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**Title:** How should *Helicobacter pylori* eradication be done in the extensive proton pump inhibitor allergy?

**Running Head:** *Helicobacter pylori* eradication with ranitidine

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## Abstract

In this presentation, we would like to discuss the path followed with pediatric allergy in the selection of drug in a case of extensive allergy to (proton pump inhibitor) PPI. A 15-year-old male patient presented with complaints of dyspepsia and epigastric pain for 4-5 years. It was learned that there were fixed drug eruption described with omeprazole and widespread rashes after lansoprazole. Famotidine was started, but the patient was unable to use the drug because of rash and itching in his body 1 hour after drug intake. On physical examination, fixed drug eruption was observed in the whole body and his gluteal region. Gastroduodenoscopy was performed. Macroscopically, the corpus and antrum were hyperemic and antrum nodular, bulbus normal, and duodenum nodular. Multiple biopsies were taken. He was consulted to pediatric allergy department for possible cross-reactions between PPIs.

The patient underwent skin prick and intradermal tests with famotidine and ranitidine. The patient also underwent skin patch tests with all available PPIs.

The pathologic result of biopsies was HP (+++) with Giemsa staining. Because of the cross sensitivity between PPIs and the positivity of the allergy tests, triple HP treatment was not considered. This is an interesting case because of the extensive allergies to all existing PPIs and no similar cases have been found in the literature. After evaluation of allergic tests, quadruple treatment without PPI (bismuth, ranitidine, metronidazole and tetracycline) was given to the patient. HP treatment was assessed after 4 weeks, two-step monoclonal stool HP antigen test was found negative.

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**Keywords:** Eradication, extensive proton pump allergy, helicobacter pylori

## **Introduction**

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Helicobacter pylori (HP) eradication usually prevents ulcer recurrence and ulcer complications after appropriate proton pump inhibitor (PPI) treatment. HP eradication is also important in the treatment of stomach disorders such as MALT lymphoma, but HP treatment is controversial in gastric cancer prevention (1). Patients with penicillin allergy are given amoxicillin-free treatments. In this presentation, we would like to discuss the path followed with pediatric allergy in the selection of drug in a case of extensive allergy to PPI.

### Case report

A 15-year-old male patient presented with complaints of dyspepsia and epigastric pain for 4-5 years. It was learned that there were fixed drug eruption described with omeprazole in 3 years ago and widespread rashes in the body after lansoprazole in the previous year. Famotidine treatment was started, but the patient was unable to use the drug because of rash and itching in his body 1 hour after drug intake. On physical examination, fixed drug eruption was observed in the his gluteal region (Figure 1a, 1b, 1c, 1d). One week later, gastroduodenoscopy was performed. Macroscopically, the corpus and antrum were hyperemic and antrum nodular, bulbus normal, and duodenum nodular (Figure 2a, 2b, 2c). Multiple biopsies were taken. He was consulted to pediatric allergy department for possible cross-reactions between PPIs.

The patient underwent skin prick tests with famotidine and ranitidine (10 mg/ml; 40 mg/ml, respectively) and intradermal tests with famotidine and ranitidine (1/100; 1/10 dilution). The patient also underwent skin patch tests with all available PPIs (10% and 30% concentration). Skin patch test was found (++) positive with 30% concentration with

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lansoprazole and esomeprazole; omeprazole was found to be negative (Figure 3). Omeprazole was not considered to be given to the patient due to fixed drug eruption described with omeprazole 3 years ago. Prick and intradermal tests was found negative with ranitidine. Oral provocation test with ranitidine was also negative. Prick and intradermal tests was negative with famotidine, but because of the recent reaction, famotidine was not given again.

The pathologic results of endoscopic biopsy was HP (+++) with Giemsa staining and there was no intestinal metaplasia. Because of the cross sensitivity between PPIs and the positivity of the allergy tests, triple HP treatment was not considered. This is an interesting case because of the extensive allergies to all existing PPIs and no similar cases have been found in the literature. Quadruple treatment without PPI (bismuth, ranitidine, metronidazole and tetracycline) was given to the patient. He had no complaint after 2 weeks. Following the completion of the treatment, HP treatment was assessed after 4 weeks, two-step monoclonal stool HP antigen test was found negative and the patient was asymptomatic.

Written informed consent was obtained from the patient and parents for the publication and presentation of case and images.

## **Discussion**

Despite the decreasing prevalence of HP infection, it still infects 30-50% of the general population in western countries (2). *Helicobacter pylori* causes active chronic gastritis in all infected persons and may cause complications such as gastric malignancies, peptic ulcers

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and dyspepsia. *Helicobacter pylori* eradication usually prevents ulcer recurrence and complications (2).

The most frequently used initial treatment for HP is triple treatment including PPI, amoxicillin, and clarithromycin. If the patient comes from a place with increased resistance to clarithromycin, metronidazole is used in place of clarithromycin (1).

All international guidelines agree that 14-day triple therapy with clarithromycin can be used as a first-line treatment for HP eradication (3).

If the strain is susceptible to clarithromycin and metronidazole in the penicillin allergy, triple treatment with standard metronidazole should be used instead of amoxicillin; if the strain is resistant to clarithromycin and the age of the patient is over 8, bismuth treatment with tetracycline should be given instead of amoxicillin (4).

HP eradication treatment is difficult because it may develop resistance. Therefore, two or three antibiotics are usually given together with PPI and / or bismuth-containing compounds for eradication (3).

The bismuth-containing quadruple-treatment includes bismuth salt, tetracycline and metronidazole additionally PPI (5). This treatment regimen has been proposed for only the second-line treatment in the past, since it is more complex than the standard treatment (6).

However, bismuth-containing quadruple therapy is a powerful weapon against antibiotic resistance as neither clarithromycin nor levofloxacin is involved. For this reason, bismuth-containing quadruple treatment has been returned in the last decade and is now also recommended as first-line treatment (7).

International guidelines recommend using 2 standard doses of PPI to increase the effectiveness of antimicrobial drugs (3). This is because high intragastric pH reduces both H.

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pylori bacterial load and minimal inhibitor concentration of antibiotics (8).

With the increasing use of PPIs, significant treatment difficulties, side effects and complications have occurred (6).

The patient was interesting because of extensive allergies to all available PPIs and we did not find a similar case in the literature. After evaluating the patient in terms of allergy test, quadruple treatment without PPI (bismuth, ranitidine, metronidazole and tetracycline) was given to the patient to increase the effectiveness of the treatment. Instead of PPIs, we used ranitidine according to the result of allergic tests. He had no complaint after 2 weeks. HP antigen in stool was negative and he was asymptomatic after one month.

## **Conclusion**

As a result, cross-reactivity between PPIs should be considered before HP treatment in PPIs allergy. The choice of treatment should be planned according to the results of allergic evaluation.

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## Figure legends

Figure 1a,b,c : fixed drug eruption described with famotidine

Figure 1d: healing period of fixed drug eruption and skin peeling

Figure 2a: hyperemic and nodular antrum

Figure 2b: hyperemic and nodular antrum

Figure 2c: nodular appearance of duodenum

Figure 3: skin patch tests with lansoprazole, esomeprazole and omeprazole (10% and 30% concentration), the left one 30% concentration, the right one 10% concentration.

L: lansoprazole, E: esomeprazole, O:omeprazole, C: control with vaseline

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