

Contact sensitization to lettuce and rocket-salad with and without systemic elicitation of dermatitis after oral challenge

Evy Paulsen¹, Mette Sommerlund² and Flemming Andersen¹

¹Department of Dermatology and Allergy Centre, Odense University Hospital, DK-5000 Odense C, Denmark and ²Department of Dermatology, Aarhus University Hospital, DK-8000 Aarhus C, Denmark

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The different cultivated varieties of lettuce (*Lactuca sativa* L.) belong to the Compositae (Asteraceae) family of plants, and are well-known causes of contact dermatitis, in spite of their low sensitizing potential (1, 2). Usually, lettuce-sensitive patients are advised to use foliage vegetables from non-related plant families, such as rocket-salad (*Eruca vesicaria* Cav. ssp. *sativa* Thell. = *Eruca sativa* Mill.) (Fig. 1) and Chinese cabbage (*Brassica rapa*, ssp. *pekinensis*), both from the Brassicaceae (mustard) family, or spinach (*Spinacia oleracea*) of the Amaranthaceae family, in their raw food salads. The following case report describes the process of diagnosing lettuce food allergy and the subtle clinical features, as well as an unexpected contact sensitization to rocket-salad.



Fig. 1. Rocket-salad leaves on a Brassicaceae plate.

Case Report

A 56-year-old male was referred to the Allergy Centre on suspicion of food allergy to lettuce, (whitloof) chicory (*Cichorium intybus* var. *foliosum*), and rocket-salad.

The patient, who was otherwise healthy, had a family, but no personal history of atopy. For 15 years, he had suffered from a gradually worsening dermatitis of exposed skin, at first summer-exacerbated, but eventually more or less constant. Furthermore, he described an urticaria-like rash with angioedema. He was diagnosed with Compositae contact allergy in 2005, and had noticed some improvement of his eczema on avoidance of lettuce, chicory and sunflower seeds in his diet. However, ingestion of lettuce or chicory elicited perioral dermatitis,

swelling of the lateral aspects of the tongue, and either exacerbation of pre-existing eczema or – if the eczema had temporarily resolved – elicitation of eczema on his back corresponding to previously affected sites. On one occasion, the patient developed burning erythema in the face and on the neck 1 hr after ingestion of a mixed green raw salad that possibly also contained rocket-salad. He had been heavily exposed to Compositae plants, both occupationally through outdoor working with telephone cables and through hobby gardening. Prior to referral, the patient had been examined at the Department of Respiratory Medicine, Aarhus University Hospital, and the examination had included measurement of specific IgE to inhalants and food allergens, with negative results. Furthermore, he had been extensively patch tested at the Department of Dermatology, Aarhus University Hospital, and this confirmed the Compositae allergy: the positive results are shown in Table 1. As patch testing with his own plants, including iceberg lettuce, chicory, and rocket-salad, and prick tests with, among other things, iceberg

Correspondence: Evy Paulsen, Department of Dermatology and Allergy Centre, Odense University Hospital, Sdr. Boulevard 29, DK-5000 Odense C, Denmark. Tel: +45 6541 2705; Fax: +45 6612 3819. E-mail: evy.paulsen@rsyd.dk

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Table 1. Positive reactions at the first patch testing, November 2012

Allergen	Maximum reaction
Fragrance mix I* 450 µg/cm ²	++
<i>Narcissus poeticus</i> 2% pet.	+
Wood tar mix 12% pet.	+
<i>Myroxylon perei</i> resin 10% pet.	+
Sesquiterpene lactone mix 0.1% pet.	+++
Roman chamomile (<i>Anthemis nobilis</i>) extract 1% pet.	+++
Arnica (<i>Arnica montana</i>) extract 0.5% pet.	+++
Yarrow (<i>Achillea millefolium</i>) extract 1% pet.	+++
Pyrethrum (<i>Chrysanthemum cinerariifolium</i>) extract 1% pet.	+++
Tansy (<i>Tanacetum vulgare</i>) extract 1% pet.	+++
Alantolactone 0.033% pet.	+++
Parthenolide 0.1% pet.	+++
Dandelion (<i>Taraxacum officinale</i>) extract 2.5% pet.	++
Carvone 5% pet.	++

*Fragrance mix I consists of cinnamyl alcohol, cinnamal, eugenol, α -amyl cinnamal, hydroxycitronellal, geraniol, isoeugenol, *Evernia prunastri* absolute, and sorbitan sesquioleate.

lettuce, chicory, rocket-salad, and sunflower seeds, gave negative results, he was referred for further investigations.

At the Allergy Centre, the patient was first prick tested again with the standard series of inhalant allergens, as well as a series of food items, supplemented with lettuce and rocket-salad: all tests gave negative results. Specific IgE antibodies to lettuce were not detected, and a histamine release test (RefLab Aps, Copenhagen, Denmark) gave a negative result for lettuce, but a positive result for rocket-salad. Two months later, an open oral challenge with 21.8 g of rocket-salad did not elicit any symptoms. The patient was patch tested again with the baseline series, which included True Test Panel 1–3 and selected pet.-based allergens (except for sesquiterpene lactone mix 0.1% pet. and parthenolide 0.1% pet.) supplemented with romaine lettuce (*L. sativa* var. *longifolia*) and rocket-salad. The allergens were applied to the back for 2 days with Finn Chambers® on Scanpor® tape (SmartPractice®, Phoenix, AZ, USA), and read on D3 and D7, in accordance with the criteria of the ICDRG (3). The positive results are shown in Table 2. Patch tests with romaine lettuce leaves, wetted with water and ethanol, gave no reactions. Two slices of romaine lettuce stalk, wetted with water and ethanol, respectively, were tested in 5 consecutive eczema patients, and rocket-salad wetted with water and ethanol were tested in another 10 consecutive eczema patients. None of the controls showed positive reactions, but, in 5 of the patients tested with rocket-salad, a few follicular papules appeared under the water-wetted leaf.

