

An atypical presentation of an acute gastric *Helicobacter felis* infection

K. Ghysen^{1*}, A. Smet^{2*}, P. Denorme³, G. Vanneste⁴, F. Haesebrouck^{5**}, W. Van Moerkercke^{6,7**}

(1) Department of Internal Medicine, University Hospital Leuven, Belgium ; (2) Laboratory of Experimental Medicine and Pediatrics (LEMP), Faculty of Medicine and Health Care, University of Antwerp, Belgium ; (3) Department of Dermatology, University Hospital Leuven, Belgium ; (4) Department of Pathology, AZ Groeninge, Kortrijk, Belgium ; (5) Department of Pathology, Bacteriology, Avian Diseases, Ghent University, Merelbeke, Belgium ; (6) Department of Gastroenterology, University Hospital Leuven, Belgium ; (7) Department of Gastroenterology, AZ Groeninge, Kortrijk, Belgium.

* Shared first authorship. ** Shared senior authorship

Abstract

Helicobacter pylori is a Gram negative bacterium that has been associated with a wide variety of gastric pathologies in humans. Besides this well studied gastric pathogen, other *Helicobacter* spp. have been detected in a minority of patients with gastric disease. These species, also referred to as “*H. heilmannii sensu lato*” or “non *Helicobacter pylori* *Helicobacter* spp. (NHPH)”, have a very fastidious nature which makes their *in vitro* isolation difficult. This group comprises several different *Helicobacter* species which naturally colonize the stomach of animals. In this article we present a case of a patient with severe gastritis in which *H. felis* was identified. The necrotic lesions observed at gastroscopy differ from the less active and less severe lesions generally associated with NHPH infections in human patients. The patient was successfully treated with a combination of amoxicillin, clarithromycin and pantoprazole. Infections with NHPH should be included in the differential diagnosis of gastritis when anatomopathological findings show an atypically shaped helicobacter. (*Acta gastroenterol. belg.*, 2018, 81, 436-438).

Introduction

H. pylori is the most prevalent *Helicobacter* species in the stomach of humans and has been associated with a wide range of gastric disorders (1).

However, other *Helicobacter* bacteria have over the years also been associated with gastric diseases in humans like gastritis, ulcer and even neoplasia (1). These microorganisms, which may be referred to as non-*H. pylori* *Helicobacter* species (NHPH) or *H. heilmannii sensu lato*, were similar to bacteria earlier reported in the stomach of pigs, cats, dogs and non-human primates (2,3,4). Analysis of the 16S rRNA gene of these bacteria resulted in their classification into the genus *Helicobacter* (4). Further investigation of the 16S rRNA gene sequence produced the reclassification of these gastric helicobacters into “*H. heilmannii*” type 1 and “*H. heilmannii*” type 2. Although the name *H. heilmannii* has for many years been used to refer to the long spiral-shaped bacteria in the human stomach, it was not formally recognized as a valid species name until recently (5). The former “*H. heilmannii*” type 1 is identical to *H. suis*, which naturally colonizes the stomach of pigs (4). *H. heilmannii* type 2 is more complex. It does not represent one single species, but rather a group of species naturally colonizing the canine and feline gastric mucosa, such as *H. bizzozeronii*, *H. felis*, *H. salomonis*, *H. cynogastricus*, *H. baculiformis*, *H. heilmannii (sensu stricto)* and *H.*

ailurogastricus. Living in close proximity to animals has been suggested to be a risk factor for humans to contract a NHPH infection (4).

Case presentation

This case concerns a 39 year old male presenting at the emergency department with acute abdominal pain, nausea and vomiting of brown fluid. The pain was located in the epigastric region. There was no use of nonsteroidal anti-inflammatory drugs. An important medical history was absent. He stopped smoking two years ago. He used approximately 15 units of alcohol a day during the weekend. He had a guinea pig and a parakeet as pets. On examination, the patient’s blood pressure was 144/73 mmHg, his pulse was 84 bpm and his temperature was 36°C.

Auscultation of heart and lungs was normal. Palpation of the abdomen was painful, especially in the epigastric region with focal tenderness. Both hypochondric regions were also painful. The remainder of the physical examination was normal.

A blood examination showed a slightly elevated C-reactive protein of 8.4 mg/L (reference range 0.00-5.0 mg/L). The white blood cell count, platelet count, white cell differential count, hematocrit and hemoglobin level were normal, as were also the liver and kidney function, the electrolytes (potassium, sodium, chloride) and the lipase level. At this moment the differential diagnosis consisted of an acute gastric ulceration with possible perforation or an acute alcoholic pancreatitis.

