

The Journal of Dermatology / Early View

LETTER TO THE EDITOR | [Full Access](#)

## Minocycline-induced anaphylaxis mediated by antigen-specific immunoglobulin E

Rie Nakamura , Akio Tanaka , Hitomi Kinoshita, Kaori Ishii, Michihiro Hide

First published: 09 November 2021

<https://doi-org.bibliosan.clas.cineca.it/10.1111/1346-8138.16228>

Dear Editor,

Drug-induced anaphylaxis can be caused by mechanisms that do not essentially involve immunoglobulin (Ig)E. Minocycline has been reported to occasionally cause anaphylaxis. However, whether this reaction is mediated by IgE remains unclear.<sup>1,2</sup> Herein, we report a case of minocycline-induced anaphylaxis with antigen-specific IgE.

A 67-year-old woman was treated for common cold with minocycline, an antitussive medication containing codeine phosphate hydrate, and an anti-flatulent. Thirty minutes after receiving the medications orally, she developed generalized erythema and dyspnea. These symptoms rapidly improved with the administration of i.m. epinephrine and supplemental fluids.

She had taken minocycline twice in the past and had experienced dizziness immediately after the second dose. However, she did not develop any adverse effects to the antitussive medication on the past several occasions. Skin prick tests showed a positive response for minocycline (0.5 mg/mL) and codeine phosphate hydrate (10 mg/mL), with wheal sizes of 3.5 mm and 3.0 mm, respectively. Based on previous literature, a wheal diameter of 3 mm or more was considered positive.<sup>3</sup> Skin prick tests for all the other drugs consumed before the appearance of anaphylactic symptoms were negative. We then performed a histamine release test (HRT) by a previously described method using basophils from the patient.<sup>4</sup> No histamine release was observed in response to these drugs in the absence of autologous serum. However, minocycline caused a concentration-dependent release of histamine in the presence of the patient's serum (Figure 1a). In contrast, histamine was only marginally released following the stimulation of basophils with 1% codeine phosphate hydrate (Figure 1a), leading to the diagnosis of minocycline-induced anaphylaxis. With the autologous serum, basophils from three healthy controls did not release histamine in response to

minocycline (Figure S1). The dot blot assay, performed according to a previously described method,<sup>4</sup> revealed the specific binding of IgE to minocycline in the presence of the patient's serum (Figure 1b). However, IgE in the patient's serum did not show any specific binding to codeine phosphate (data not shown). She then took codeine phosphate hydrate and did not show any allergic symptoms. Informed consent was obtained from the patient for the publication of her clinical and laboratory data.

