

Lymphomatoid contact dermatitis caused by limonene hydroperoxides confirmed by an exposure provocation test with the involved personal hygiene products

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Lymphomatoid contact dermatitis is an uncommon inflammatory disorder of the skin that is classified as a pseudolymphoma. It is probably an under-reported entity, combining the clinical and histological features of cutaneous T cell lymphoma (CTCL) with some characteristics of allergic contact dermatitis. Aetiologically, it has been linked to several haptens, such as phosphorus sesquisulfide (1, 2), gold, nickel, dimethyl fumarate, methylisothiazolinone, and azo dyes. Delayed-type hypersensitivity is regarded as the key in pathogenesis; avoidance of the hapten usually leads to resolution, and clonality cannot be proven in most cases. We report on the first case of lymphomatoid contact dermatitis in relation to limonene hydroperoxides (LimOOHs).

Case Report

A 35-year-old non-atopic female was referred to us with a pruritic eruption that had started 4 months earlier. Her family history revealed parapsoriasis in her mother. Lesions, consisting of erythematous well-circumscribed plaques with thin scales, initially involved her lower abdomen, and eventually spread to her lower limbs (Fig. 1a). The eruption partially responded to a methylprednisolone aceponate ointment. According to the

clinical features and her family history, an early onset of a CTCL was suspected. Cutaneous pathology showed a perivascular and perifollicular slightly atypical lymphoid infiltrate with focal epidermotropism (Fig. 1c). Immunostaining highlighted the presence of mostly CD3⁺ CD8⁺ T cells (Dako, Glostrup, Denmark) (Fig. 1d) within the epidermis. However, T cell receptor (TCR) gene rearrangements could not be identified by polymerase chain reaction (PCR).

The patient was patch tested with the Spanish Contact Dermatitis Research Group (GEIDAC) baseline series with TRUE Test[®] and supplementary allergens supplied by AllergEaze (Calgary, Canada), a cosmetic series (Chemotechnique, Vellinge, Sweden), and five of her own hygiene products 'as is'. The allergens were prepared on Curatest[®] chambers (Lohmann & Rauscher, Neuwied, Germany), applied on the patient's back, and fixed with an adhesive tape (Omnifix E[®]; Hartmann, Heidenheim, Germany). The exposure time was 2 days, and readings were performed and scored according to ESCD guidelines (3). Positive results were obtained with LimOOHs 0.3% pet. [+ on day (D) 4], and with one of the patient's own products ('The hair pack') (+ on D2 and D4) (Fig. 1b). She claimed to suffer from severe pruritic papules when she used it.

Limonene was identified on the labels of several of the patient's hygiene and household products, such as the above hair pack, a shower gel, a moisturizing cream, a shampoo, a washing-up liquid, and a floor mop. Topical corticosteroids and sun exposure (5 min daily) were recommended, and she was given a recommendation to avoid limonene. These measures led to complete clearance of the lesions within a few months.