A CT-scan was performed for further differentiation (Fig. 1). This scan revealed an important thickening of the antral and pyloric gastric mucosa with a discrete infiltration of the adjoining mesenteric area. The other intra abdominal organs were normal.

A gastroscopy was performed and showed a massive antral gastritis with focal necrosis of the gastric mucosa (Fig. 2). Biopsy specimens were obtained from the

Correspondence to : Katrien.Ghysen, Handelskaai 1C bus 31 8500 Kortrijk.
E-mail : katrien.ghysen@uzleuven.be

Submission date : 31/08/2016
Acceptance date : 02/02/2017

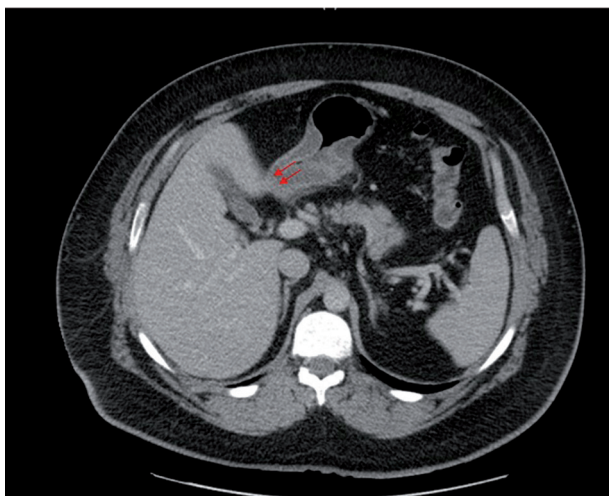


Fig. 1. — CT-scan of the abdomen.

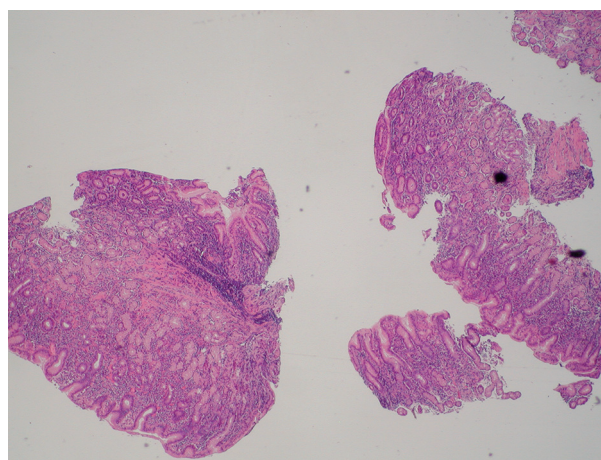


Fig. 3a. — Histopathological image, hematoxylin/eosin staining.

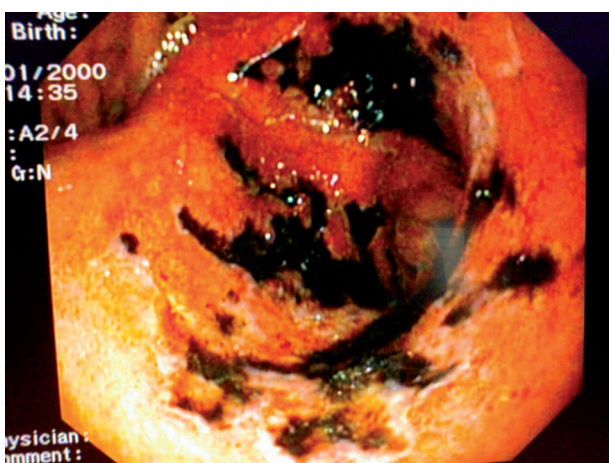


Fig. 2. — Endoscopic image of the antrum.

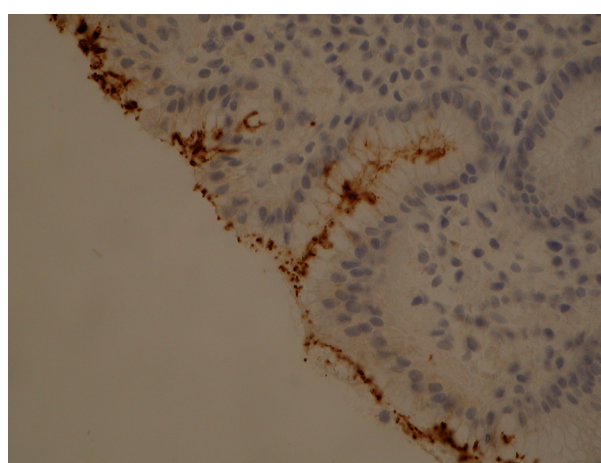


Fig. 3b. — Histopathological image, HP colouring.

gastric antrum and body. These specimens were fixed in 10% formalin and subsequently embedded in paraffin for further analyses.

