Capryloyl glycine: A polyfunctional cosmetic ingredient and potential skin sensitizer

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Amino acid alkyl amides (AAAAs) are polyfunctional cosmetic ingredients, some of which also have preservative properties. Here, we report a case of allergic contact dermatitis caused by a body lotion containing an AAAA, namely, capryloyl glycine (CG) (synonyms: caprylyl glycine and *N*-octanoylglycine; CAS no. 14246-53-8) (Figure 1).

CASE REPORT

A 50-year-old atopic man, who was known to have hand dermatitis and who had recently been diagnosed with contact allergy to methylisothiazolinone (MI), methylchloroisothiazolinone/MI, fragrances (*Myroxylon pereirae* and fragrance mix II), and ricinus oil, developed an itchy, papular skin eruption on his arms and legs after the application of a body lotion (Figure 2A,B). He had also suffered from a similar skin eruption after the use of two sunscreens. However, none of these products contained any of his known contact allergens, so he was referred to us for additional patch tests. These were performed with the three suspected products, tested "as is," along with the separate ingredients of the body lotion, kindly provided by the manufacturer (L'Oréal, Clichy, France), a photopatch series (Chemotechnique Diagnostics, Vellinge, Sweden), and ingredients of the suncreens that were commercially available as patch test preparations. Allergeaze patch test chambers (SmartPractice, Calgary, Canada) were used, and, following occlusion for 2 days with Fixomull stretch (BSN Medical, Hamburg, Germany), all tests were read, according to published guidelines, on day (D) 2, D4, and D7.[1] The photopatch tests were occluded for 2 days, and, upon removal, one of two identical series was irradiated with 5 J/cm^2 ultraviolet (UV) A; readings were performed on D2, D4 and D7 following application of these tests. Positive patch test reactions were observed to the body lotion (++), and to its ingredient CG 1% 50% aq./50% ethanol. (+) (Figure 3). A repeated patch test with this allergen confirmed the positive reaction, with the same degree of reactivity (+). An additional patch test with CG 1% aq., retrieved from a different cosmetic company, gave only a doubtful reaction (?+). Twenty control patients had completely negative test results with both CG 1% aq. and CG 1% 50% aq./50% eth. Our patient also had positive reactions to patch tests with the two sunscreens (+), although to a lesser extent (?+) when these were irradiated with UVA, and to the chemical filter benzophenone-10 (+), which, according to the packaging, was not present in these products. As both sunscreens contained caprylic/capric triglyceride, that is, glycerol esterified with one part capric acid and two parts caprylic acid, the latter being an acid that is also used in the manufacture of CG, additional tests were performed with caprylic/capric triglyceride (10% pet.; obtained from Pierre Fabre, Paris, France); however, these did not yield a positive reaction, so the culprit ingredient(s) of the two sunscreens could not be identified. However, contact allergy to the body lotion, and its ingredient CG, was effectively detected, and, out of interest, we additionally patch tested a "medical device" cream for psoriasis and a cream used to treat scars, also containing CG; both of these gave positive reactions, ?+ and +, respectively, on D4. We thus advised the patient, in addition to his already known contact allergens and benzophenones, to avoid products containing CG. From our departmental database, we retrieved five other patients who had developed dermatitis following the use of the same body lotion. All of these patients had reacted to the body lotion "as is" (+ to ++), and some of them had also previously been tested with the separate ingredients, yielding, however, no positive reactions to CG 1% 50% aq./50% eth.

DISCUSSION

We report, to our knowledge, the first case of contact allergy caused by CG, a polyfunctional ingredient in cosmetic leave-on and rinse-off products, and household detergents. It is an *N*-acyl α-amino acid, composed of glycine acylated with caprylic acid chloride in aqueous

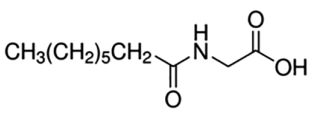

FIGURE 1 Capryloyl glycine

Evelyne A. Mangodt and Ella Dendooven contributed equally to this work.

