

CASE REPORTS

Erythema multiforme-like eruption due to carbamates and thiuram

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ABSTRACT

Report of a case of erythema multiforme-like eruption due to the use of rubber gloves. After several complementary studies, including epicutaneous and skin prick tests, we concluded that the eruption was secondary to sensitization to carbamates and thiuram. The main differential diagnosis in this case was allergic contact dermatitis to latex in natural rubber gloves. This entity is less frequent than might be expected, because it is usually due to intermediate chemical compounds used in rubber manufacturing, such as vulcanization accelerators; among of these latter compounds are thiurams and carbamates. Erythema multiforme-like eruption is a rare manifestation of contact dermatitis. Several cases have been reported, most of which have been due to contact with plants, metals or topical non-steroidal anti-inflammatory drugs. Its mechanism is still unclear, but it seems to be a type IV hypersensitivity reaction.

Key words: Erythema multiforme. Thiuram. Carbamates. Latex rubber gloves.

CLINICAL CASE

A 38 years old woman, without personal or familiar history of atopy. She presents with mildly pruritic, erythematous and edematous plaques, from 1 to 1.5 centimeters, involving her hands and forearms, in their dorsal and ventral aspects, covering almost the whole surface of the affected region, with a perfect clear proximal border, at the middle third of the forearms, like a glove, since 2 weeks ago. Some of the lesions have a target-like appearance. Lesions weren't eroded nor excoriated. She didn't present any lesion at other sites of her body (fig. 1).

Giving the distribution of the lesions, we made a directed anamnesis, looking for any kind of contact which may produced contact dermatitis, and our patient referred using a new rubber gloves brand for houseworking since 1 month before. She didn't report any other suspicious contact. She had never suffered from herpes simplex.

A provisional diagnosis of erythema multiforme-like contact dermatitis was made. To confirm this, skin biopsy, epicutaneous tests and prick tests with latex was performed, and latex-specific IgE in serum determined.

The skin biopsy showed a lichenoid pattern, with necrotic keratinocytes, basal vacuolar changes, spongiosis and linfocitic inflammatory infiltrate at mid and papillary dermis, and at dermo-epidermal junction, being, therefore, compatible with our first clinical diagnosis. Prick test and specific IgE were negative. We made patch tests with standard series of the GEIDC (Grupo Español de Investigación en Dermatitis de Contacto) (TRUEstest®, Alk-Abelló, Madrid), with readings at 48 and 96 hours; positive results to carbamates mix (+ + / + + +), and to thiuram mix

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Figure 1.—Aspect of the lesions.

(+ + / + + +), following ICDRG guidelines (International Contact Dermatitis Research Group) were obtained (fig. 2).

Definitive diagnosis of erythema multiforme-like contact dermatitis was established. Lesions cleared after gloves substitution.

DISCUSSION

We present a case of erythema multiforme-like contact dermatitis to carbamates and thiuram. They are substances used in transforming natural rubber, material useful to make several industrial and home rubber instruments; among these are natural rubber gloves.

Natural rubber comes from the tree *Hevea brasiliensis*, from the Amazonic region. Through incisions along the bark, pours a milky substance, called latex, because of its appearance. This raw material must be modified for its better use in factories, passing through a series of transformations, such as coagulation, vulcanization, moulding, ... till the desirable physical and chemical properties are reached. To get this, several intermediary substance are used, like accelerators, preservers or stabilizers. The most common vulcanization accelerators are carbamates



Figure 2.—Result of patch tests.

and thiuram, often involved in type IV hypersensitivity reactions as sensitizers¹.

Main differential diagnosis in our case is urticaria to latex, secondary to a type I reaction to its peptides, that can manifest as a broad spectrum from urticaria to anaphylactic reactions and death. There were been made a lot of assays to determine its protein concentration³, find the main epitopes responsables of this reactions², get clear the relationship between type I reactions latex and cross reactivity against other allergens, and also to determine if a type IV reaction against latex exists⁴.

Some peptides, with different body weight, were identified as main allergens of latex, and were denominated as Hev b, following of a number from 1 to 6. Some of these peptides were associated with several entities, as occurs between Hev b1 and 3 and bifid spine. Nevertheless, there are many other known and unknown allergens that probably have a paper in reactions to latex, and it's calculated that 20 to 50 per cent of cases are due to these secondary allergens. Examples of these secondary peptides are profilin, chitinase, enolase, lisozime, also present in some fruits and vegetables, as banana², melon⁶ or orange, and probable responsables of cross reaction between latex and fruits.

