

A rare case of *helicobacter pylori* mix infections and recurrence of duodenal ulcers

Abstract

Introduction: Since *Helicobacter pylori* (*H. pylori*) infection is a major cause of gastroduodenal ulcers, it is normal to expect successful eradication drastically reduces ulcer recurrence.

Case presentation: We present a case of a 45-year-old woman with no history duodenal ulcer in her family who was referred to the hospital with epigastric pain. A gastroduodenoscopy was then performed, and revealed two active duodenal ulcers, both measuring 10mm in size. She was prescribed with 14days *H. pylori* standard therapy, but no confirmation test concerning bacterial clearance was performed. Ten months later, she was admitted to the hospital again and complained about intense epigastric pain and vomiting. Gastroscopic findings showed a new 11mm duodenal ulcer. However, because of positive rapid urease test (RUT), further microbiological analysis was prescribed. Strikingly, *H. pylori* mix infections was observed. With prescription of second-line therapy against *H. pylori*, after 4weeks, positive ¹³C-urea breath test became negative and her duodenal ulcer was also completely cured.

Conclusion: Our cases strongly suggest that frequency of *H. pylori* mix infections is not only considerable but also it can drastically affect the final outcome of clinical manifestations such as duodenal ulcer. Conclusively, current report insists that gastroenterologists should pay more attention to the possibility of presence of *H. pylori* mix infections in the management of patients with duodenal ulcers. Additionally, after an initial antibacterial treatment, an obligatory follow up system is recommended.

Keywords: *helicobacter pylori*, duodenal ulcer, mixed infection

Volume 1 Issue 1 - 2014

Amin Talebi Bezmin Abadi, Ashraf Mohabbati Mobarez, Tarang Taghvaei

Department of Bacteriology, Tarbiat Modares University Tehran, Iran

Correspondence: Amin Talebi Bezmin Abadi, Department of Bacteriology, Tarbiat Modares University, Tehran, Iran 14115-111, Email mmmobarez@modares.ac.ir

Received: October 14, 2014 | **Published:** November 13, 2014

Abbreviations: *H. pylori*, *helicobacter pylori*; RUT, rapid urease test; PPI, proton pump inhibitor

Introduction

Helicobacter pylori (*H. pylori*) is a spiral Gram-negative bacterium that colonizes approximately one-half of the world's population. Since its groundbreaking discovery in 1982 by Barry Marshall, *H. pylori* has been the topic of extensive digestive research. The infection is involved in the development of various gastroduodenal diseases including duodenal ulcer and gastric cancer.¹ However, to everyone's surprise, *H. pylori* infection in human stomach evades strong immune responses, leading to ineffective bacterial clearance.² It has been firmly established that *H. pylori* colonization is associated with 90% of duodenal ulcers.³ In clinical setting, as a general rule, *H. pylori* testing is not recommended for asymptomatic individuals. However, there is no well-established guideline for symptomatic digestive patients infected with *H. pylori*. At the beginning, lack of this guideline was not thought to be a potential problem. Those patients with duodenal ulcers can usually be distinguished by severe clinical outcomes including bloating, lack of appetite, nausea and vomiting, particularly if left untreated.⁴ Along these lines, we report the case of a patient with duodenal ulcers in whom *H. pylori* had not been successfully eradicated. Undoubtedly, this report elucidates the rationale that *H. pylori* mixed infections should also be considered in the context of a patient's clinical history and also further examination after first-line therapy to improve management of patients with duodenal ulcers. The low frequency of reports on duodenal ulcers linked with *H. pylori* mix infections motivated the presentation of the current case.