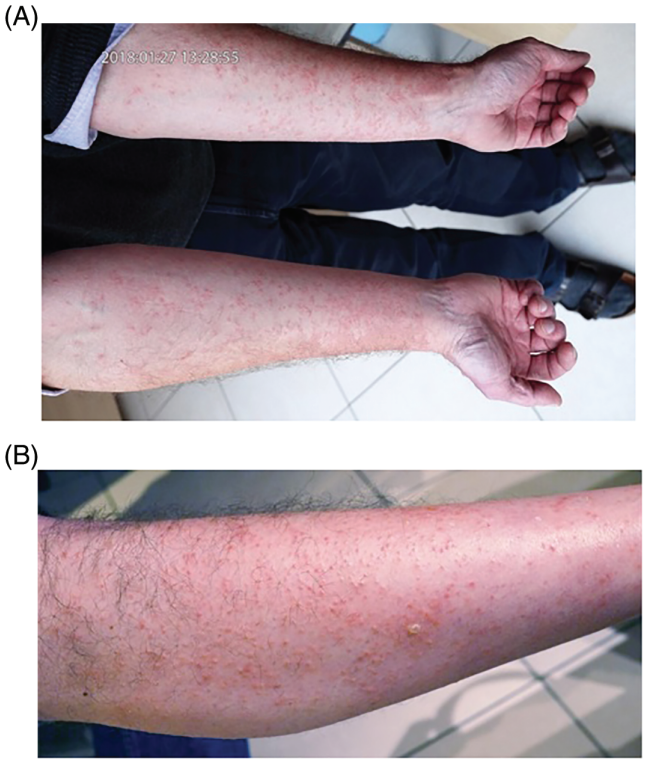

FIGURE 2 Acute, papular rash on the arms following the use of a capryloyl glycine-containing body lotion

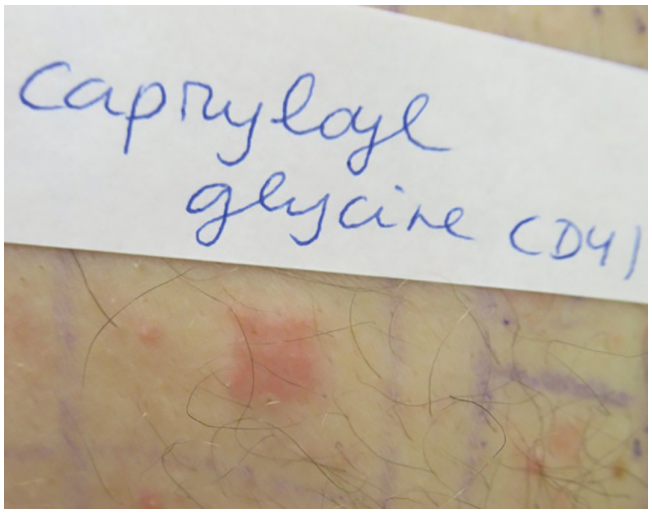

FIGURE 3 Positive patch test reaction (+) to capryloyl glycine 1% in 50% aq./50% ethanol on day 4

medium.[2,3] In cosmetics, besides being a skin and hair conditioning agent, it is a surfactant and has antimicrobial properties. Despite the fact that CG inhibits the proliferation of *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Propionibacterium acnes*, and *Pityrosporum ovale*, and is thus included in products marketed for the treatment of acne-prone skin and dandruff, it is not considered to be a full-fledged preservative. However, this glycine derivative is often used together with other preservative agents to obtain a synergistic preservative effect.[3,4] With regard to the test results obtained with CG 1% aq. (?+), as opposed to CG 1% in 50% aq./50% eth. (+) in our patient, we hypothesize that the vehicle might have influenced the test results: CG has a pK_a of ~4.0, and in the CG 1% aq. solution, with a pH of 7.0, most of the molecule is negatively charged, hence negatively influencing skin penetration and possibly resulting in a weaker, or potentially even false-negative, patch test reaction[2,3,5]; we could not determine whether this solution had been neutralized to obtain a pH of 7. However, CG 1% in 50% aq./50% eth., as received by the manufacturer of the body lotion, has a low pH of 3.3, indicating that a smaller amount of negatively charged CG is present, hence ensuring better skin penetration and thus potentially provoking a (possibly stronger) positive patch test reaction. Moreover, bearing in mind that CG is used in cosmetics up to a maximum concentration of 2%, higher test concentrations than 1% might be necessary.[3,6] Altogether, when patch tests in general are performed, and with CG in particular, it is useful to question which particular vehicle and concentration might be the most appropriate ones to use. Although we were unable to obtain the raw material of CG, it might be worthwhile, in the work-up of future cases, to patch test CG in pet., a lipophilic vehicle, and then preferably at 2%, as this would correlate with almost 100% uncharged CG, making skin penetration and possible detection of contact allergy to CG more reliable. Moreover, taking into account its surfactant properties, pet.-based vehicles might also be less irritating, although none of our control patients showed any irritant patch test reactions to the aqueous or aqueous/ethanolic preparations. Our patient presented with clinically very pronounced allergic contact dermatitis, reflecting potentially strong sensitization, which probably led him to react even to potentially less adequate patch tests containing CG, at only 1%, and in a pure aqueous solution. In retrospect, we cannot exclude the possibility that the negative patch test reactions to CG 1% 50% aq./50% eth. in some of the other patients who had previously experienced a skin reaction after using the same body lotion were false-negative reacions, possibly related to the above-mentioned factors of concentration and vehicle. We have no clue as to which ingredient was potentially the culprit sensitizer in the two sunscreens that our patient could not tolerate. Although we suspected a potential link with the caprylic/capric triglyceride contained in these, a substance that, like CG, is manufactured with the use of caprylic acid, patch test results with caprylic/capric triglyceride 10% pet. remained negative, making a possible relationship between CG and caprylic/capric triglyceride unlikely.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

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