For histopathological examination, 5 µm sections were stained with hematoxylin/eosin. The biopsy of the antrum showed a normal architecture with a well differentiated epithelium. Locally there was a necrotic sludge. There was no intestinal metaplasia. At the lamina propria there was an inflammatory infiltrate (Fig 3a). In the lumens of the glands, *Helicobacter pylori* like specimens were present (Fig. 3b).

Afterwards an anti *H. pylori* staining (with polyclonal rabbit anti *Helicobacter pylori* antibody) was performed revealing large spiral shaped *Helicobacter* like bacteria. Based on this finding, the assumption of a NHPH infection was made. To further characterize the identified *Helicobacter* bacteria at species level, quantitative PCR (q-PCR) was performed. In the biopsy specimens, roughly 100 *H. felis* bacteria per mg tissue were detected. The patient was treated with amoxicillin 2 times 1 g a day, clarithromycin 2 times 500 mg a day and pantoprazole 2 times 40 mg a day for fourteen days. A new gastroscopy performed 3 weeks later showed almost complete disappearance of the lesions and only

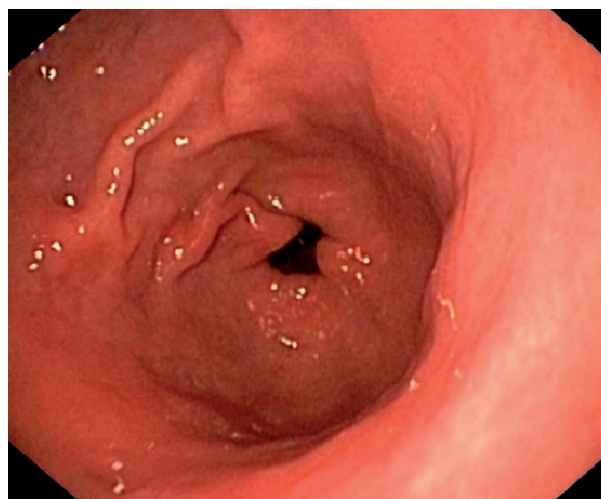


Fig. 4. — Endoscopic image after therapy.

slightly hyperemic gastritis (Fig. 4). New biopsies were taken and histopathological examination could not demonstrate the presence of spiral shaped bacteria.

Discussion

H. pylori is assumed to be the most frequent cause of chronic bacterial infections in humans. In developing countries, more than 80 % is infected with *H. pylori*. When compared with the developed countries there is a distinct difference since the prevalence of this pathogenic agent generally remains under 40 % (6). The prevalence of NHPH infections in humans is considerably lower and varies from 0.1 to 6 % with a higher incidence in Asian countries, such as China and Thailand (7,8).

In the present case, a 39-year old male suffering from severe gastritis was shown to be infected with *H. felis*. This pathogen has frequently been described in clinically healthy and diseased pets, with a prevalence of 62.8% and 52.6% in Belgian cats and dogs, respectively (9). *H. felis* DNA has been detected in the saliva of cats and dogs highlighting that the oral cavity of these animals may act as a source of infection with this agent for humans (4). The patient in the current study had a parakeet and a guinea pig at home, but no dog or cat. To the best of the authors' knowledge, the possible presence of *H. felis* in the stomach of guinea pigs and parakeets has not yet been thoroughly examined and the source of infection of the current case remains unclear.

NHPH infections are assumed to be less aggressive than *H. pylori* infections (8,10). Indeed, peptic ulcerations and erosions are more common in patients infected with *H. pylori* (8,10). NHPH-associated gastritis has been described to be most frequently localised in the antrum of the stomach and to be less active and less severe, while in patients infected with *H. pylori*, gastritis 2 may be more diffuse (8,10). In the present case, the gastritis was indeed localised in the antrum. It was, however, an atypical presentation of an NHPH infection, since gastroscopy revealed the presence of severe, necrotic lesions, comparable with the image of a caustic gastritis.