Latex sensitization is more frequent among health-care workers, factory workers who handle latex products, and people who have had several surgical operations; all these people have in common a very intense or repeated contact with latex⁸. There have been reported cases of latex allergy before contact with gloves, balloons, condoms, needles for insuline injection, and also due to aerotransportated latex particles⁹. This latter mechanism is secondary to products derived of cornflour, with low molecular weight, recently introduced as part of the inner powder in several trades of latex gloves; these products link gently to latex particles, releasing them into the air. It has been demonstrated that, like happens in children with spina bifida, the more the number of surgical operations, the more the probabilities of become sensitized².

The best tests to diagnose latex allergy are prick tests and specific IgE in serum, because it's a type I hypersensitivity. Results must be correlated with clinical findings, as there have been found a 12 % of healthy controls with positive specific IgE; a positive result in prick test is more specific. These data suggest that there may be presensitized, but clinically asymptomatic, people⁶.

Latex sensitization is less common than we can expect, since most of the patients referred to a dermatologist who suffer from contact dermatitis to rubber products, are due to other substances used in the rubber elaboration as preservatives or vulcanization accelerators; among of the latter are carbamates and thiurams^{1,5}. In the last decade, thiurams were being substituted for carbamates, since these are less allergenic⁵. A reduction in sensitization to thiuram mix in healthcare workers, determined by patch test, supports this situation¹; however this sensitization shows a recent slight elevation, probably due to the use of cheaper rubber gloves brands⁵.

In clinical studies made among people with high risk to develop contact dermatitis to rubber gloves, like odontologists, nurses, hairdressers or cleaning workers, thiurams are the most common allergens, especially tetraethylthiuramdisulfide (TETD), followed by dithiocarbamates and, at more distance, mercaptobenzothiazole and thioureas. There are patients sensitized to both thiurams and carbamates; it's common that almost all patients sensitized to carbamates are also to thiurams; this is not true at the other way round; this means that many people sensitized to thiurams could use gloves containing carbamates⁵.

Sensitization to carbamates and thiurams causes a type IV hypersensitivity reaction, so it should be diagnosed by patch testing. Standard series used in Spain contains a thiurams mix, formed by tetram-

ethylthiuramdisulfide (TMTD), tetraethylthiurammonosulfide (TETM), tetraethylthiuramdisulfide (TETD) y dipentamethylenethiuramdisulfide (DPTD). Carbamates mix, part of standard series, includes 1,3 diphenylguanidine (DPG), Zn-diethyldithiocarbamate (ZDEC) and Zn-dibutyldithiocarbamate (ZDBC). The most common clinical presentation is like hand contact dermatitis. Our case presented like an erythema multiforme like eruption.

Contact erythema multiforme-like eruption is a rare manifestation of non-eczematous allergic contact dermatitis. It was also called urticarial papules and plaques eruption⁹. Clinical presentation is variable, from localized affectation of the contact area, like our case, to disseminated eczema and even toxic epidermic necrolysis. It's believed that the main mechanism is a type IV cell-mediated hypersensitivity, after exposure to strong allergens, or repeated exposures to mild allergens^{12,16}. There have been implicated lots of allergens, like several metals, topical steroids, topical NSAIDs, plants, exotic woods or industrial chemical products^{10,12,15}. A case similar to ours was reported in 2001, but without patch testing nor biopsy¹¹. When biopsy was taken, in almost all the cases histopathology findings was similar to those seen in typical erythema multiforme¹². Diagnosis of contact erythema multiforme should be made considering clinical findings, with characteristic lesions, and positive patch testing, and excluding other causes of urticarial eruptions. It must be taken in mind that there were reported some cases with disseminated lesions after patch testing^{9,12}. Once diagnosed, therapeutic approaches are similar to those taken in typical erythema multiforme, in addition to avoid the responsible allergen.

Given the frequency of contact dermatitis to rubber gloves, other kind of materials gloves are appearing; but there have already been described contact dermatitis to these new products, like polyethylene or nitrile gloves^{13,14}.

CONCLUSIONS

We present a case of contact erythema multiforme-like eruption to carbamates and thiuram, two vulcanization accelerators, often implicated in contact dermatitis. In fact, most of the cases of troubles with natural rubber things, are due to these components rather than latex. Taking in mind that sensitization is easier after repeated contacts, health authorities should act in critical sectors like healthcare workers, to avoid contact dermatitis related morbidity.

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