

Contact urticaria caused by carmine-containing eyeshadows; the causative allergen is carminic acid rather than CC38K

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CASE REPORT

A 24-year-old woman without atopic dermatitis, hand eczema, and pollinosis sometimes experienced urticaria without anaphylaxis. Three years ago, she bought eyeshadow A but stopped using it because her eyelids turned red after application. A year ago, she noticed itchy erythema on her eyelids 3 hours after applying eyeshadow B. She had the same symptoms after applying eyeshadow C, purchased 2 months ago. Other than these eyeshadows, she used cosmetics without having any symptoms. She noticed that only eyeshadows A, B, and C contained carmine.

We performed skin prick tests (SPTs) using 1% normal saline solution (aq.) carmine (Thermo Fisher Scientific, Waltham, Massachusetts), 1% aq. carminic acid (MP Biomedicals, Santa Ana, California), 1% aq. cochineal dye (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan), saline, and 10 mg/mL histamine dihydrochloride (Torii Pharmaceutical, Tokyo, Japan). The results were evaluated as described previously.¹ She reacted positively to carmine, carminic acid, cochineal dye, and histamine dihydrochloride (mean wheal diameter: 4.5, 5.5, 4, and 5 mm, respectively; Figure 1) and negatively to saline. We performed immunoblotting against *Dactylopius coccus* Costa and carmine using the patient's serum and found specific immunoglobulin E antibodies binding to proteins in both (Figure 2A).

In addition, we performed an inhibition enzyme-linked immunosorbent assay (ELISA) to assess the *D. coccus* Costa, carmine, carminic acid, and cochineal dye antigenicities; importantly, the binding of immunoglobulin E antibody to *D. coccus* Costa and carmine was inhibited by *D. coccus* Costa, carmine, cochineal dye, and carminic acid (Figure 2B). The investigation was approved by the Ethics Committee of Fujita Health University (approval no. HM20-385 and HM20-204), and the informed consent was obtained from the patient.

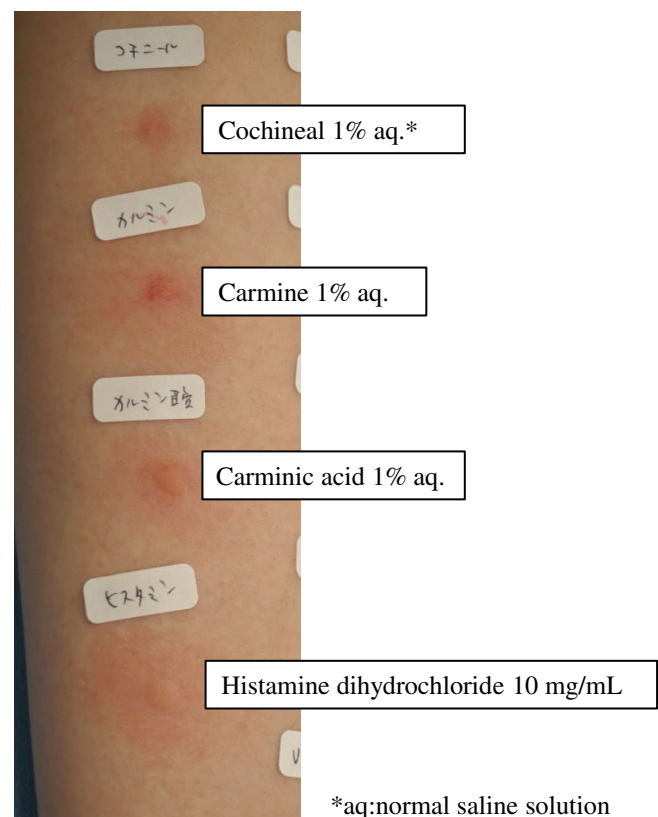


FIGURE 1 Skin prick test results

DISCUSSION

The main component of the cochineal dye is carminic acid, with carmine being a derivative. Cochineal was first reported in 1974 as the