As mentioned in the review of the Cochrane analysis of 2013 (11), treatment regimens (for *H. pylori*) with triple therapy with a proton pump inhibitor and two antibiotics during 14 days was associated with a significantly higher eradication rate when compared with 7 to 10 days. In the present case, after the 14day treatment of the patient, NHPH were no longer detected in gastric biopsy samples, indicating that such treatment regime is also effective for eradication of *H. felis*.

There is a lack of clinical trials and only few reports deal with antimicrobial susceptibility of gastric NHPH. Van den Bulck et al. studied the susceptibilities of animal derived *H. felis*, *H. bizzozeronii*, and *H. salomonis*

isolates against 10 antimicrobial agents. Between these different *Helicobacter* species, no consistent differences were noticed (12).

Conclusion

This case of the 39-year old male with severe gastritis showed a more acute and aggressive course of an *H. felis* infection than described in literature for other NHPH infections. In our case there was an excellent response to the conventional triple therapy as used for the treatment of infections with *H. pylori*. This diagnosis is frequently missed because of its atypical clinical presentation although the anatomopathological findings are easy to recognize by the pathologist. It is merely interesting on a scientific basis since the treatment for an typical *H. Pylori* infection is the same.

References

1. MONTECUCCO C, RAPPUOLI R. Living dangerously : how *Helicobacter pylori* survives in the human stomach. *Nat. Rev. Mol. Cell. Biol.*, 2001, **2** : 457-466.
2. MENDES EN, QUEIROZ DM, ROCHA GA, MOURA SB, LEITE VH, FONSECA ME. Ultrastructure of a spiral microorganism from pig gastric mucosa ("Gastrospirillum suis"). *J. Med. Microbiol.*, 1990, **33** : 61-66.
3. QUEIROZ DM, ROCHA GA, MENDES EN, LAGE AP, CARVALHO AC, BARBOSA AJ. A spiral microorganism in the stomach of pigs. *Vet. Microbiol.*, 1990, **24** : 199204.
4. Haesebrouck F, Pasmans F, Flahou B, Chiers K, Baelle M, Meyns T. *et al.* Gastric Helicobacters in Domestic Animals and Nonhuman Primates and Their Significance for Human Health. *Clin. Microbiol. Rev.*, 2009, **22** : 202-223.
5. MÉNARD A, PÉRÉVÉDRENNE C, HAESEBROUCK F, FLAHOU B. Gastric and Enterohepatic Helicobacters other than *Helicobacter pylori*. *Helicobacter*; 2014, **19** (Suppl 1) : 59-67.
6. KUSTERS J, VAN VLIET A, KUIPERS E. Pathogenesis of *Helicobacter pylori* Infection. *Clin. Microbiol. Rev.*, 2006, **19** : 449-490.
7. OKIYAMA Y, MATSUZAWA K, HIDAKA E, SANO K, AKAMATSU T, OTA H. *Helicobacter heilmannii* infection: Clinical, endoscopic and histopathological features in Japanese patients. *Pathol. Int.*, 2005, **55** : 398-404.
8. JOO M, KWAK JE, CHANG SH, KIM H, CHI JG, KIM KA. *et al.* *Helicobacter heilmannii* associated Gastritis: Clinicopathological Findings and Comparison with *Helicobacter pylori* associated gastritis. *J. Korean Med. Sci.*, 2007, **22** : 63-69.
9. De Groote D, Van Doorn LJ, Van den Bulck K, Vandamme P, Vieth M, Stolte M. *et al.* Detection of Nonpylori *Helicobacter* Species in "Helicobacter heilmannii" infected Humans. *Helicobacter*; 2005, **10** : 398-406.
10. STOLTE M, KROHER G, MEINING A, MORGNER A, BAYERDÖRFFER E, BETHKE B. A Comparison of *Helicobacter pylori* and *H. heilmannii* Gastritis. A matched control study involving 404 patients. *Scand. J. Gastroenterol.*, 1997, **32** : 28-33.
11. YUAN Y, FORD AC, KHAN KJ, GISBERT JP, FORMAN D, LEONTIADIS GI. Optimum duration of regimens for *Helicobacter pylori* eradication. *Cochrane Database of Systematic Reviews*, 2013, **12** : CD008337.
12. Van den Bulck K 1 , Decostere A, Gruntar I, Baelle M, Krt B, Ducatelle R. *et al.* In Vitro Antimicrobial Susceptibility Testing of *Helicobacter felis*, *H. bizzozeronii*, and *H. salomonis*. *Antimicrob Agents Chemother*; 2005, **49** : 2997-3000.