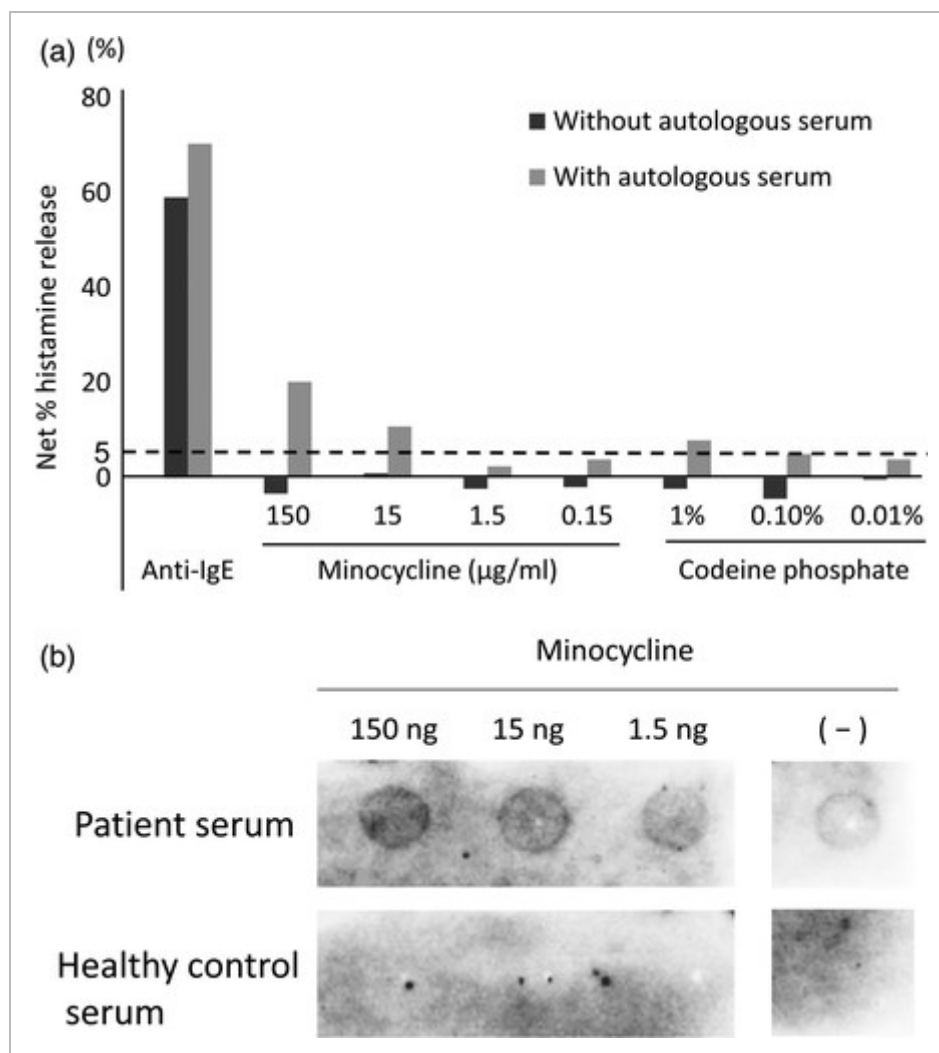


**FIGURE 1**

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(a) The HRT (using patient basophils) for minocycline (150, 15, 1.5, and 0.15 µg/mL), codeine phosphate (1%, 0.1%, and 0.01%), and anti-IgE (positive control). Shaded and filled bars show data obtained with and without autologous serum, respectively. The positive response of net histamine release was defined as 5% or more. (b) Dot blot analysis of IgE binding to minocycline. Minocycline-bound IgE antibodies in the patient's serum were detected by HRP-conjugated goat antihuman IgE. In contrast, binding of IgE was not detected in the presence of serum of healthy controls. The total IgE levels of the patient's serum and that of the control serum were 93.3 IU/mL and 55.7 IU/mL, respectively. HRP, horseradish peroxidase; HRT, histamine release test; IgE, immunoglobulin E.

Several cases of hypersensitivity reactions to minocycline have been reported.<sup>2,3,5</sup> However,

they identified minocycline as the cause of immediate allergy/anaphylaxis based on the results of skin and oral challenge tests.<sup>2,3</sup> Although these tests can confirm an individual's hypersensitivity to minocycline, they cannot determine whether the reaction was mediated by antigen-specific IgE and histamine. In our case, the HRT showed that minocycline elicited no response from basophils in the absence of autologous serum. Owing to its small molecular weight 493.94, minocycline cannot directly cross-link multiple IgE antibodies, which may partially explain why the patient's basophils did not respond to minocycline in the absence of serum (Figure 1a). In this case, basophils released histamine upon stimulation with minocycline in the presence of autologous serum, suggesting the presence of minocycline–haptic carrier proteins in the patient's serum. In conclusion, this report indicates that minocycline can cause IgE-mediated type I allergic reactions.

## ACKNOWLEDGMENTS

None.

## CONFLICT OF INTEREST

None declared.

