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Reasons for Two Consecutive *Helicobacter pylori* Treatment Failures

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Abstract

The present case focuses on a symptomatic patient with two consecutive *Helicobacter pylori* treatment failures. *H. pylori* strain isolated from the patient was susceptible to amoxicillin, metronidazole, tetracycline and rifampin, but was resistant to clarithromycin and ciprofloxacin/levofloxacin. The first treatment failure could be the consequence of a suboptimal treatment regimen (esomeprazole, amoxicillin and tetracycline) despite *in vitro* susceptibility of the isolate to both antibiotics. The second eradication attempt (esomeprazole, amoxicillin, levofloxacin and colloidal bismuth subcitrate) was unsuccessful due to *in vitro* resistance of the isolate to quinolones. In conclusion, not all antibiotics can be successfully co-administered simultaneously for *H. pylori* eradication despite the *in vitro* susceptibility. The patients should inform clinicians about their previous clinical and paraclinical evaluations, including the bacterial susceptibility testing results to receive the most appropriate treatment regimen.

Key words: *Helicobacter pylori,* eradication, failure, suboptimal, regimen, resistance

Резюме

Настоящият случай фокусира симптоматичен пациент с две последователни неуспешни терапии за *Helicobacter pylori*. Щамът *H. pylori* изолиран от пациента беше чувствителен към amoxicillin, metronidazole, tetracycline и rifampin, но резистентен към clarithromycin и ciprofloxacin/levofloxacin. Първият неуспех на терапията може да бъде следствие от субоптималния режим (esomeprazole, amoxicillin и tetracycline) въпреки in vitro чувствителността на изолата на двата антибиотика. Вторият опит за ерадикация (esomeprazole, amoxicillin, levofloxacin и колоидален бисмут субцитрат) беше неуспешен поради in vitro резистентността на щама към хинолоните. В заключение, не всички антибиотици могат да бъдат успешно комбинирани за ерадикация на *H. pylori* въпреки in vitro чувствителността. Пациентите трябва да информират клиницистите за техните предишни клинични и параклинични резултати, включително тези от тестовете за бактериалната чувствителност, за да получат най-подходящия режим на лечение.

Introduction

Helicobacter pylori eradication is difficult to achieve and the treatment success of first-line triple therapy has decreased over time (Smith *et al.,* 2014). Key reasons for treatment failure are poor patient compliance owing to complicated treatment regimens and *H. pylori* antibiotic resistance (Smith *et al.,* 2014), and an additional factor can be the use of inappropriate antibiotic regimens.

Case report

On 13 August 2014, a 46-year-old man with complaints of abdominal pain was admitted to the Gastroenterology Unit of Department of Surgery, Medical University-Sofia for a gastroscopic evaluation. The gastroscopy showed the presence of reflux esophagitis, hiatal hernia and erosive gastroduodenitis. Gastric biopsy specimens were sent to the microbiology laboratory for *H. pylori* diagnostics.

H. pylori strain was isolated and identified as reported previously (Boyanova *et al.,* 2008) and the antibiotic susceptibility of the strain was tested by a breakpoint susceptibility testing method (Boyanova *et al.,* 2008) using Mueller-Hinton agar plates (Oxoid, Basingstoke, UK) with 5% sheep blood and one of the following antibiotic concentrations: amoxicillin 0.12, 0.25. 0.5,1 or 2

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mg/L, metronidazole 4, 8 or 16 mg/L, clarithromycin 0.25, 0.5, 1, 2 or 4 mg/L, tetracycline 1 or 2 mg/L, and ciprofloxacin 1 or 10 mg/L. Susceptibility testing for ciprofloxacin was performed as a marker for the strain susceptibility to levofloxacin (Boyanova *et al.,* 2008). Rifampin susceptibility was tested by rifampin 5-μg/disk (Oxoid, Basingstoke, UK). The antibiotics were obtained from Sigma-Aldrich, St. Louis, MO (amoxicillin, metronidazole, and tetracycline); Abbott Laboratories, Illinois (clarithromycin); and Actavis, Sofia, Bulgaria (ciprofloxacin).

The plates were incubated microaerophilically (CampyGen, Oxoid, UK) at 37° C for 2-3 days. Control strains were used for the susceptibility testing methods as previously described (Boyanova *et al.,* 2008). Resistance breakpoints were 8 mg/L metronidazole, 0.5 mg/L clarithromycin, 0.12 mg/L amoxicillin, 1 mg/L tetracycline and 1 mg/L levofloxacin (EUCAST, 2015). Strains with inhibition zone diameters of ≥21 mm were classified as rifampicin/rifabutin susceptible (Glocker *et al.,* 2007).

The isolated *H. pylori* strain was susceptible to amoxicillin, metronidazole, tetracycline and rifampin, but was resistant to clarithromycin and ciprofloxacin/levofloxacin.

Treatment was administered for 10 days with esomeprazole 20 mg bid, tetracycline 500 mg qid and amoxicillin 1000 mg bid.

On 18 December 2014, *H. pylori* eradication of the patient was assessed by a ^{13}C urea breath test (*Helicobacter* Test INFAI via mass spectrometric analysis) and the result was positive (difference 8.737) for *H. pylori* infection.

On 10 March 2015, due to absence of his treating gastroenterologist, the patient visited another physician and was administered esomeprazole 40 mg bid, amoxicillin 1000 mg bid, levofloxacin 250 mg bid and colloidal bismuth subcitrate 120 mg tid for 10 days.

On 29 April 2015, the patient underwent a stool antigen test for *H. pylori* (Premier Platinum HpSA PLUS, Meridian Bioscience, Cincinnati, OH, USA) and the result was positive (0.200 U/mL).

Discussion

In the present study, the first treatment regimen with esomeprazole, amoxicillin and tetracycline was unsuccessful. Similarly, Perri *et al.,* (2002) reported a low (35%) eradication rate by amoxicillin 1000 mg bid plus tetracycline 500 mg qid and lansoprazole 30 mg bid for 14 days.

The second treatment regimen of the patient (esomeprazole, amoxicillin, levofloxacin and colloidal bismuth subcitrate) was also unsuccessful because the strain was *in vitro* resistant to quinolones, however, the patient did not report the susceptibility testing results to the physician. *H. pylori* fluoroquinolone resistance has been reported to decrease the success of the fluoroquinolone-based eradication of regimens by 41.7-66.7% in comparison with that of susceptible strains (Perna *et al.,* 2007; Nishizawa *et al.,* 2009).

An appropriate regimen for the patient can be the bismuth-containing quadruple therapy used with eradication success of 86% and 81.1% according to the intention-to-treat and per-protocol analyses, respectively (Gokcan *et al.,* 2015). The regimen includes bismuth salts, tetracycline, metronidazole and a proton pump inhibitor. Another suitable eradication regimen can be the rifabutin-based triple therapy, including a proton pump inhibitor, rifabutin and amoxicillin (Papastergiou *et al.,* 2014). In Korean patients (53 subjects), the eradication success of the regimen including lansoprazole (60 mg bid), amoxicillin (1000 mg tid) and rifabutin (150 mg bid) for 7 days was 96.3% according to the intention to treat analysis and 100% according to the per-protocol analysis (Lim *et al.,* 2014).

Conclusion

Two main conclusions can be drawn from the results of this case. Firstly, not all antibiotics to which the isolate is susceptible can be successfully co-administered simultaneously for *H. pylori* eradication. Secondly, the patients should inform the clinicians about their previous clinical and paraclinical evaluations, including the susceptibility testing results in order to obtain the optimal *H. pylori* eradication regimen.

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