Case report

A 45-year-old woman had been admitted to the hospital presented with vomiting and epigastric pain of seven months duration and without specific histories in her family. A gastroduodenoscopy was then performed, and revealed two active duodenal ulcers, both measuring 10mm in size. Furthermore, histopathological examination showed an acute inflammation and *H. pylori* infection. Subsequent bacterial culture and PCR assay confirmed identity of *H. pylori* infection.⁵ Thus, she was treated for fourteen days with *H. pylori* standard therapy based on proton pump inhibitor (PPI)-amoxicillin-clarithromycin. Because of the likely poor patient adherence of medication, no clear records were available about her first admission. Due to absence of the patient and intense emotional stress, clearance of *H. pylori* infection after first-line therapy was not confirmed by a negative ¹³C-urea breath test or even a negative stool antigen test. Strikingly, 10months later, she again referred to the hospital due to the intense epigastric pain. Endoscopic findings confirmed new 11mm duodenal ulcer. Because of positive rapid urease test (RUT) at endoscopic room, further microbiological analysis prescribed.⁶ Since possible risk of mix infection, bacterial culture was performed to investigate *H. pylori* mix infections. In brief, from original plate (Figure 1), five different colonies were picked and restreaked in new plates according to the standard protocols.^{7,6} PCR of virulence genes, (e.g. *cagA*, *iceA1*, *homb*, *baba2* and *cagE*) were carried out to detect and draw genetic variability panel of those *H. pylori* strains.⁸⁻¹⁰ Primer sequences, sizes, and conditions of PCR amplifications of the *glmM* gene for detection and confirmation of *H. pylori* and the other genes

(i.e., *homB*, *cagA*, *cagE*, *iceA1* and *babA2*), were carried out using the conditions described previously (Table 1).^{6,9,8} This time, after starting second-line therapy (levofloxacin-based therapy), within 4 weeks, positive ¹³C-urea breath test became negative and her duodenal ulcer was also completely cured.¹¹ The presence of *H. pylori* virulence genes was directly determined by specific sensitive PCR method, then

results were compared per single strain (Table 2). The distribution of various *H. pylori* genotypes as shown in Table 2 indicates presence of mix infections. In a follow up system for this interesting case of up to 12 months, no new abdominal pain, vomiting or any evidence to *H. pylori* infection were observed.

Table 1 Primer sequence and PCR conditions

Genes	PCR product	PCR conditions	Reference
<i>cagA</i>	298bp	95°C, 1min; 61°C, 1min; 72°C, 1min (33cycles)	7
<i>iceA₁</i>	247bp	95°C 1min; 55°C, 1s; 72°C, 50 sec (35cycles)	10
<i>babA₂</i>	271bp	95°C, 1min; 48°C, 1min; 72°C, 1min (32cycles)	10
<i>homB</i>	161bp	95°C, 1min; 56°C, 1min; 72°C, 1min (30cycles)	9
<i>cagE</i>	508bp	95°C, 1min; 52°C, 48s; 72°C, 55 s (30cycles)	9
<i>glmM</i>	294bp	94°C, 1min; 57°C, 1min; 72°C, 1min (30cycles)	7

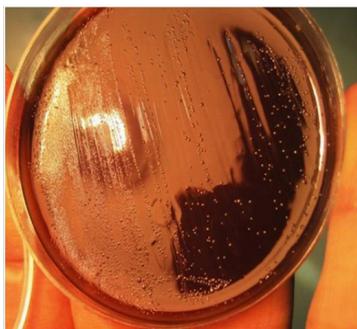


Figure 1 Original plate harboring at least 5 different *H. pylori* strains isolated from 45-years-old women.

Table 2 Distribution of various virulence genes among five different picked colonies from original *H. pylori* plate

<i>H. pylori</i> Strains	<i>cagA</i>	<i>iceA₁</i>	<i>homB</i>	<i>babA₂</i>	<i>cagE</i>
A1	+	-	+	-	+
A2	+	+	+	-	-
A3	-	+	+	-	+
A4	+	-	-	+	-
A5	-	-	-	+	+

Discussion

It should be noted that since differences exist in *H. pylori* DNA contents obtained from the same patient, the mixed infections might actually affect clinical outcome. However, an undeniable fact is that the majority of patients with duodenal ulcers are infected with *H. pylori*. Despite the long period of time that we have known about *H. pylori* we are not aware of main route of transmission. At least in developing countries, childhood is accepted as the most likely time of the first exposure with this persistent bacterium. Not enough evidence for zoonotic transmission of *H. pylori* infection is available yet.^{12,13} Collectively, human-human direct contact is considered the most possible route for *H. pylori* transmission. However, colonization of the human stomach by more than one strain at the same time is not an abnormal phenomenon in *H. pylori* microbiology. Concerning *H. pylori* treatment, around 25% of individuals are not cured completely;