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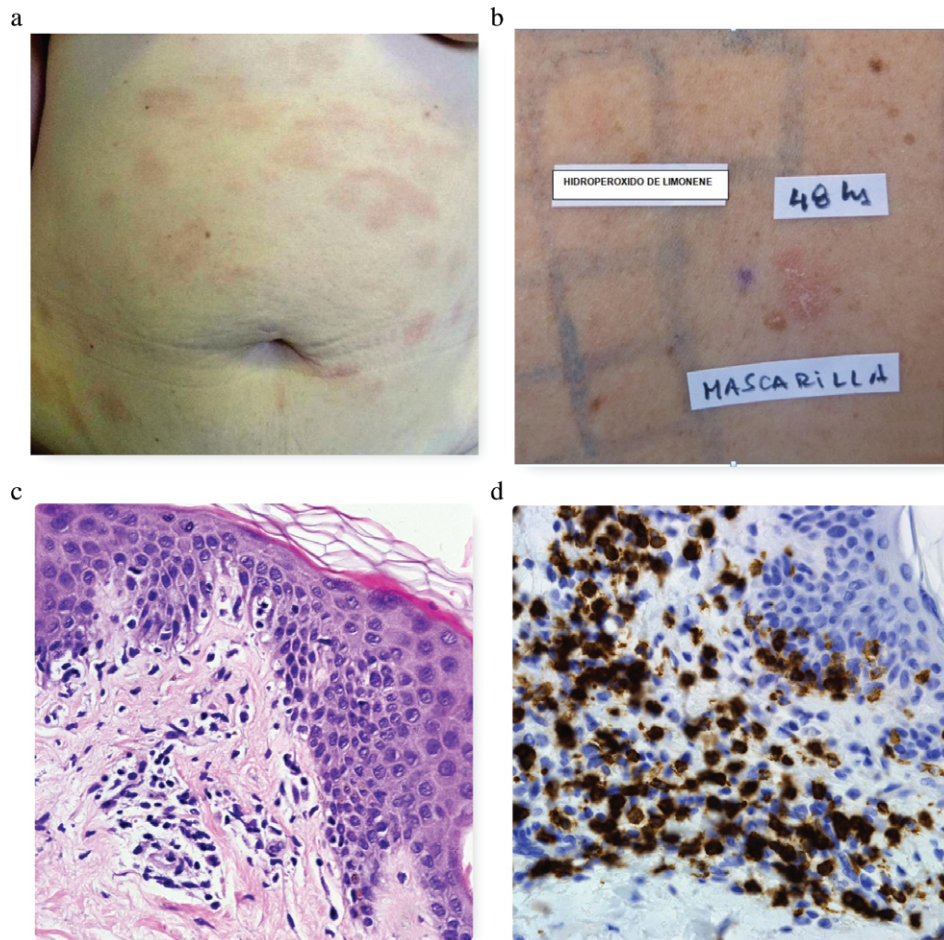


Fig. 1. (a) Numerous erythematous, well-delimited, maculopapular lesions scattered over the abdomen. (b) Patch test results: limonene hydroperoxides 0.3% pet., ?+ on day (D) 2; patient's own hair mask product ('The hair pack'), + on D2. (c) Histopathological examination shows slight epidermotropism of atypical lymphocytes and minimal spongiosis without eosinophils (haematoxylin and eosin: $\times 400$). (d) Immunostaining highlighting the presence of CD8⁺ T cells within the epidermis ($\times 400$).

After the patient had strictly avoided contact with limonene and had been completely asymptomatic for 15 months, she gave informed consent for a cutaneous provocation test. She used her former shampoo, shower gel and a moisturizing cream containing limonene for 1 month. A flare-up of lesions similar to the previous ones appeared over the same previously affected abdominal locations (Fig. 2a). The patient was patch tested a second time with LimOOHs 0.3% and linalool hydroperoxides 1%. Positive results were obtained with LimOOHs 0.3% pet. (+) on D2 and D4 (Fig. 2b). Patch tests with limonene 10% pet. (Chemotechnique) gave negative results on D2, D4, and D7. A new biopsy showed focal parakeratosis and lymphoid dermal infiltrates with focal epidermotropism (Fig. 2c) of mostly CD3⁺ CD8⁺ T lymphocytes (Dako) (Fig. 2d) with isolated eosinophils. Polyclonal TCR gene

rearrangements were identified by PCR. The use of topical corticosteroids and limonene avoidance resulted in rapid improvement.

Discussion

Limonene is a common fragrance terpene with a fresh citrus odour, and is widely used in the cosmetic, household and hygiene industries. It has recently been recognized as a prehapten, that is, a substance that is prone to become a more potent allergenic compound through air oxidation (autooxidation). LimOOHs have been described as important contact haptens. According to a recent study, the prevalence of LimOOH sensitization in the patch tested population in Spain is 5.1%, and LimOOHs 0.3% pet. have been proposed to be useful for screening (4). To the best of