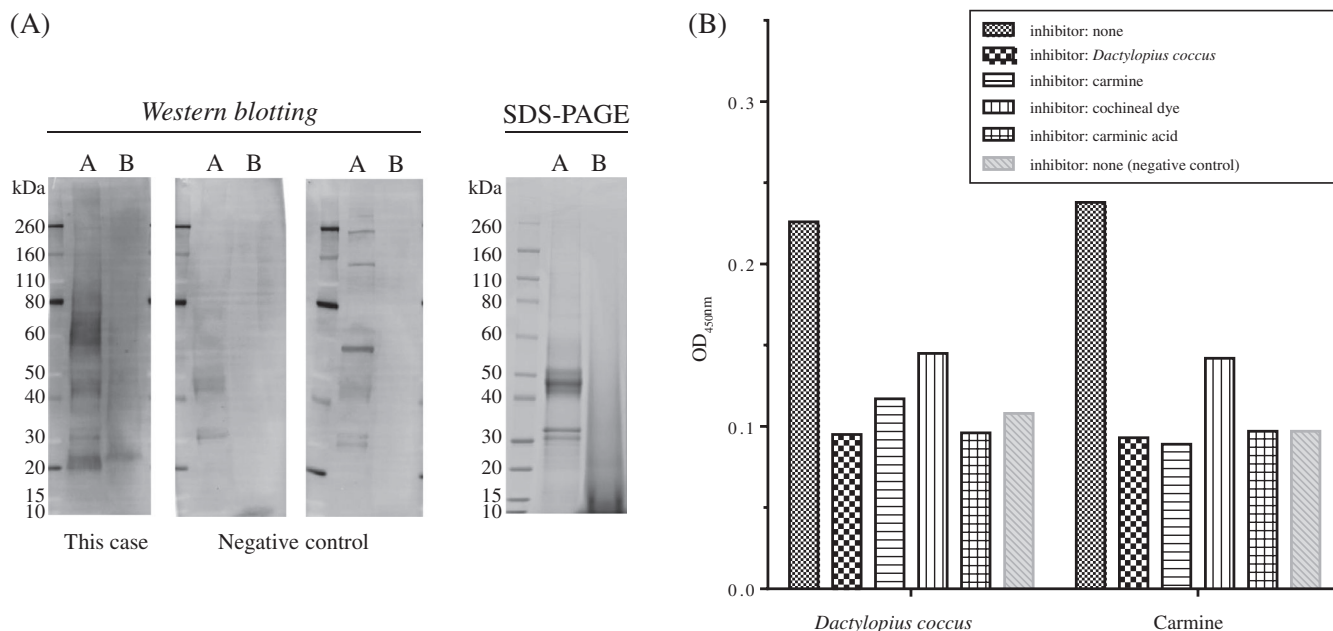


FIGURE 2 (A) Immunoblotting against *Dactylopius coccus* Costa and carmine. Sensitization of cochineal and carmine proteins confirmed by immunoblot. (B) ELISA to assess antigenicity of *D. coccus* Costa, carmine, carminic acid, and cochineal dye. ELISA confirmed that protein and carminic acid are antigens. ELISA, enzyme-linked immunosorbent assay; SDS-PAGE, sodium dodecyl sulfate-polyacrylamide gel electrophoresis

causative allergen of occupational asthma.² The first case of anaphylaxis due to carmine-containing foods was reported in 1994.³ Since then many cases of anaphylaxis caused by ingesting carmine- or cochineal dye-containing foods have been reported.⁴ Of note, most of the non-occupational cochineal dye sensitization cases are associated with females.⁴ Previously, cases have been diagnosed after the onset of systemic urticaria or anaphylaxis upon ingesting cochineal dye-containing foods. No patient diagnosed with only localized symptoms to carmine, without anaphylaxis, as in this case, has been reported.

Ohgiya et al⁵ reported CC38K as the causative protein of cochineal allergy in 3 cases. Sugimoto et al⁶ and Osumi et al⁷ reported that histamine release occurs because of basophil stimulation with high-purity carminic acid; a hapten of carminic acid may also cause cochineal allergy. We considered that the causative allergen in this case was a protein derived from *D. coccus* Costa and/or carminic acid according to the SPTs, ELISA, and immunoblotting results.

CONFLICTS OF INTEREST

KM is an endowed chair of Hoyu Co. Ltd. The other authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

Kayoko Suzuki: Conceptualization; data curation; investigation; resources; visualization; writing-original draft. **Kyoko Futamura:** Investigation; writing-review and editing. **Nayu Sato:** Data curation; investigation; resources; writing-review and editing. **Masashi Nakamura:** Data curation; investigation; resources; writing-review and editing. **Kayoko Matsunaga:** Funding acquisition; supervision; writing-review and editing. **Akiko Yagami:** Funding acquisition; project administration; supervision; writing-review and editing.

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