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CONTACT DERMATITIS

Review Article

Allergic contact dermatitis from modified colophonium in wound dressings

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This study concerns a 69-year-old female patient with a longstanding history of venous ulcerations on both lower legs and multiple sensitivities, who developed eczematous lesions with the hydrocolloid dressing Combiderm® (Convatec Ltd., a Bristol-Myers Squibb division, Ickenham, Middlesex, UK). Epicutaneous tests were positive to this dressing and to a modified colophonium derivative, i.e. glyceryl rosinate, however not to the unmodified colophonium from the standard series. A review of the literature showed several case reports about sensitization to similar hydrocolloids being distributed under various brand names in different countries and which contain the pentaerythritol ester of the hydrogenated rosin as the tackifying agent. Some of the patients described did, while others did not, react to colophonium but only to a modified derivative. In our patient, the reaction to glyceryl rosinate most probably represent cross-sensitivity with the modified colophonium derivative used in Combiderm®, the presence (but not the exact nature) of which was showed by the company. In patients where allergic contact dermatitis from hydrocolloid dressings is strongly suspected and colophonium tests negatively, patch testing to modified colophonium derivatives should therefore be performed. As the complete composition of wound dressings is most often unknown, we urgently advocate legal requirements for labelling of those and in fact all medically used devices.

Key words: allergic contact dermatitis; colophonium; glyceryl rosinate; leg ulcer; modified colophonium; patch test; rosin; treatment; wound dressings. © Blackwell Munksgaard 2007.

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Leg ulcers represent a chronic condition affecting more than 1.7% of the population older than 65 years (1). Because healing is difficult to achieve, these patients are exposed to many topical drugs and dressings for long period of time. Sensitization therefore occurs in these patients and increases with duration of the ulcer (2). Over the past years, because of their sophisticated composition, hydrocolloids dressing have been introduced routinely in the treatment of various types of wounds, which may be clean, granulating or necrotic, or with low to moderate exudates. They provide a moist environment, promoting autolytic debridement, and stimulation of angiogenesis. While these dressings may be more expensive, if used correctly, they are cost-effective because they have a longer wear time. However, long-term application often leads to inflammation of the skin in the immediate neighbourhood of the ulcer, being an irritant dermatitis in many cases, but sometimes also leads to contact sensitization.

Case Report

A 69-year-old female patient presented with a longstanding history of severe venous insufficiency and venous ulcerations on both lower legs, with recurrent eczematous dermatitis. Patch tests had already been carried out twice, both in the Leuven Contact Allergy Unit, 23 years ago, and by a private dermatologist, 2 years ago, and had showed multiple sensitivities: para-phenylenediamine, parabens, wool alcohols, clioquinol, neomycin, nickel sulfate, *Myroxylon pereirae* (balsam of Peru), fragrance mix, budesonide, phenoxyethanol, cetylalcohol, nonoxynol, bacitracine, and benzocaine.

In August 2005, the patient again presented to the Leuven outpatient Chronic Wound Clinic because of an ulcer on the left lower leg of 6 month duration. She had applied Duoderm® hydroactive bandage and later on Combiderm® (both from Convatec, a Bristol-Myers Squibb division, UK), but the ulcer got worse, became weeping and more painful. An allergic contact dermatitis was

suspected, and she was asked to apply the adhesive part of both hydrocolloids to her forearms, the adhesive part of the Combiderm® clearly producing an eczematous reaction 3 days later (Fig. 1). Patch tests were again performed in September 2005 with Combiderm® (tested as is), colophonium (Trolab, Reinbeck, Germany) as present in the standard series and other allergens possibly present in adhesives, such as polyethylene glycol 400 20% aqua, acrylate components, and modified colophonium (Table 1), i.e. glyceryl rosinate [20% petrolatum (pet.)] that was available to us from Reckitt Benckiser (Massy, France) (3). Positive reactions were obtained to this hydrocolloid as well as to the modified colophonium derivative (Fig. 2).

Convatec informed us that Combiderm® consists of 2 elements: a non-adhesive layer based on polypropylene in contact with the wound (to which the patient did not react positively) and an adhesive part having a similar composition as Duoderm extra thin® (also from Convatec), which contains the pentaerythritol ester of rosin (Pentalyn®), a modified colophonium derivative that is not present in the regular Duoderm (4) to which our patient had not reacted on her forearm.