### Supporting Information



| Filename                                                          | Description |
|-------------------------------------------------------------------|-------------|
| <a href="#">jde16228-sup-0001-FigureS1.jpg</a> JPEG image, 978 KB | Figure S1   |

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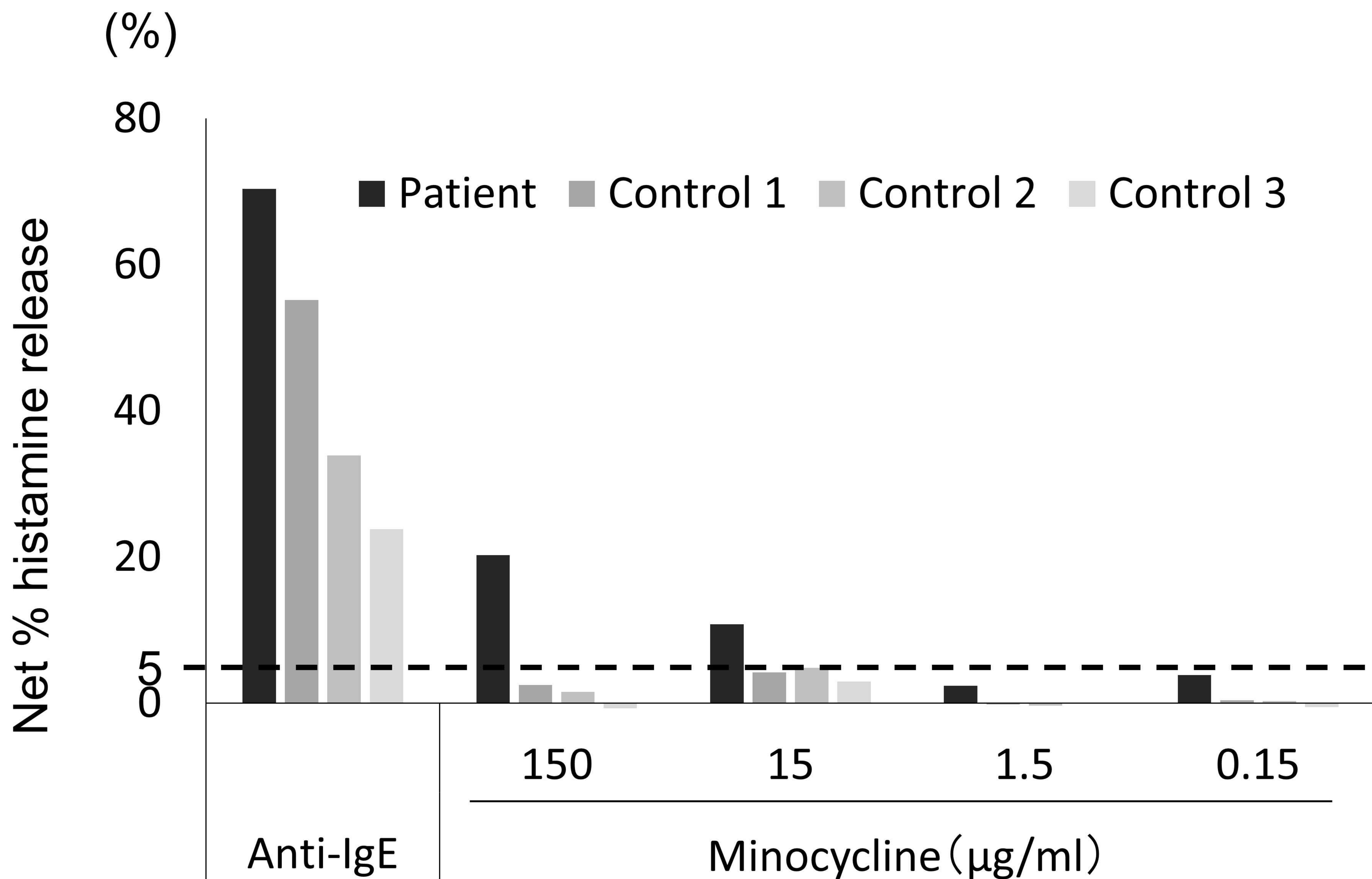


**Figure S1. The histamine release tests with autologous serum for minocycline.**

Histamine was released from basophils of the patient (Patient) in response to minocycline, but not from basophils of 3 healthy controls (Control 1-3). The positive response of net histamine release was defined as 5% or more. Anti-IgE was a positive control.