *H. heilmannii* infection causes chronic gastritis in children and is reported to be asscociated with gastric ulcer[18] or anemia.[15] *H. heilmannii* induces chronic inflammation in the gastric mucosa but the degree is generally milder than with *H. pylori*.[7] In addition, *H. heilmannii* colonization is commonly focal and restricted to the antrum.[7] In our case, previous *H. pylori* infection showed chronic active gastritis with grade 2 infiltration of neutrophils in the antrum, whereas the following *H. heilmannii* infection showed chronic gastritis without neutrophil infiltration.

Table 2. Pediatric cases with *Helicobacter heilmannii* infection reported in the English literature

Case no.	Age (years)	Sex	Main GI symptoms	Diagnosis[a]	Pet animals	Eradication therapy[b]	Reference no.
1	14	F	Abdominal pain, bloating	Gastritis	—	ND	9
2	14	M	Epigastric pain, fat intolerance	Gastritis	—	ND	9
3	7	—	Epigastric pain, vomiting	Gastritis	None	ND	10
4	10	M	Nausea, substernal discomfort	Chronic gastritis	Cat and dog	Bismuth + A	11
5	3	M	Abdominal pain, nausea, anorexia	Chronic gastritis	Cat and dog	Bismuth + ranitidine + A	11
6	12	F	Epigastric pain, vomiting	CAG (NG)	Dog	Bismuth + antibiotics	12
7	1	F	Vomiting	CAG (NG)[c]	Dog	Bismuth + AM	13
8	15	F	Abdominal pain	CAG (NG)	Dog	Ranitidine + AM (S)	14
9	5	M	Dysphagia	CAG	Dog	ND	14
10	9	F	Abdominal pain, vomiting	CAG (NG)	Cat	Ranitidine + AM	14
11	14	M	Anemia	CAG (NG)	Cat and dog	Omeprazole + AC (S)	15
12	11	F	—	Gastritis	—	—	16
13	5	M	Abdominal pain, faiture to thrive	CAG	Cat	Omeprazole + AC (S)	17
14	14	F	Epigastric pain, hematemesis	Gastric ulcer	None	Omeprazole + AM (S)	18
15	11	M	None	Chronic gastritis[d]	None	Lansoprazole + AC (S)	Present case

ND, Not done; —, not described
[a] CAG, chronic active gastritis; NG, nodular gastritis
[b] A, amoxicillin; C, clarithromycin; M, metronidazole; S, successful eradication
[c] Celiac disease
[d] Previous history of *H. pylori*-associated duodenal ulcer

In the present review of pediatric cases, neutrophil infiltration (chronic active gastritis) was found in seven cases,[12–15,17] but was not found in three cases including ours.[11] In the adult population, neutrophil infiltration was observed in 65% of *H. heilmannii* gastritis.[7] As in *H. pylori* gastritis, endoscopic nodularities, so-called nodular gastritis, were shown in six of seven children with chronic active gastritis. Lymphoid aggregates were also seen regularly in adulthood *H. heilmannii* gastritis.[21] Eradication of *H. heilmannii* leads not only to ulcer healing[6] but also to regression of the tumor in gastric MALT lymphoma.[8] It appears that *H. heilmannii* is easier to eradicate than *H. pylori*. In one study in which *H. heilmannii* was cultured,[23] the organism was susceptible to amoxicillin, tetracycline, and erythromycin but resistant to metronidazole. In the pediatric population, *H. heilmannii* was successfully eradicated by regimens with amoxicillin plus metronidazole or clarithromycin (Table 2). However, it remains unclear whether patients with *H. heilmannii* gastritis should be treated and what is the optimal regimen.

At present, it is extremely difficult to culture *H. heilmannii*. Therefore, the diagnosis of *H. heilmannii* infection is generally done by the detection of its characteristic morphology in gastric biopsy specimens. Although *H. heilmannii* expresses variable urease activity, ^{13}C-UBT and urease test are thought to be less sensitive than in *H. pylori* infection. Furthermore, it is impossible to distinguish *H. pylori* and *H. heilmannii* infection by these test using urease activity. In our case, who had positive urease test at the diagnosis of *H. heilmannii* infection, ^{13}C-UBT was negative. The stool enzyme-linked immunosorbent assay (ELISA) test using *H. pylori* polyclonal antigens may cross-react with antigens of other *Helicobacter* species such as *H. heilmannii*;[24] however, our case continued to show negative results of the stool antigen test after *H. pylori* was initially eradicated.

In summary, when the cause of chronic gastritis is unknown or when results of *H. pylori* tests are discrepant, that is, *H. pylori* culture is negative and other tests positive or borderline, physicians should take *H. heilmannii* infection into account. The increased recognition of *H. heilmannii* infection would deepen the understanding of gastric *Helicobacter* infection in humans.

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