Table 1. Patch tests results

Patch tests	D2	D4
Combiderm® (as is)	+	+
Colophonium 20% pet.	−	−
Modified colophonium (glyceryl rosinate, 20% pet.)	+	+
Polyethylene glycol 400, 20% aqua	−	−
Acrylate components: methyl methacrylate 2% pet., 2-hydroxyethylacrylate 2% pet., hydroxyethylmethacrylate 2% pet., ethyleneglycol dimethacrylate 2% pet., and epoxy-acrylate 0.5% pet. (all from Chemotechnique, Malmo, Sweden)	−	−

Pet., petrolatum; D, days.

The ulcer was first treated with $KMnO_4$ compresses (dilution 1/4000) and zinc oxide paste, and compressive therapy was given. Because of

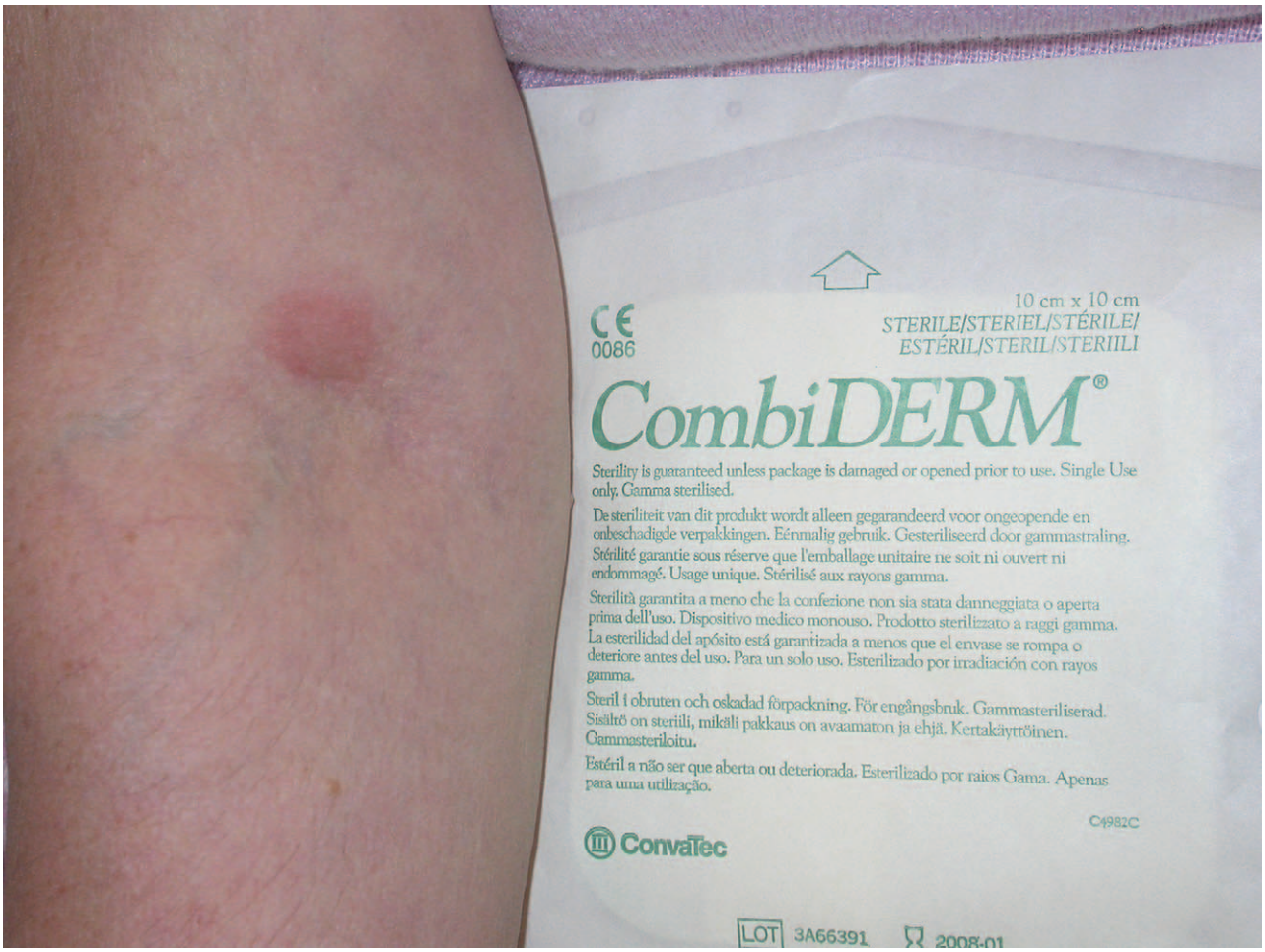

Fig. 1. Positive 'use' test with Combiderm® (reading at 3 days).