in this case, second line therapy is mostly recommended.¹⁴ nowadays, a therapeutic dilemma exists for patients who failed in first line antibacterial therapy.¹⁵ In fact, recurrence of *H. pylori* after primary therapeutic is not rare in developing countries. Current knowledge is not quite conclusive that recurrence is caused by re-colonization of the same strain or recurrence of infection should be considered likely responsible by new *H. pylori* strain.¹⁵ Treatment of duodenal ulcers is strongly affected by successful clearance of *H. pylori* infection. The worst-case scenario would be that the *H. pylori* mix infections be incorporated. Altogether, the risk of carrying multiple resistant strains will be simultaneously increased,¹⁶ if primary *H. pylori* colonization is left uncured. We think if having mixed infection can influence the risk of DU recurrence; thereby it should be an alarming signal for clinicians and microbiologist to consider these types of strains as a risk factor to increase the clinical manifestations affected by *H. pylori*. In conclusion, recurrence of *H. pylori* re-infection should be taken into consideration. In other words, our findings support the notion that reliable approach for follow-up after *H. pylori* eradication should be used at least in regions such as developing countries, due to the relatively high rate of re-infection and mix infections. Because of easy and relatively free access of antibiotics in the developing countries, and also an increasing trend of antimicrobial resistance; an accurate follow-up system to confirm bacterial clearance (e.g. UBT or serologic tests) seems necessary in diagnostic procedures.

Acknowledgements

None.

Conflict of interest

The author declares no conflict of interest.

References

- Hatakeyama M, Brzozowski T. Pathogenesis of *Helicobacter pylori* infection. *Helicobacter*. 2006;11(Suppl 1):14–20.
- Blaser MJ, Atherton JC. *Helicobacter pylori* persistence: biology and disease. *J Clin Invest*. 2004;113(3):321–333.
- Graham DY, Lew GM, Klein PD, et al. Effect of Treatment of *Helicobacter pylori* infection on the long-term recurrence of gastric or duodenal ulcer a randomized, controlled study. *Ann Intern Med*. 1992;116(9):705–708.

4. Ernst PB, Gold BD. The disease spectrum of *Helicobacter pylori*: the immunopathogenesis of gastroduodenal ulcer and gastric cancer. *Annu Rev Microbiol.* 2000;54:615–640.
5. Espinoza MG, Vazquez RG, Mendez IM, et al. Detection of the *glmM* gene in *Helicobacter pylori* isolates with a novel primer by PCR. *J Clin Microbiol.* 2011;49(4):1650–1652.
6. Talebi Bezmin Abadi A, Mobarez AM, et al. Antibiotic resistance of *Helicobacter pylori* in Mazandaran, North of Iran. *Helicobacter.* 2010;15(6):505–509.
7. Megraud F, Lehours P. *Helicobacter pylori* detection and antimicrobial susceptibility testing. *Clin Microbiol Rev.* 2007;20(2):280–322.
8. Abadi ATB, Taghvaei, T, Mobarez AM, et al. High correlation of *babA2*–positive strains of *Helicobacter pylori* with the presence of gastric cancer. *Intern Emerg Med.* 2013;8(6):497–501.
9. Abadi ATB, Rafiei A, Ajami A, et al. *Helicobacter pylori homB*, but not *cagA*, is associated with gastric cancer in Iran. *J Clin Microbiol.* 2011;49(9):3191–3197.
10. Abadi AT, Taghvaei T, Wolfram L, et al. Infection with *Helicobacter pylori* strains lacking *dupA* is associated with an increased risk of gastric ulcer and gastric cancer development. *J Med Microbiol.* 2012;61(Pt 1):23–30.
11. Talebi Bezmin Abadi A. Therapy of *Helicobacter pylori*: present medley and future prospective. *Biomed Res Int.* 2014;2014:124607.
12. Brown LM. *Helicobacter pylori*: epidemiology and routes of transmission. *Epidemiol Rev.* 2000;22(2):283–297.
13. Rowland M. Transmission of *Helicobacter pylori*: is it all child's play? *Lancet.* 2000;355(9201):332–333.
14. O'connor A, Gisbert JP, McNamara D, et al. Treatment of *Helicobacter pylori* infection. *Helicobacter.* 2010;15:46–52.
15. Gispert JP. “Rescue” regimens after *Helicobacter pylori* treatment failure. *World J Gastroenterol.* 2008;14(35):5385–5402.
16. Saracino IM, Zullo A, Holton J, et al. High prevalence of primary antibiotic resistance in *Helicobacter pylori* isolates in Italy. *J Gastrointestin Liver Dis.* 2012;21(4):363–365.