

Correspondence

Reply

To the Editor:

We thank Dr Kawai for his comments¹ on our study² on hypersensitivity to *Helicobacter pylori* induced during eradication therapy that results in skin manifestations. Dr Kawai raised a question about the results of lymphocyte transformation tests (LTTs) for patients with skin eruptions after *H pylori* eradication therapy. He showed a high frequency of positive LTT results in patients with skin eruptions and suggested that this difference is caused by the timing of the LTTs. At his institution, the LTTs were performed once within 3 days after onset, whereas at our institution, the drug LTTs were performed at least 3 times, with the first time being at least 1 week after clinical recovery. As Dr Kawai suggests,¹ the LTTs or CD154 expression assays in our patients might also have had a high frequency of positive results if these tests had been performed in the acute phase. LTT results are known to differ depending on the timing of the test. Furthermore, nonspecific positive results are occasionally detected, especially in the acute phase.³ Thus LTTs should be performed repeatedly at various timings.³ In addition, amoxicillin and certain other drugs produce positive LTT results, even in nonexposed subjects, suggesting these drugs can stimulate lymphocytes directly.³ These facts indicate that LTT results for amoxicillin in the acute phase might not reveal “true” sensitization.

Dr Kawai notes that the mechanism of skin eruption occurrence after *H pylori* eradication therapy is similar to that of skin eruption occurrence caused by amoxicillin administration in patients with infectious mononucleosis (ie, transient reversible hypersensitivity to the drug). However, unlike skin eruptions after *H pylori* eradication therapy, skin eruptions caused by amoxicillin administration in patients with infectious mononucleosis appear during administration of that drug. If degraded *H pylori* were inducing

transient hypersensitivity to the drug, it would be unlikely for the skin eruptions to appear after cessation of that medication.

Our report revealed that *H pylori* components degraded by using eradication therapy induce an anti-*H pylori* immune reaction. In skin eruptions after *H pylori* eradication therapy, it is indistinguishable whether skin eruptions are caused by a pathogen or drug administration. It is difficult to identify the cause of skin eruptions with use of only drug LTTs. As our report indicated, the CD154 expression assay was useful for identifying pathogen-specific hypersensitivity. A CD154 assay to identify drug-specific hypersensitivity also was performed, and it successfully detected the cause of drug hypersensitivity.⁴ We are performing further analyses of the clinical usefulness of the CD154 assay. We expect that the combined use of LTTs and CD154 assays will enable us to differentiate between drug hypersensitivity and pathogen hypersensitivity with high accuracy.

Akito Hasegawa, MD
Riichiro Abe, MD, PhD

From the Division of Dermatology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan. E-mail: aberi@med.niigata-u.ac.jp.

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Kawai K. Amoxicillin sensitization rate in patients with eruptions after *Helicobacter pylori* eradication therapy. *J Allergy Clin Immunol* 2019 ■■■:■■■.
2. Ito T, Shiromizu T, Ohnishi S, Suzuki S, Mabe K, Hasegawa A, et al. Potential role of extracellular vesicle-mediated antigen presentation in *Helicobacter pylori* hypersensitivity during eradication therapy. *J Allergy Clin Immunol* 2018;142: 672-6.e12.
3. Pichler WJ, Tilch J. The lymphocyte transformation test in the diagnosis of drug hypersensitivity. *Allergy* 2004;59:809-20.
4. Higuchi T, Satoh T, Yokozeki H. Using CD40 ligand expression to detect antigen-specific T cells in patients with drug eruptions. *Acta Derm Venereol* 2014;94:86-7.

<https://doi.org/10.1016/j.jaci.2019.02.012>