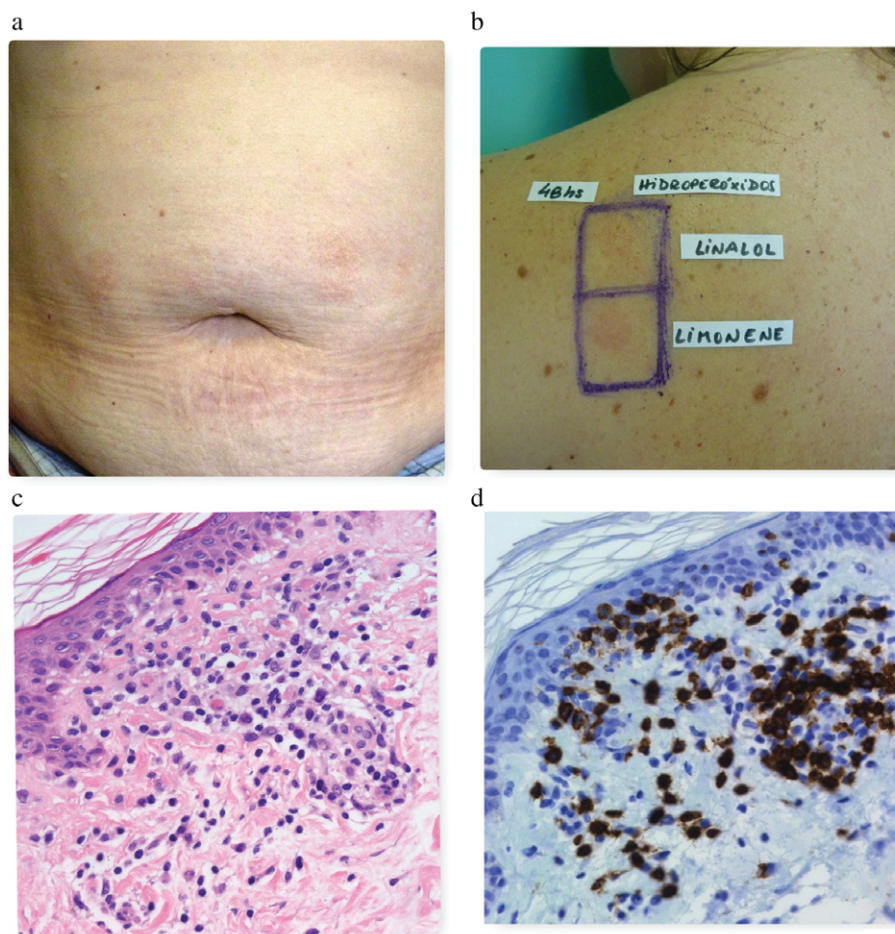


Fig. 2. (a) Scarce erythematous, well-delimited, macular lesions involving the abdomen. (b) Patch test results: limonene hydroperoxides 0.3% pet., + on day 2. (c) High-power view showing limited epidermotropism with atypical lymphocytes and minimal spongiosis (haematoxylin and eosin: $\times 400$). (d) Immunohistochemistry highlighting the presence of CD8⁺ T cells within the epidermis ($\times 400$).

our knowledge, no other cases of lymphomatoid contact dermatitis caused by LimOOHs have been previously reported.

Lymphomatoid contact dermatitis was originally described in 1976 by Gómez-Orbaneja et al. (1), involving 4 patients who developed cutaneous lesions from the matchboxes they carried in their pockets. Biopsies were consistent with CTCL, and the culprit allergen was suspected to be phosphorus sesquisulfide in the matchboxes. Lesions resolved after avoidance of further contact. In 2014, a literature review was published by Knackstedt and Zug (5). In these 23 cases, lymphomatoid contact dermatitis was more frequent in male patients (median age: 58.5 years). Fourteen different haptens were identified. The most frequent locations were the thighs, head and neck, buttocks, and groin. Most cases (68.1%) showed strong (++) or extreme positive (+++) patch test reactions, and only 31.9% had weak reactions (+). In most cases (80%), recovery was achieved with topical steroids

and allergen avoidance. Airborne-induced lymphomatoid contact dermatitis caused by methylisothiazolinone has also been reported (6). In accordance with the literature, our patient improved after avoiding the allergen. Unlike previous reports, our case involved a female patient showing more generalized lesions, and patch test reactions were weaker (+). We believe that allergen re-exposure tests could be the way to diagnose sensitization from ubiquitous allergens such as fragrances like LimOOHs, especially when, as in our case, patch test reactions are not strong. In these cases, clinical relevance is difficult to determine, and complete allergen avoidance is hard to accomplish.

We stress the importance of considering the diagnosis of lymphomatoid contact dermatitis in lesions resembling early-onset mycosis fungoides, especially in those cases with pruritic lesions, an atypical body distribution, and polyclonal infiltrates, and recommend that patch tests be performed with a broad allergen panel.

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