

# Increases in Nonspecific Immunoglobulin E and Eosinophils after *H. pylori* Eradication

Yoshihiro Matsukawa<sup>a</sup> Yasuhiro Gon<sup>b</sup> Akihiro Hemmi<sup>c</sup>  
Jin Takeuchi<sup>a</sup> Shigemasa Sawada<sup>a</sup> Izumi Hayashi<sup>d</sup>

<sup>a</sup>Division of Hematology and Rheumatology, Department of Medicine, <sup>b</sup>Division of Molecular Cell Immunology and Allergology, Department of Advanced Medical Science, and <sup>c</sup>Department of Pathology, Nihon University School of Medicine, Tokyo; <sup>d</sup>Kanifukuoka-Kyodo Clinic, Fujimino, Japan

## Key Words

Nonspecific immunoglobulin E · Eosinophils · *H. pylori* eradication

## Abstract

*Helicobacter pylori* infection has been reported to be inversely associated with allergic disorders. We by chance experienced a patient with atrophic gastritis who presented marked elevations of both nonspecific serum immunoglobulin E and eosinophil counts after *H. pylori* eradication. A 49-year-old Japanese man received eradication of *H. pylori* using lansoprazole 60 mg/day, amoxicillin 1,500 mg/day, and clarithromycin 400 mg/day for 7 days. Serum immunoglobulin E increased to more than four times its pretreatment level, 306 → 485 → 1,325 U/ml, and peripheral eosinophil counts increased to more than three times, 99 → 139 → 298 per  $\mu$ l. Deducing from the current case, *H. pylori* eradication might develop allergic disorders in some patients.

## Introduction

Recently, *Helicobacter pylori* (*H. pylori*) infection has been increasingly reported to be inversely associated with allergic diseases [1–3], although some study groups proposed discrepancies in the data, i.e. improvement or no improvement in allergic symptoms after the eradication [4–6]. We by chance checked nonspecific serum immunoglobulin E (IgE) and found a marked rise in its titers following *H. pylori* eradication therapy.

## Case Report

A 49-year-old Japanese man, ex-smoker without allergic disorders, visited Kamifukuoka-Kyodo Clinic checking for low serum pepsinogen (PG) levels: PG I 40.8 ng/ml, PG II 15.7 ng/ml, and PG I:PG II ratio 2.60, suggesting possible gastric cancer. Gastrofiberscopic examination did not reveal gastric cancer, but showed atrophic gastritis with *H. pylori* infection, i.e. positive results for rapid urease test and pathologic findings. The patient wanted to eradicate *H. pylori*, and a triple drug regimen using lansoprazole 60 mg/day, amoxicillin 1,500 mg/day, and clarithromycin 400 mg/day for 7 days was initiated in February 2008. He additionally received lansoprazole 30 mg/day for 7 more weeks. Following informed consent to check laboratory data on anti-*H. pylori* antibody titers and immunohematologic parameters, complete blood counts, leukocyte differentials, and serum levels of immunoglobulin (IgG, IgA, IgM, and IgE) were serially measured. Eight weeks later, a second endoscopic examination confirmed successful eradication: negative results for both rapid urease test and pathologic findings. At that time, the titer of anti-*H. pylori* IgG antibody, neutrophil counts, and monocyte counts had decreased. On the contrary, peripheral counts of lymphocytes, eosinophils, basophils, and platelets had increased (table 1). In addition, serum levels of IgG, IgA, IgM, and IgE had all risen. 10 more weeks later, the level of serum IgE increased to four times its pretreatment level: 306 → 485 → 1,325 U/ml (normal <170). Along with these increases, the number of peripheral eosinophils also increased to triple: 99 → 139 → 298 per  $\mu$ l. In addition, we pathologically evaluated IgE-containing cells and mast cells in the gastric mucosa (fig. 1, fig. 2). The density of mast cells apparently increased in the antrum, although that of IgE-containing cells did not show any difference on the posttreatment specimen. The patient neither began to keep animals nor did he receive any additional medications, and was free from any signs of allergic disorders by December 2008.

## Discussion

Infiltration of both neutrophils and lymphocytes into the gastric mucosa is a well-known phenomenon among *H. pylori*-infected patients. In addition, monocytes, eosinophils and basophils also have been reported to infiltrate into the gastric mucosa in *H. pylori*-infected persons [7–9]. These observations suggest that *H. pylori* infection can upregulate the peripheral numbers of such leukocytes in infected patients. We therefore presume that eradication of *H. pylori* decreases the numbers of these leukocytes and of immunoglobulins in the peripheral blood. Unexpectedly, only neutrophils and monocytes decreased with a successful eradication in the patient. Serum IgE and eosinophils were continuously increased afterwards. The precise mechanism of this phenomenon is unclear, but the following is able to explain the phenomenon: (1) skewed differentiation of helper T cell seen in *H. pylori*-infected patients, (2) hygiene hypothesis, and (3) the influence of lansoprazole on serum immunoglobulins.

*H. pylori* infection is now accepted to skew T helper differentiation toward type 1 (Th1) property (production of interleukin-2, interferon- $\gamma$ , and tumor necrosis factor- $\alpha$ ) that counteracts the Th2-dependent process [10, 11]. Actually some cell contents of *H. pylori* have been reported to downregulate Th2 inflammation in experimental models [12]. As a result of successful eradication, the liberation of Th1 property could enhance humoral immunity to upregulate immunoglobulin production, and this regain may finally exert upregulation of serum IgE and eosinophilic inflammation induced by the Th2-dependent process.