Table 2. Positive reactions at the second patch testing, October 2013

Allergen	Maximum reaction
Fragrance mix I* 450 µg/cm ² /8% pet.	+/+++
Methyldibromo glutaronitrile 0.5% pet.	+
Textile mix [†] 6.6% pet.	++
Oxidized linalool 1% pet.	++
Rocket-salad wetted with ethanol	+
Romaine lettuce stalk wetted with water	+++
Romaine lettuce stalk wetted with ethanol	++

*Fragrance mix I consists of cinnamyl alcohol, cinnamal, eugenol, α -amyl cinnamal, hydroxycitronellal, geraniol, isoeugenol, *Evernia prunastri* absolute, and sorbitan sesquioleate.

[†]Textile mix consists of Disperse Blue 106, Disperse Blue 124, Disperse Blue 35, Disperse Yellow 3, Disperse Orange 1, Disperse Orange 3, Disperse Red 1, and Disperse Red 17.

Discussion

Usually, the term 'food allergy' connotes an immediate-type hypersensitivity, and this has been reported previously for both lettuce and chicory (4, 5). In light of the clinical features, with erythema and oral symptoms after ingestion of lettuce and chicory, and the negative patch test reactions to iceberg lettuce and chicory, it was necessary to rule out immediate-type reactions. However, the patient also reported either exacerbation or elicitation of eczema after eating lettuce, suggesting a systemic reaction, an incognito lettuce dermatitis. Aggravation of dermatitis, including a rash around the lips, lip swelling, and symptoms in the oral mucosa, after ingestion of lettuce has been reported previously (6). The fact that dermatitis in other areas of the body became worse is especially interesting, as this cannot be explained by direct contact with lettuce, which otherwise might account for perioral dermatitis, cheilitis, or mucosal symptoms. Oliwiecki et al. even suggested that this systemic reaction may be more common than previously recognized (6). Although the present patient was highly sensitive to Compositae, having strongly positive reactions to plant extracts that rarely give positive reactions in Danish Compositae-allergic patients, such as Roman chamomile and pyrethrum, the reactions to romaine lettuce stalk were most likely not cross-reactions, as he had grown both lettuce and rocket-salad for years and prepared them for salads. The heavy exposure to the weakly allergenic lettuce thus accounts for the development of contact sensitization that is usually more common in occupationally exposed persons (7). The two important sesquiterpene lactone allergens of lettuce and chicory, lactucin and lactucopicrin, are not commercially available. To diagnose lettuce contact sensitization, it is recommended to patch test with either leaf or the milky

sap 'as is', or to use a short ether extract 10% in pet. (7). The present case emphasizes the main problem with patch testing with lettuce 'as is': a risk of false-negative reactions. According to Hausen et al., lactucin is rather sensitive to ultraviolet irradiation, especially in aqueous solution, which degrades the allergen (2). Thus, patch testing with lettuce leaves that are wet or not completely fresh may result in false-negative reactions, as was the case with our patient at both test sessions. Patch testing with a slice of freshly cut stalk, however, seems to be more reliable.

Rocket-salad has not previously been reported as a contact sensitizer in its own right. However, Taramira oil, which is made from the seeds of *E. sativa*, may cause allergic dermatitis and photodermatitis of the scalp, neck and skin around the ears when applied to the hair (8). Possible allergens in the Brassicaceae family include isothiocyanates (mustard oils) (8). These compounds, which are bound in the plants as glucosinolates, are soluble in ethanol, but not in water, which may account for the positive patch test reactions to rocket-salad leaves wetted with ethanol and the absence of reactions to leaves wetted with water. The slight follicular reactions in controls may reflect an irritant potential, although they reacted to water-wetted pieces of leaf. Likewise, the positive histamine release test result with rocket-salad seems to be a non-specific response, as there was no other evidence for immediate-type hypersensitivity. There are several possible explanations for the negative oral challenge result with rocket-salad. First, on the basis of the patch test results, the sensitization to lettuce was

much stronger than that to rocket-salad, and perhaps only the strongest allergens are able to elicit systemic reactions. Second, the oral challenge at the Allergy Centre is designed to detect immediate-type food allergy by ingestion of small amounts of food, and the challenge is therefore considered to be negative if nothing happens after a few hours. The patient was instructed to report any late-occurring reactions, but, according to his medical record, none was reported. Therefore, the amount of rocket-salad may have been too small to elicit any reactions. Third, the allergen contents of the rocket-salad used for oral challenge and patch testing may have differed considerably from each other. It is well known that both cultivation conditions and post-harvest storage affect the levels of both flavonoids and glucosinolates (9). Contact sensitization to both Compositae and Brassicaceae was reported in a chef who had positive patch test reactions to chicory oleoresin, lettuce, lettuce extract 10%, lactucin, lactucopicrin, and cabbage (10). As in the present case, these findings probably represent co-sensitization rather than cross-reactions.

In conclusion, the case report emphasizes (i) that food allergy in adults is not always caused by immediate-type reactions, (ii) that lettuce may not only cause contact reactions in or around the mouth, but also elicit/exacerbate eczema as a systemic reaction, (iii) that patch testing with lettuce stalk is more reliable than patch testing with lettuce leaves for the diagnosis of lettuce sensitization, and (iv) that rocket-salad may be added to the list of sensitizing vegetables.

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