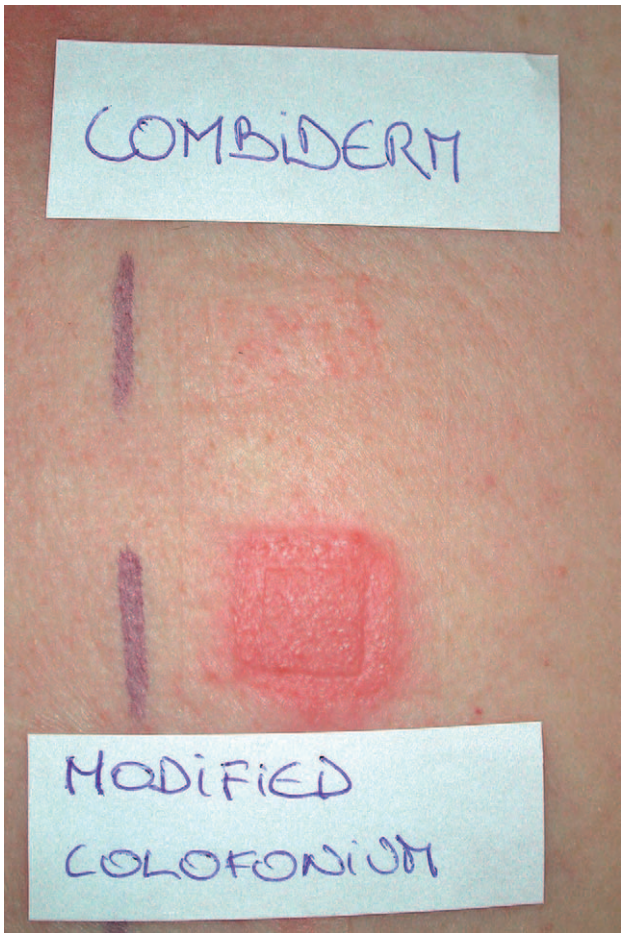

Fig. 2. Positive patch tests to both Combiderm® and glyceryl rosinate (modified colophonium).

Staphylococcus aureus infection, she was given antibiotic therapy with erythromycin ethyl succinate (Erythroforte®; Abbott, Ottignies, Belgium). The dermatitis cleared, and the ulcer became better but did not heal completely before May 2006.

Discussion

Investigations on the sensitizing potential of modern wound dressings are few and focus only on single sensitizing agents. In a study by Gallenkemper et al. (5), 20 different wound dressings were tested in 36 patients with chronic venous insufficiency and positive reactions were observed in 3 of them, i.e. 8.3%. All the cases were related to propylene glycol as an ingredient of hydrogels. They did not detect sensitization to hydrocolloids, alginates or polyurethane foams. Later on, Tavadia et al. (6) and Machet et al. (2) have obtained similar results and observed very low rates of sensitivity to the newer dressings, with the exception of hydrogels. They did observe positive reactions to colophonium; however, they did not test modified colophonium derivatives.