In recent decades, the decreased prevalence in infectious diseases had led to a rapid increase in the prevalence of allergic diseases especially in Western societies, and such observation has been explained with the hygiene hypothesis [13]. Exposure to some pathogens, including bacteria and viruses, is proven to induce Th1 skew that could be preventive for the induction of allergic diseases through counteraction against Th2 cells [14, 15].

We stained IgE-containing cells and mast cells in the pretreatment and posttreatment gastric mucosa. As a result, an increase in mast cell density was observed in the posttreatment specimen (fig. 2a, b). Mast cells have been reported to involve gastric mucosal damage in patients with gastritis, especially those infected with *H. pylori* [16]. We thus presumed the decreased density of mast cells in the posttreatment specimen, we however could not confirm such decrease microscopically. The specimen showed the increased density of mast cells after the eradication therapy. Since mast cells involve allergic response in humans, this observation may represent *H. pylori* eradication-induced allergy.

Concerning serum immunoglobulins, we recently reported increases in serum IgG and IgM in *H. pylori*-infected patients treated with lansoprazole, suggesting the altering ability on Th1 shift [17]. We however confirmed continuous increases in lymphocytes, eosinophils, basophils, IgG and IgE in the peripheral blood at follow-up. Since the patient was free from lansoprazole on follow-up, the continuous increases in both IgE and eosinophil should be an aftereffect induced by *H. pylori* eradication.

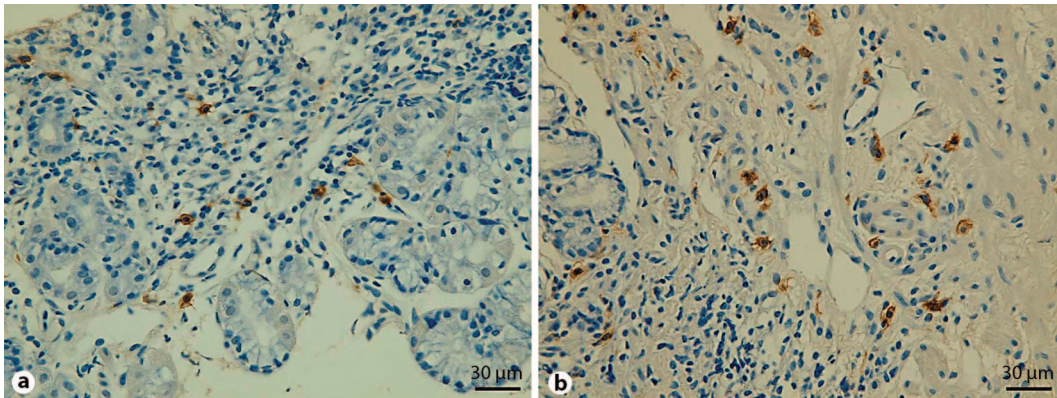
This case presentation suggests that some patients are able to develop allergic disorders through *H. pylori* eradication. Since a sole case presentation cannot be applied for an exact explanation for the phenomenon, further evaluations using sufficient numbers of patients should be performed.

**Table 1.** Changes in immunohematologic parameters after eradication

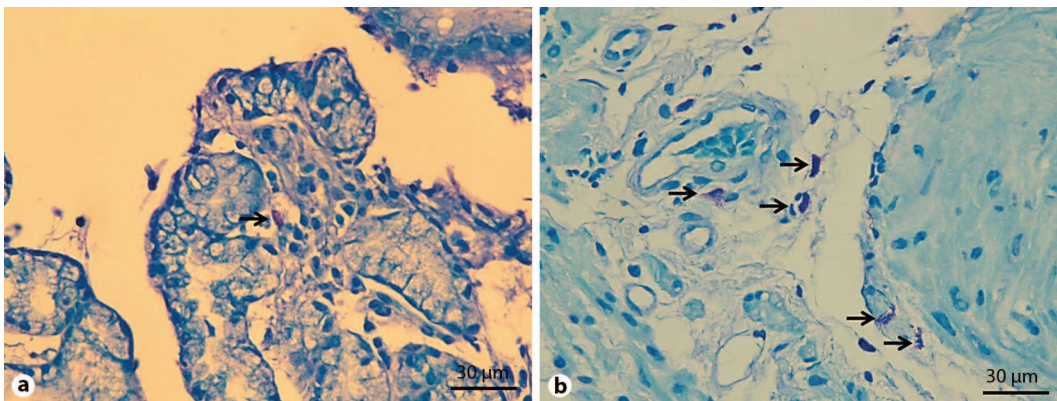
	Pre	Post	Follow-up
WBC, / $\mu$ l	4,310	3,880	4,330
Neutrophils, / $\mu$ l	2,853	2,409	2,502
Lymphocytes, / $\mu$ l	1,091	1,122	1,209
Monocytes, / $\mu$ l	228	159	251
Eosinophils, / $\mu$ l	99	139	298
Basophils, / $\mu$ l	39	51	70
Platelets, $\times 10^4$ / $\mu$ l	24.3	24.6	23.6
$\alpha$ - <i>H. pylori</i> *, U/ml	12.8	11.8	7.4
IgG, mg/dl	1,100	1,196	1,217
IgA, mg/dl	278	282	280
IgM, mg/dl	103	108	105
IgE**, IU/ml	306	485	1,325

\* Less than 10.0 are considered to be negative. \*\* Normal less than 170 IU/ml.

**Fig. 1.** **a** IgE-containing cells in the antrum of the pretreatment specimen. **b** IgE-containing cells in the antrum of the posttreatment specimen.



**Fig. 2.** **a** Mast cells in the antrum of the pretreatment specimen (toluidine-blue staining). **b** Mast cells in the antrum of the posttreatment specimen (toluidine-blue staining). Arrows indicate stained cells.



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