

Correspondence

Amoxicillin sensitization rate in patients with eruptions after *Helicobacter pylori* eradication therapy

To the Editor:

I read with interest the recent article by Ito et al.¹ The authors reported that only 2 of 15 patients with skin eruptions after eradication therapy for *Helicobacter pylori* using amoxicillin, clarithromycin, and a proton pump inhibitor had positive results on repeated drug lymphocyte transformation tests (LTTs), and in another patient CD4⁺ T cells expressed CD154 in response to the drugs. They elegantly demonstrated that a significant proportion of the patients with negative drug-specific responses (9/12) exhibited *H. pylori*-specific immune responses.¹

Table I summarizes 11 patients with skin eruptions after *H. pylori* eradication therapy in our hospital during the last 3 years. Similar with the previous studies,^{1,2} in most patients generalized maculopapular rash developed after completing the 7-day eradication therapy (Table I). In our patients, however, all but 1 exhibited positive LTT responses to amoxicillin (Table I).

The difference in the rate of positive drug LTT responses might be explained by the difference in timing of the onset of skin eruptions. Ito et al.¹ showed that skin eruptions occurred earlier (≤ 9 days from start of treatment) in patients with positive drug-specific responses than in patients with positive *H. pylori*-specific responses. The proportion of the patients in whom skin eruptions occurred 9 days or less from the start of treatment was greater in our patients compared with patients in the study by Ito et al.¹ However, 3 patients in whom skin eruptions occurred 10 or more days from the start of treatment also exhibited positive LTT responses to amoxicillin (Table I).

An alternative reason for the higher rate of positive drug LTT responses in our patients might be the difference in timing of the LTTs. The results of drug LTTs performed during the recovery phase or after resolution of skin eruptions associated with *H. pylori* eradication therapy were frequently negative in the

previous studies.^{2,3} Although exact intervals from the onset of skin eruption to LTTs were not mentioned in the article by Ito et al.,¹ we performed drug LTTs within 3 days from onset in most patients (Table I).

Our results suggest that amoxicillin sensitization was detectable only transiently during the acute phase in some patients with skin eruptions after *H. pylori* eradication therapy. As with amoxicillin-induced exanthema in patients with infectious mononucleosis,⁴ positive LTT responses to amoxicillin during the acute phase of skin eruptions after *H. pylori* eradication therapy might be caused by not only persistent true sensitization but also transient reversible hypersensitivity to the drug. Degraded *H. pylori*, *H. pylori*-specific T cells, and/or recirculation of mucosal T cells into the blood could be responsible for the transient breakdown of immune tolerance to or ignorance of the drug. Although we have not performed repeated drug LTTs or other *in vitro* or *in vivo* tests for amoxicillin sensitization after resolution of skin eruptions in our patients, it will be important to determine whether positive drug LTT responses during the acute phase are true drug sensitization in patients with skin eruptions after *H. pylori* eradication therapy to prevent unnecessary drug avoidance.

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TABLE I. Characteristics of patients with skin eruptions after *H. pylori* eradication therapy

	Age (y)	Sex	Interval from start of treatment to onset (d)	Medications	Result of drug LTTs	Interval from start of treatment to LTTs (d)
Patient 1	47	F	11	ACV	Amoxicillin (670%)	27
Patient 2	65	F	10	ACV	Amoxicillin (270%)	10
Patient 3	66	F	10	ACV	Amoxicillin (310%)	15
Patient 4	73	F	9	ACR	Amoxicillin (380%)	10
Patient 5	66	F	9	ACR	Amoxicillin (400%)	10
Patient 6	69	M	9	ACV	Amoxicillin (480%)	10
Patient 7	58	F	9	ACV	All negative	9
Patient 8	61	F	8	ACV	Amoxicillin (420%)	9
Patient 9	71	F	8	ACV	Amoxicillin (340%)	10
Patient 10	61	F	8	ACL	Amoxicillin (260%)	9
Patient 11	59	F	7	ACL	Amoxicillin (590%)	10

ACL, Amoxicillin, clarithromycin, and lansoprazole; ACR, amoxicillin, clarithromycin, and rabeprazole; ACV, amoxicillin, clarithromycin, and vonoprazan; F, female; M, male.