Nevertheless, a review of the literature shows several isolated case reports of sensitization to similar hydrocolloids being produced by the same manufacturer but distributed under various brand names in different countries. This concerns case reports about Duoderm E® or CGF® (3 cases) (4) and 1 case to Varihesive® (Duoderm E) (7), all containing the pentaerythritol ester of the hydrogenated rosin (Pentalyn®) as the tackifying agent. In these cases, positive patch test reactions were observed to the dressings as well as to colophonium. However, none of the patients was tested to the ester of hydrogenated rosin (modified colophonium), but the authors assumed that the patients became sensitized to this compound, in view of their concomitant reaction to colophonium. Mallon and Powell (8) identified Pentalyn®, i.e. the pentaerythritol ester of hydrogenated rosin (diluted 10% and 20% pet.), as the responsible allergen in 2 patients with allergic contact dermatitis from Granuflex E® that also reacted positively on patch testing. They also obtained positive reactions to colophonium and ester gum resin (glycerol ester). Schliz et al. (9) performed patch tests with Varihesive E® and Comfeel® (Coloplast BV, Peterborough, UK) in 41 consecutive patients with leg ulcers, 8 of whom reacted to one or both dressings; they identified the contact allergen Pentalyn® in 1 patient and a derivative of polyisobutylene in another patient. In the other 6 cases that patch tested positively to hydrocolloid dressings, the authors could not identify the responsible allergen. Mollin (10) tested 25 consecutive patients hospitalized for chronic venous ulcers and found 13 patients with positive patch test reactions to various types of Duoderm® dressings: among them, 10 reacted to Duoderm E® and 8 were allergic to Pentalyn®. However, they did not address the question of cross-sensitization with unmodified colophonium nor mentioned the allergen responsible in the other cases.

Some authors have reported cases in which, as in our patient, in contrast to a positive test to a modified colophonium derivative, unmodified colophonium did not react (11, 12). Downs et al. (11) described 7 patients with allergic contact dermatitis from Granuflex®: patch testing was positive to unmodified colophonium and the hydrogenated pentaerythritol-esterified gum rosin in 3 patients but positive only to the latter in another 2 patients. In 1270 patients with leg ulcer tested, by Salim and Shaw (12), with both colophonium and ester gum rosin, positive reactions to both colophonium and ester gum rosin were observed in 31% of the patients and to colophonium alone in 29% but to ester gum rosin alone in 40% of the patients.

Colophonium (rosin) derived from pine resin, tall oil and stump extractives. It is used as is or in chemically modified forms: hydrogenated, disproportionated, esterified, polymerized, as salt, or reaction products with maleic anhydride or formaldehyde. The pentaerythritol rosinate is an ester gum derived from rosin (mostly abietic acid) and pentaerythritol (13). Modifications of colophonium form new potent allergens not found in unmodified colophony. Hausen et al. (14) performed patch testing with 6 types of unmodified colophonium and 12 types of modified colophonium products and found that 17 of 137 patients did not react to the unmodified colophonium but responded to 1 or more of the modified products. The hydrogenated pentaerythritol rosinate is likely to be a complex blend of chemicals because hydrogenation of gum rosin will produce a mixture rich in dihydro-, tetrahydro-, and dehydroabietic acids (15). These modifications of gum rosin do not appear to alter its allergenicity after pentaerythritol esterification because cross-reactivity with fully hydrogenated pentaerythritol rosinate is preserved.

In our case, the patch testing was positive to the glyceryl rosinate, but we failed to identify the exact nature of the ester gum derivative present in Combiderm®. Major allergens have been identified and synthesized from glycerol-modified, fumaric acid-modified, and maleic anhydride-modified gum rosins that do not cross-react with colophonium (16). This explains why unmodified colophonium (in the standard series) is often negative in patients sensitized by modified rosin derivatives, the latter being probably more potent sensitizers.

Due to their resistance to oxidation and discolouration (16), colophonium derivatives are used as 'tackifiers' in natural and synthetic rubber, in adhesives for lamination of paper and in several other protective coating compositions. In medicine, besides hydrocolloids, they are found in adhesive tapes, plasters, bandages and medicated creams and ointments. Unfortunately, these tackifiers – as all other ingredients – are not declared ingredients of medical devices including wound dressing.

Conclusion

As in several literature reports, this case illustrates that unmodified gum rosin or colophonium 20% pet., as present in the European standard series, often fails to detect contact allergy to hydrocolloids and that patch testing should include modified colophonium derivatives such as glycerol esters present in them. Moreover, in the Leuven Contact Allergy Unit, we already did observe several patients with leg ulcer suspected to suffer from allergic contact dermatitis when hydrocolloids were used on damaged skin but for whom patch testing with the dressing itself failed to produce a positive reaction on normal skin. As the complete composition is in most cases not known, it is not possible to identify the responsible allergens nor to give advice for safer alternatives. Therefore, we advocate that medical devices, including wound dressings, bandages, adhesives, etc., that are used medically and applied on damaged skin, should be labelled with their complete qualitative composition (as is the case for all cosmetic products, which are applied to normal skin!).

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